ESTIMATIVA DO VALOR DO NÚMERO REPRODUTIVO BÁSICO DA COVID-19 E DO EFEITO DAS MEDIDAS ANTI-EPIDÊMICAS E DO “FATOR SAZONAL” NESTE VALOR

ESTIMATION OF THE VALUE OF THE COVID-19 BASIC REPRODUCTIVE NUMBER AND THE EFFECT OF ANTI-EPIDEMIC MEASURES AND “SEASONAL FACTOR” ON THIS VALUE

ОЦЕНКА ВЕЛИЧИНЫ РЕПРОДУКТИВНОГО ЧИСЛА R_0 ПРИ COVID-19 И ВЛИЯНИЯ НА НЕГО ПРОТИВОЭПИДЕМИЧЕСКИХ МЕРОПРИЯТИЙ И СЕЗОННОГО ФАКТОРА

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RESUMO

Introdução: O surgimento do COVID-19 tem levado a uma maior atenção aos modelos matemáticos da epidemiologia sendo um dos principais parâmetros o número reprodutivo básico R_0 . O seu valor determina a dinâmica da incidência e o nível das medidas antiepidêmicas. É desejável ter um método bastante preciso para avaliar R_0 para cada dia. **Objetivo:** desenvolver uma metodologia para avaliar o valor de R_0 para COVID-19, levando em consideração uma mudança bastante rápida e significativa em seu valor ao longo do tempo. **Métodos:** foi proposto um método de cálculo do número de reprodução R_0 para avaliação do COVID-19 levando-se em consideração a mudança na contagiosidade das pessoas infectadas durante o processo infeccioso. **Resultados e Discussão:** Na Rússia, em junho-agosto de 2020, a taxa de reprodução era ligeiramente inferior a 1, mas, em setembro, o R_0 começou a crescer, ultrapassou 1, o que causou um aumento notável na incidência. Durante junho, no Brasil, R_0 estabilizou em um valor 1. A atividade de transmissão do patógeno é influenciada por mudanças sazonais na taxa de reprodução R_0 , bem como no nível de estado imunológico da comunidade. Com base na avaliação da dinâmica da incidência de outras pneumonias, verificou-se que a variação do R_0 durante o ano é de cerca de 10%, com um mínimo no verão. **Conclusões:** embora mantendo a atividade atual de medidas antiepidêmicas devido a fatores sazonais da atividade do mecanismo de transmissão e acúmulo de indivíduos imunes nos próximos meses, a situação na Federação Russa se agravará com um aumento na incidência que dobrará em seis meses e, no Brasil, em seis meses - melhora com diminuição da incidência em 10 vezes. No entanto, a dinâmica da incidência será determinada principalmente pelo trabalho da administração e das autoridades sanitárias e pela conscienciosidade dos cidadãos.

Palavras-chave: COVID-19, avaliação do R_0 , modelos matemáticos do processo epidêmico

ABSTRACT

Background: The emergence of COVID-19 has led to increased attention to mathematical models of epidemiology, one of the main parameters of which is the basic reproductive number R_0 . Its value determines both the dynamics of the incidence and the level of anti-epidemic measures. Therefore, it is desirable to have a fairly accurate method for assessing R_0 for each day. **Aim:** Develop a methodology for determining the R_0 value for COVID-19, taking into account a reasonably rapid and significant change in its value over time. **Methods:** a method for calculating reproduction number R_0 was proposed for assessing COVID-19 R_0 , taking into account the change in the contagiousness of the infected people during the infectious process. **Results and Discussion:** In Russia in June-August 2020, the reproduction rate was slightly less 1, but in September R_0 began to grow, exceeded 1, which was caused a noticeable increase in the incidence. During June in Brazil, R_0 stabilized at a value of 1. The activity of transmission of the pathogen is influenced by seasonal changes in the reproduction rate R_0 and the level of community immune status. Based on the assessment of the dynamics of the incidence of other pneumonia, it was found that the change of R_0 during the year is about 10%, with a

minimum in summer. **Conclusions:** while maintaining the current activity of anti-epidemic measures due to seasonal factors of the activity of the transmission mechanism and accumulation of the immune individuals in the coming months, the situation in the Russian Federation will worsen with an increase in the incidence doubled within six months, and in Brazil in six months — improve with a decrease in the incidence ten times. However, the dynamics of the incidence will be determined primarily by the work of the administration and health authorities and the conscientiousness of citizens.

Keywords: COVID-19, R_0 estimation, mathematical models of the epidemic process

АННОТАЦИЯ

Введение. Появление COVID-19 привело к повышенному вниманию к математическим моделям эпидемиологии, одним из основных параметров которых является число репродукции R_0 . Его величина определяет как динамику заболеваемости, так и уровень противоэпидемических мероприятий. Желательно иметь достаточно точную методику оценки R_0 на каждый день. **Цель:** разработать методологию оценки значения R_0 для COVID-19 с учетом довольно быстрого и значительного изменения его значения с течением времени. **Методы.** Метод расчета репродуктивного числа R_0 был предложен для оценки COVID-19 R_0 с учетом изменения заразности инфицированных людей в ходе инфекционного процесса. **Результаты.** В России в июне-августе 2020 года коэффициент воспроизводства был немного меньше 1, но в сентябре R_0 начал расти, превысив 1, что вызвало заметный рост заболеваемости. В течение июня в Бразилии R_0 стабилизировался на уровне 1. На активность передачи патогена влияют сезонные изменения скорости воспроизводства R_0 , а также уровень иммунного статуса сообщества. На основании оценки динамики заболеваемости другими пневмониями установлено, что изменение R_0 в течение года составляет около 10% с минимумом летом. **Заключение:** при сохранении текущей активности противоэпидемических мероприятий за счет сезонных факторов активности механизма передачи и накопления иммунных особей в ближайшие месяцы ситуация в Российской Федерации будет ухудшаться с увеличением заболеваемости вдвое в течение шести месяцев, а в Бразилии через полгода - улучшение со снижением заболеваемости в 10 раз. Однако, динамика заболеваемости будет определяться, прежде всего, работой администрации и органов здравоохранения и сознанием граждан.

Ключевые слова: COVID-19, оценка R_0 , математические модели эпидемического процесса

1. INTRODUCTION:

1.1. Background

The onset of the pandemic disease caused by the new coronavirus COVID-19 has drawn attention to mathematical models of the epidemic process, as only with their help the dynamics of incidence of a new disease under different scenarios of anti-epidemic measures can be predicted. In particular, a “contact number” or “basic reproductive number” terms, traditionally referred to as R_0 , has come into use (WHO, 2020; WHO, March 5, 2020; Euro WHO, 2020; Madabhavi, 2020; CDC, 2020; Anderson and May 1992; Li *et al.*, 1999).

The basic reproductive number is defined as the average number of infected from one infected at universal susceptible. Similar terms exist in population biology and are defined as the ratio of populations of offspring and parents under the most favorable conditions: food excess, absence of predators, and parasites (Svirezhev and Logofet, 1978).

Since the activity of the transmission mechanism depends on both the properties of the pathogen and the characteristics of the host population, including both biological and social aspects, the attention to mathematical models of the epidemiology, one of the main parameters of which is the basic reproductive number even for the same pathogen varies in different cities and countries and changes over time has increased. Typhoid fever is an example. Even 100 years ago, there was mass infection for typhoid fever. However, after introducing the practice of disinfecting food and water, the incidence of typhoid fever began to decline. Currently, in most countries, there are isolated cases of typhoid fever (WHO, 2018).

1.2. Basic models of the epidemic process and their development in the models of the COVID-19 epidemic process.

The first models of the epidemic process date back to the first half of the 20th century (Kermack and McKendrick, 1927). Their use was limited, as the successful use of mathematical

models requires a fairly good understanding of the phenomenon under study (Longini, 1978; Olsen, 1988; Qiu, 2020; Zhao, 2020). Progress in epidemiology is accompanied by increasingly active use of mathematical models of the epidemic process. (Cabore *et al.*, 2020; Carvalho *et al.* 2019).

The reason for this is that mathematical models use incidence data and knowledge about the epidemiology of the disease under study. As knowledge accumulates, the models and prognoses created on their basis are refined. So, in early 2020, it was believed that most of the infected patients with COVID-19 fall ill in severe form, with a mortality rate of more than 5% (Zhou *et al.*, 2020; Guo *et al.*, 2020). As a result, the obtained prognosis of damage from a pandemic in the absence of active anti-epidemic measures gave a situation of a global catastrophe (Diop *et al.*, 2020) with the number of deaths in several hundred million people. Now, from the reports of the Moscow Government on the results of mass screening of city residents the presence of antibodies to COVID-19 is about 20% (Mos.ru, 2020). It was also found that the likelihood of disease and its severity dramatically increases with age (Giordano *et al.*, 2020; Zheng *et al.*, 2020; Han *et al.*, 2020; Ge *et al.*, 2020; Silva *et al.*, 2020; Sharma *et al.*, 2020; CDC, 2020).

As a result, the estimate of the maximum damage decreased by about ten times. On the other hand, the mathematical models of the COVID-19 epidemic correctly predicted that if no effective measures are taken to limit the spread of the pathogen, the incidence will grow exponentially with an increase in the number of cases in a month several tens of times until a significant proportion of the population will be infected (Ngonghala *et al.*, 2020). At the same time, the maximum incidence will be such that the number of patients who need hospitalization will be many times higher than the capacity of health care. Furthermore, estimates of the activity of the transmission mechanism unambiguously showed that the spread of the pathogen will not be limited to one country but will be global.

Therefore, projections based on mathematical models served as one of the factors that prompted the health care system and government to take immediate practical measures to limit the rate of increase in the incidence (Euro WHO, 2020; WHO, March 5, 2020; Billah *et al.*, 2020; Zhang *et al.*, 2020).

However, at the same time, it is still unknown how long the immunity will be after the disease (Zhang and Guo, 2020; Chams, 2020). Therefore, there is no data required to create mathematical models of long-term dynamics of incidence or mathematical models of the epidemic process of COVID-19. We have to limit ourselves to models of the COVID-19 epidemic for no more than several years.

Formally, the mathematical model of the epidemic is obtained from the model of the epidemic process, if we do not take into account the process of the population turnover due to the birth of new members of the population or the loss of specific immunity in some of those who have been ill. Therefore, the epidemic model can be used for short-term or medium-term prognosis, for not more than several years, even for infectious diseases with an expressed lifelong immunity.

1.3. Compartmental models in epidemiology

Traditionally, models of the epidemic process are divided according to a set of possible states. The most commonly used model is SIR (Matveev, 2020), in which members of a population can be in one of three states (S – Susceptible; I – Infectious; R – Recovered). Transition $S \rightarrow I$ — infection of a susceptible person, $I \rightarrow R$ — recovery, $R \rightarrow S$ — population turnover.

Population turnover occurs due to the loss of specific immunity or a pair of events "death of the insusceptible person" + "birth of a new member of the population". The SI model corresponds to infectious diseases from which one cannot recover, ending in death or life-long carriage; SIS model — diseases that do not have post-infectious immunity. In the SEIR model, another state is "sterile infected", "Exposed" — in the stage of the disease before the onset of the shedding of the pathogen. One more condition has been added in the MSIR and MSEIR models, corresponding to children with passive immunity due to breastfeeding (Matveev, 2020).

The specificity of the disease course may necessitate further complications of the model by introducing additional states and transition stages. So, for tuberculosis, an infected person is in a "healthy carrier" state. From this state, a transition to the state of an active infectious process is possible. The state of active tuberculosis can be divided into several variants: with and without bacterial excretion, with or

without active drug treatment, and so on (Avilov, 2007).

The epidemic model differs from the epidemic process model in that it does not account for the RS update process $R \rightarrow S$. It should be noted that the selection of conditions in the models under consideration is done from the point of view of an epidemiologist, not a clinician. Being in the "Infectious" state ends with the end of the pathogen shedding and not with clinical recovery, that is, the disappearance of the clinical signs of the disease. Accordingly, the transition $E \rightarrow I$ is the beginning of the release of the pathogen, and not the appearance of clinical signs of the disease, that is, the duration of stay in the "Infectious" state does not coincide with the duration incubation period.

However, the classification of the infected persons into the "Exposed"/"Infectious" states is rather rough since the increase and decrease in the contagiousness of the infected occur gradually. Therefore, within the framework of this work, for a more accurate assessment of the activity of the transmission mechanism, we will consider the average contagiousness of an infected person as a function of the time elapsed after infection.

The dynamics of incidence, that is, the $S \rightarrow I$ transition activity, is determined not only by the current proportion of the infected persons, their contagiousness, and the activity of the pathogen transmission mechanism but also by the level of the community immune status. When comparing the results obtained using mathematical modeling with actual data, the following should be considered: (1) In the mathematical model, I is the proportion of those infected persons (not sick). For most infectious diseases, the number of cases, those diagnosed and officially reported, is only a small proportion of the total number of infected persons, since most infections are asymptomatic or without medical resource utilization. The ratio between sick and infected patients can be obtained using screening studies to assess the proportion of the immune proportion of the population and compare its value with the incidence; and (2) The value of community immune status is determined not so much by the total proportion of the immune persons as by the proportion of the immune persons in high-risk groups.

The following criteria can determine risk groups: A high risk of infection, by high infectivity, and by severe disease. The first two criteria

relate to the spread of the disease, the third to the severity of the complications.

The risk groups for infection and contagiousness traditionally include healthcare providers (Wang W., 2020). The risk group for disease severity for COVID-19 consists of older adults, high body mass index, and chronic diseases (Zhou, 2020; Du, 2020). Unfortunately, it is challenging not only for COVID-19 but even for well-studied diseases to obtain an estimate of the distribution of members of the population in terms of individual infectiousness and risk of infection (Wang X. *et al.*, 2020). The main part of this article is devoted to assessing the rate of increase in the incidence and the activity of the spread of the pathogen. For this part of the article, these difficulties in interpreting the simulation results do not affect the obtained conclusions. Also, these difficulties do not affect the analysis of the initial phase of the epidemic, when the proportion of the immune is still small in all groups, including the risk group. However? These difficulties should be considered when highlighting the influence of the community immune status on the dynamics of morbidity at a sufficiently high incidence rate. This paper concerns the analysis of the current incidence of COVID-19 in Moscow, where the proportion of seropositive persons is already about 25% (Mos.ru, 2020).

The convenience of using a reproductive number lies in the comprehensibility of interpretation. If $R_0 < 1$, then the number of sick people will decrease, and the pathogen will naturally be eliminated. If $R_0 > 1$, in the absence of additional anti-epidemic interventions, the incidence will increase until a high enough level of collective immune status is reached. To reach it, a large enough part of the population must be immune. (Billah *et al.*, 2020; Van Damme *et al.*, 2020; Ngonghala *et al.*, 2020).

1.4. Simplest homogeneous model and collective immune status.

Under the simplest homogeneous model, the level of collective immunity is given by the fraction of the susceptible portion of the population S , so that from one infected, an average of $S \times R_0$ susceptible are infected, and if $S \times R_0 > 1$, the incidence increases, and if $S \times R_0 < 1$, it decreases. With constant incidence $S = 1/R_0$. To protect the population from mass incidence by vaccination, it is necessary to vaccinate in a way that more than $(1 - 1/R_0)$ proportion of the population obtains post-vaccinal immunity,

infecting against infestation. For example, if $R_0=5$, it is necessary to vaccinate the population so that at least 80% of the population has strenuous immunity. At the same time, vaccination coverage should be higher, as not all vaccinated produce the necessary level of immune response (Zimmermann and Curtis, 2019).

It is advisable to vaccinate with some reserve, as one case of brought disease will trigger on average $(S \times R_0)/(1 - S \times R_0)$ contacted. For example, with $R_0=5$ and a proportion of immunes equal to 85%, one brought case will account for an average of 3 contacted (Horn *et al.*, 2016). Similarly, the necessary intensity of other anti-epidemic measures, including those aimed at social disintegration and the active detection and isolation of those affected, can also be estimated. Since for COVID-19, the basic reproductive number is slightly less than 3, it is necessary to reduce the number of contacts by more than 3 times to control morbidity (Liu *et al.*, 2020). However, to produce a high enough level of collective immune status, not most of the population needs to be immune — enough is that only high-risk groups in the probability of infection and contagion have immunity (Gerasimov, 2008; Munday, 2018).

In estimating the expected level of morbidity, it is also necessary to consider that the formation of collective immunity means the immunity of all those infected, not just those infected in a manifested form (Yu and Yang, 2020). During the study of the COVID-19 pandemic, estimates of the proportion of cases with pronounced symptoms have changed significantly. In January-February, researchers believed that prominent symptoms accompanied virtually all cases. This was due both to the complexity of laboratory diagnosis of the disease and to the fact that the causative agent COVID-19 was considered an analog of other coronaviruses, SARS and MERS, in which virtually all cases of infections led to disease in a severe form (Wang Y. *et al.*, 2020).

Then asymptomatic forms were identified, and estimates of the proportion of expressed cases began to decrease to 80%, then to 50%, and then to 20% (Yu and Yang, 2020). According to mass research of residents of Moscow, the proportion of expressed cases is about 10% - at the beginning of July about 220,000 cases were recorded at about 20% of seropositivity among residents of Moscow. Accordingly, if at first it was expected

that about half of the inhabitants of the Earth would suffer new coronavirus infection (with pronounced clinical symptoms), now the prognosis is ten times lower.

Individual protection and social separation measures have a positive impact on the incidence of COVID-19. Still, their long and intensive appliance by most countries' leadership is considered unacceptable because of the grievances of citizens and the negative impact on the economy. At the moment, methods for assessing the average value of the reproductive number R_0 for pathogens of infectious diseases are actively used, provided that the conditions of the course of the epidemic process of process remain unchanged (Wells *et al.*, 2020). For COVID-19, these methods are not very successful, since in this case active anti-epidemic measures are used, the set of which and the intensity of their use are constantly changing over time.

At the same time, it cannot be said that the infectivity of COVID-19 is very high. Estimating the reproduction rate R_0 for COVID-19 gives a value of no more than 3 (see text below). At the same time, for measles, mumps, diphtheria, and many other infectious human diseases R_0 is higher (Anderson and May 1922). This, in particular, offers good prospects for controlling the spread of COVID-19 through vaccination. However, since the causative agent COVID-19 is new to the human population and it has not yet passed the stage of evolutionary adaptation to the host organism, the emergence of new, more infectious variants of the pathogen is also quite likely (Belyakov *et al.*, 1987).

The need for constant monitoring of the situation and quick action follows from the experience of the initial stage of the COVID-19 epidemic. The incidence increased tenfold in a month. This technique will make it possible to assess the effectiveness of the anti-epidemic measures used and predict morbidity dynamics under different scenarios. The development of a more perfect mathematical model of the epidemic process by calculating the rapidly and significantly changing reproductive (contact) number of R_0 is an urgent task of modern epidemiology.

This study aimed to develop a methodology for assessing the value of the reproductive (contact) number R_0 for COVID-19, taking into

account a fairly rapid and significant change in its value over time.

2. MATERIALS AND METHODS

2.1. Mathematical modeling

The study used epidemiological and mathematical modeling methods for studying the proposed mathematical model using the example of the incidence of COVID-19 in Russia and Brazil in the period of March-September 2020. The study used open data from official sources on the incidence of COVID-19 in Russia (<https://covid.observer/> and <https://yandex.ru/covid19/stat>) and Brazil (Painel coronavirus - <https://covid.saude.gov.br/>).

At the initial stage of development of the epidemic of a new disease, when no noticeable immune layer has formed, and no anti-epidemic measures were taken, the incidence grew exponentially, as $c \times e^{\lambda t}$, where c is the constant, λ is the exponential growth rate, t is the time in days. At the same time, the ratio of the number of people who fell ill for this and the previous day is equal $e^{\lambda t} - 1$.

Within the simplest homogeneous model (MacIntyre and Heslop, 2020), the number of infected $J(t)$ dynamics at the first stage is described by equation 1.

$$\frac{dJ}{dt} = \frac{(R_0 - 1)}{T} J \quad (\text{Eq.1})$$

Substituting the (1) $J(t) = c \times e^{\lambda t}$, it turns out equation 2.

$$R_0 = 1 + \lambda T \quad (\text{Eq.2})$$

Therefore, for a new infectious disease, the reproduction rate R_0 can be estimated from the rate of increase in the incidence and duration of the disease. So, for SARS with a characteristic duration of the disease of about ten days at the initial period of the epidemic, the incidence doubled in about three weeks, which corresponds to a reproduction rate of about 1.5 (Liu *et al.*, 2020). This is an estimate obtained using a highly simplified "standard" model. We further propose a more accurate assessment method and compare our values with these.

2.2. Statistical Analysis

Statistical analysis of the data was carried out using the statistical software package IBM SPSS Statistics 22.0.

3. RESULTS AND DISCUSSION:

At the initial stage of exponential growth, under conditions maintained, both the number of ill patients per day and the total number of patients (incident and prevalence), the number of hospitalized, and the number of deceased shall increase at the same rates. For example, figure 1 shows that from late March to mid-April, the incidence of COVID-19 in Russia and Brazil grew exponentially, so that on the logarithmic scale, the incidence graph was close to linear, after which the rate of morbidity began to decrease.

No new cases were reported for May 20 in Brazil, and there were more than usual on May 19 and 21. Since the logarithm of zero is infinite, the data for May 19-21 were averaged for further calculations. Also, Figure 1 clearly shows the difference in the used disease registration system. In Brazil, the number of reported cases of COVID-19 on weekends is several times lower than on weekdays. There are no such differences in Russian Federation and Moscow.

The dynamics of the incidence of COVID-19 has changed. From March 31 to May 15 — a period of exponential growth; From May 16 to June 30 — the incidence continues to change, but at a slower rate; From July 1 to August 31 — the incidence is relatively stable; From September 1 to September 18 — an increase in the incidence began in the Russian Federation.

For the period from March 31 to May 15, the average exponential growth rate for Moscow was $\lambda \approx 0.0735$, for Russia excluding Moscow $\lambda \approx 0.0958$ and for Brazil $\lambda \approx 0.0389$, which corresponds to a 7.63%, 10.05% and 3.97% increase in the number of patients per day, respectively (Gerasimov, 2020). If the average duration of the disease is ten days, for Moscow, it is $R_0 \approx 1.735$, for Russia except for Moscow - $R_0 \approx 1.958$ and for Brazil - $R_0 \approx 1.398$. However, an estimate of the average R_0 value over a relatively long period is only of relative value, since the situation with the spread of COVID-19 changes in a matter of days. Therefore, the obtained estimates R_0 1.735 for Moscow, 1.958 for Russia except for Moscow, and 1.398 for Brazil need to be clarified.

In determining the duration of the disease, clinicians focus on clinical symptoms the appearance and disappearance of which may not coincide with the beginning and end of the release of the pathogen. Epidemiologists give the maximum duration of the contagious period, as needed to determine the quarantine period. In this case, the dependence of the average contagiousness of the infected on time after infection is required.

Then if $K(n)$, $n = 1, 2, \dots$ is the relative average in n days after infection case, $K(1) + K(2) + \dots = 1$, then the dynamics of the number of infected per day N is given by equation 3

$$A(N) = R_0(A(N-1)K(1) + A(N-2)K(2) + \dots) \quad (\text{Eq.3})$$

Now there are at least two approaches to determining the dynamics of contagiousness $K(n)$, $n = 1, 2, \dots$: by the disease picture and by the deviation of the incidence dynamics from the exponential. It is believed that for manifested cases, the release of the pathogen begins on the second to third day after infection and is increasing as the severity of the clinical picture increases, which corresponds to increase in the content of virions in the body of the patient. The diagnosis is made on 5th-7th day, after that the number of contacts of a sick person drastically decreases (both when hospitalized and treated at home). Further, the average contagion continues to decrease, including through recovery or death, and by mid of the third week, it becomes small (Lauer *et al.*, 2020; Liu *et al.*, 2020; Madabhavi *et al.*, 2020; Zhai *et al.*, 2020).

For asymptomatic cases, discharge begins a few days later, and ends in 2-3 weeks after infection, and is less intense. In general, the average number of infected from one asymptomatic carrier is lower than from one person with a pronounced form of the disease, but since the proportion of cases expressed is less than half, the proportion of infected patients with pronounced symptoms and asymptomatic are comparable (Giordano *et al.*, 2020).

Table 1 shows the dependence of the average infectivity of the infected $K(n)$ (contagiousness of patients with COVID-19) on the number of days n , which have passed since the moment of infection. These are used below to analyze the actual data. Another approach of

$K(n)$ estimation is based on the deviation of dynamics from the predicted model based on Eq.3. Since in the case of development of mass COVID-19 morbidity active anti-epidemic activities were introduced, the value R_0 in equation 3 should not be considered as a constant value but as a function of time.

In this case, the expected number of cases $a(N)$ per day N is shown in equation 4.

$$a(N) = R_0 E(N) (A(N-1)K(1) + A(N-2)K(2) + \dots) \quad (\text{Eq.4})$$

Further, based on actual data on disease patterns, different countries address the following challenge: at what function the $K(n)$ the expected values of $a(n)$ will be as close as possible to the actual values of $A(n)$ with the simplest form of the functions $E(n)$.

Both approaches give the same results — starts to differ from zero after two days, grows to the 7th day, then begins to decrease, with the rate of reduction about one and a half or two times less than the build-up speed contagion. Unfortunately, at the moment, it is not possible to provide links to publications on the second approach. Such calculations became possible only after the transition of the morbidity dynamics to the second (the slowdown in the incidence compared to the exponential) and the third (the stabilization and reduction of the incidence) stage and require quite long calculations using supercomputers, so here it has to rely on the results of the articles reviewed, including not yet published, reports and private messages.

According to equation (Eq.3) the expected value of the contact number for day N can be calculated as shown in equation 5

$$R_0(N) = \frac{A(N)}{A(N-1)K(1) + A(N-2)K(2) + \dots} \quad (\text{Eq.5})$$

where $A(k)$ is the number of cases per day number k .

Figure 2 shows that before May 15, there was a decrease in pathogen transmission activity, after which it remained at the same level. From May 16 to June 30, the average R_0 for Moscow was 0.783, which resulted in an about ten times decrease of the incidence. In contrast, for Russia, excluding Moscow, the average R_0

was 1.033, and the incidence remained at the same level, while for Brazil, the average R_0 was 1.213, resulting in continuing rapid growth of morbidity.

For Moscow, for the period July 1 — August 31, the average R_0 value was 0.969 and the incidence rate remained approximately at the same level. For Russian Federation (excluding Moscow), the average R_0 was 0.953, which led to a decrease in the incidence by about 20%. In the period from 1 to September 18 in Moscow the average value of R_0 was 1.034, in Russia (excluding Moscow) 1.058. By itself, an increase in the reproduction rate to a value of 1.05 corresponds to an incidence rate of about 15% per month, however, the alarming moment is that the value of R_0 in September is constantly growing.

For Brazil, the average R_0 value for the period from July 1 to September 18 is 1.025, which corresponds to a slow increase in the incidence. The average value of the change per day R_0 -0.00205, the correlation between the R_0 value and the date is statistically insignificant, $p = 0.298$. In addition to anti-epidemic measures, the dependence of the activity of the transmission mechanism on the time of year and the accumulation of immune ones affect the dynamics of morbidity given by equation (3), as shown in equation 6

$$R_0(t) = \bar{R}_0 S(t) E(t) V(t) \quad (\text{Eq.6})$$

where $\bar{R}_0$ is the “base” value of the basic reproductive number estimated above $S(t)$ is the proportion of the susceptible part of the population $E(t)$ is the current effectiveness of the anti-epidemic activities. The function $V(t)$ corresponds to the dependence of the activity of the transmission mechanism on the season. For an unambiguous definition, it is assumed that its average value is equal to one.

The dynamics of morbidity in the absence of anti-epidemic measures can be described by equations 7 and 8 (Yu,1927)

$$I(N) = \bar{R}_0 S(N-1) V(N) \sum_{n=1} K(n) I(N-n) \quad (\text{Eq.7})$$

$$S(N) = S(N-1) - I(N) + \gamma(1 - S(N-1)) \quad (\text{Eq. 8})$$

where $I(N)$ is the proportion of infected per day number N , $S(N)$ is the proportion of infected per day number N , $1/\gamma$ is the average life expectancy in days for infections with strenuous lifetime immunity or the average duration of immunity retention for infections of temporal immunity.

Numerical calculations show that the logarithm of the ratio of maximum and minimum intra-annual morbidity depends almost linearly on the amplitude of fluctuations in the activity of the transmission mechanism, that is, if $V(N) = 1 + \alpha \times f(N)$, the ratio of maximum and minimum morbidity is almost equal to $e^{\alpha\beta}$ where β is determined by values R_0 , γ , $K(n)$, and the form of function f . For life expectancy of 75 years of the contagiousness given above the $K(n)$ and the sinusoidal dependence of transmission mechanism activity on the time of year at $R_0=2$ we get that $\beta \approx 16.17$, and at $R_0=3$ $\beta \approx 16.43$.

During the year, the incidence of out-of-hospital pneumonia in Russia changes by about four times (Bondarenko *et al.*, 2016). Since the duration of the disease and the activity of the transmission mechanism for COVID-19 and other out-of-hospital pneumonias are quite similar from the ratio obtained above as shown in equation 9

$$\alpha = \frac{\ln 4}{\beta} \quad (\text{Eq.9})$$

This gives $a \approx 0.0857$ for $R_0=2$ and $a \approx 0.0843$ for $R_0=3$. Consequently, the expected value of seasonal variation in transmission mechanism activity for COVID-19 is about 8.5%.

By mid-spring, the contact number for Moscow, Russia, and Brazil was roughly 2.5. For Moscow, reduction of activity of the transmission mechanism due to accumulation of the immune layer can be estimated at 0.8, and due to reduction of activity of the transmission mechanism from mid-spring to mid-summer — 0.915 times, which in total according to (Eq.6) gives a reduction in the activity of the transmission mechanism by 1.366 times. In fact, the activity of the transmission mechanism decreased from about 2.75 to 0.759, that is 3.62 times. Consequently, due to anti-epidemic measures and the decrease in the social activity of the population, the activity of transmission of the virus decreased by 2.65 times.

If 228.678 cases were registered in Moscow at present, then in Russia as a whole — 720.547, which at a manifestation of 10% gives the share of immune in Russia except Moscow at a level of 4.2%. As shown above, now Moscow has R_0 of about 0.82 and Russia except Moscow — of about 1. From the difference of 0.23 due to differences in the severity of the immune layer, $0.2 - 0.042 = 0.158$ can be explained. About 2/3 of the difference in the activity of propagation of the pathogen is explained by differences in the immune layer.

Suppose the incidence present at the beginning of July lasts for the whole summer until the beginning of autumn, about 30.000 cases of COVID-19 will be recorded in Moscow. In that case, taking into account not manifested cases will increase the proportion of the immune layer by another about 2.5%. For Russia except for Moscow, the increase in the immune layer will also be approximately 2.5% if the incidence remains at the same level as it is now. Since due to seasonal change of R_0 , in autumn the activity of propagation of the pathogen will be about 9%, the overall situation with the incidence of COVID-19 will deteriorate even with the preservation of existing anti-epidemic activities.

For Brazil, the situation is also quite unfavorable. On July 29, 2.552.265 cases were recorded, which at 10% manifesto yields to about 12.3% seropositive (Amorim Filho *et al.*, 2020; Aguas *et al.*, 2020; Vieira *et al.*, 2020; Hallal *et al.*, 2020). Therefore, the current R_0 value of 1.192, taking 10% amplitude of the transmission mechanism activity fluctuations, will increase to about 1.3 by mid-autumn. Consequently, doubling the proportion of seropositive will make R_0 less than 1. Therefore, if the current anti-epidemic activities in Brazil are maintained, it is possible to expect that by early autumn, the number of residents affected by COVID-19 will double, after which the incidence will begin to decline noticeably. So, at the initial period of the COVID-19 epidemic in Russia and Brazil, the contact number R was in the region of 2.5 - 3. However, due to the introduction of anti-epidemic measures, R_0 was reduced to about 1. Thus, the dynamics of the incidence of COVID-19 is determined, according to (Eq.6), by three components — the activity of the transmission mechanism, taking into account the anti-epidemic measures, the activity of seasonal factors of transmission, and the level of community immune status.

As of September 19, 2020, 275.354 cases of the disease were registered in Moscow, which is 2.17% of the total population. According to the statements of the Moscow Government, as a result of the screening, it was obtained that about 20% of Moscow residents have antibodies to the new coronavirus (Mos.ru, 2020). Consequently, the proportion of manifest registered cases for Moscow is about 8.7%.

Currently, about 800 cases of COVID-19 are registered in Moscow per day. Considering the obtained share of documented cases of the disease in 8.7%, this increases the share of immune Muscovites per day by 0.073%. On the other hand, due to the activation of seasonal factors, the activity of the transmission mechanism will increase at a rate of about 0.093% per day. Consequently, at the current level of morbidity, the increase in the collective immune status and the activation of seasonal factors of transmission almost completely compensate each other

For Russia, with the exclusion of Moscow from it, 821.164 cases of COVID-19 were registered, which corresponds to 0.61% of the population and gives the proportion of the immune persons at 7.05%. With the current incidence of about 5000 new cases per day, this gives an increase in the proportion of immune people by 0.043% per day, which compensates for half of the seasonal increase in the activity of the transmission mechanism and corresponds to a twofold increase in the incidence by the end of winter.

In Brazil, there are 4.495.181 registered COVID-19 cases, accounting for 2.13% of the population. Since the ratio of registered cases, as well as the magnitude of seasonal changes in the activity of the transmission mechanism in Brazil, may differ from Russia, it can be said only as a very rough estimate that due to an increase in community immunity and a seasonal decrease in the activity of the transmission mechanism, which in this case will be summed up, while maintaining the current activity of anti-epidemic measures, an approximately 10-fold decrease in the incidence of COVID-19 in Brazil is expected.

4. CONCLUSIONS:

In total, while maintaining the current activity of anti-epidemic measures, the incidence in Moscow will remain at the same level. In the Russian Federation, except for Moscow, it will

increase and in six months should increase by about two times. In Brazil, it will decrease and in six months should decrease by about 10 times. Therefore, the main factor that will determine the dynamics of incidence in the Russian Federation and Brazil is anti-epidemic measures, which must be increased compared to the current level, although this causes popular discontent.

These estimates were obtained within the framework of the simplest homogeneous model, in which community immunity is determined by the proportion of the susceptible part of the population. However, as mentioned earlier, in reality, community immunity is higher since the proportion of susceptible people in high-risk groups in terms of the probability of infection is lower than the average for the population.

5. CONFLICT OF INTEREST:

The authors declare there is no conflict of interest

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Figure 1. Dynamics of new COVID-19 cases detected per day in Moscow, Russia excluding Moscow, and Brazil.

Notes: The x-axis is the date (day. month) of registration of new cases in 2020.

Figure 2. Dynamics of reproductive number R_0 (average number of infected from one infected person) estimation for a given day.

Notes: The x-axis is the date of R_0 calculation (day.month) in 2020. The y-axis is the calculated coefficient R_0 for a given day in 2020.

Table 1. Change in contagiousness of patients ($K(n)$) with COVID-19, depending on the time (day) elapsed since the moment of infection.

n (day)	$K(n)$	n (day)	$K(n)$
1	0	15	0.0242
2	0.142	16	0.0211
3	0.142	17	0.0179
4	0.142	18	0.0147
5	0.101	19	0.0115
6	0.0477	20	0.0083
7	0.0477	21	0.0052
8	0.0452	22	0.0045
9	0.0427	23	0.0039
10	0.0401	24	0.0032
11	0.037	25	0.0026
12	0.0338	26	0.0019
13	0.0306	27	0.0013
14	0.0274	28	0.0006