

PREVENTIVE HEALTHCARE: TOPICAL ISSUES OF HEALTH RISK ANALYSIS

UDC 613; 614
DOI: 10.21668/health.risk/2023.2.01.eng



Research article

SPATIAL-DYNAMIC HETEROGENEITY OF THE COVID-19 EPIDEMIC PROCESS IN THE RUSSIAN FEDERATION REGIONS (2020–2023)

N.V. Zaitseva, S.V. Kleyn, M.V. Glukhikh

Federal Scientific Center for Medical and Preventive Health Risk Management Technologies,
82 Monastyrskaya Str., Perm, 614045, Russian Federation

The coronavirus pandemic has produced considerable effects on medical and demographic processes worldwide and in Russia in particular. The epidemic process involved a sequence of circulating SARS-CoV-2 virus strains with different mutations and this reflected in registered levels of incidence and mortality against spatial heterogeneity of socioeconomic factors in different RF regions.

The aim of this study was to analyze spatial-dynamic heterogeneity of the COVID-19 epidemic process in the RF regions in 2020–2023.

We performed retrospective analysis of incidence and mortality at the national and regional levels. The analysis relied on departmental statistical data provided by Rospotrebnadzor as well as public data that described the intensive indicators of the COVID-19 epidemic process and results obtained by sequencing of biomaterial samples to identify COVID-19 in them in 2020–2023.

In 2020–2023 we identified five ‘waves’ of the COVID-19 epidemic processes that interchanged sequentially. Within these waves, RF regions reached local peaks in incidence with different speed. According to available data, the highest primary incidence among all the RF regions in 2021–2022 was established in Saint Petersburg (12,821.8 cases and 17,341.2 cases per 100 thousand people); the highest mortality in 2021 was detected in the Tver region (427 cases per 100 thousand people) and in the Arkhangelsk region in 2022 (350.9 cases per 100 thousand people). The greatest number of the RF regions where the incidence due to the disease was higher than its average annual level was established in October, November, December 2021 and February 2022 (51, 68, 51 and 82 RF regions accordingly).

The established spatial-dynamic heterogeneity of the epidemic process may indicate that this process can be largely determined by differences in the initial socioeconomic, medical and demographic characteristics of the RF regions.

Limitations of the study are related to the used statistical data on registered incidence and mortality as well as the concept of the epidemiological ‘wave’ accepted in it.

The identified territorial differences in the COVID-19 epidemic process should be considered when developing optimal regulatory impacts including those aimed at predicting probable emergent infections.

Keywords: *epidemiological process, COVID-19, epidemiological waves, incidence, mortality, RF regions, epidemiological analysis.*

According to the WHO statistics, 763,740,140 confirmed COVID-19 cases and 6,908,554 deaths caused by the disease were registered worldwide as of April 2023¹. In absolute values, Europe accounts for 36.1 % of all the disease cases (the first rank place) and 32.2 % of all the deaths caused by it (the second rank place). The Russian Federation holds the

© Zaitseva N.V., Kleyn S.V., Glukhikh M.V., 2023

Nina V. Zaitseva – Academician of the Russian Academy of Sciences, Doctor of Medical Sciences, Professor, Scientific Director (e-mail: znv@fcrisk.ru; tel.: +7 (342) 237-25-34; ORCID: <http://orcid.org/0000-0003-2356-1145>).

Svetlana V. Kleyn – Professor of the Russian Academy of Sciences, Doctor of Medical Sciences, Head of the Department for Systemic Procedures of Sanitary-Hygienic Analysis and Monitoring (e-mail: kleyn@fcrisk.ru; tel.: +7 (342) 237-18-04; ORCID: <https://orcid.org/0000-0002-2534-5713>).

Maxim V. Glukhikh – Candidate of Medical Sciences, Junior Researcher at the Department for Systemic Procedures of Sanitary-Hygienic Analysis and Monitoring (e-mail: gluhih@fcrisk.ru; tel.: +7 (342) 237-18-04; ORCID: <https://orcid.org/0000-0002-4755-8306>).

¹ The data cover the whole COVID-19 pandemic by April 2023.

31st rank place in Europe (the 55th in the world) for incidence (5,021.1 cases per 100 thousand people) and the 19th rank place in Europe (the 32nd in the world) for mortality (90.7 cases per 100 thousand people) over 2020–2022 [1].

The WHO classification [2] states that at present (April 2023) no variants of the virus circulating now could raise some concern. Only two variants of *Omicron* line are circulating at the moment that could be of some interest, *XBB.1.5* (so called *Kraken*) and *XBB.1.16* (so called *Arc-turus*). They are potentially able to induce new epidemic waves due to their greater capability to effectively escape any immune response of the human body [3, 4]. Still, according to the available estimates [3, 4], these sub-variants are not prone to induce more severe disease than other *Omicron* lines and have smaller virulence against the previously dominating strains that induced the first epidemiological ‘waves’.

While the infections agent (*SARS-CoV-2*) as well as its mutations and variants were actively spreading all over the world, it was deemed necessary to make reliable predictions how an epidemic situation would develop. These predictions should consider not only some peculiar features of the new infection (the basic reproduction number, incubation, virus mutation, etc.) but also relevant healthcare measures (vaccination, social isolation, face mask wearing etc.) [5, 6]. The general decline in the epidemic process motivates researchers to accomplish retrospective assessments of its active phases, relevance and timeliness of accomplished measures aimed at the disease control within epidemiological ‘waves’. All this is done to identify the most effective strategies for fighting against similar threats in future [7]. Despite there is no clear unambiguous definition of a ‘wave’², six COVID-19 waves have already been identified in Russia³ and each of

them has mostly been caused by specific variants of the virus and had its specific peaks in incidence and mortality.

The analysis of the research in the field has revealed that in Russia the COVID-19 epidemic process was estimated as per specific ‘waves’ / periods during which incidence and mortality were growing. However, such studies and analysis often focused either at the national level [8–10] or on just one or several RF regions / Federal Districts [11–13]. Some studies addressed identification and comparative analysis of *SARS-CoV-2* genetic variants that were detected in Russia during different periods of the COVID-19 epidemic process [14, 15]. Some studies established regional peculiarities and regularities lying in differences associated with multiple environmental factors able to modify the epidemic process, its intensity and duration [16, 17].

Despite some relevant studies in the field, only limited data are available in scientific literature that describe peculiarities of the COVID-19 epidemic process in RF regions or provide comparative inter-region assessments of it relying on the concept of epidemiological waves caused by consistent changes between several dominating *SARS-CoV-2* strains.

The aim of this study was to analyze spatial-dynamic heterogeneity of the COVID-19 epidemic process in the RF regions in 2020–2023.

Materials and methods. We have conducted retrospective epidemiological analysis of indicators related to the COVID-19 epidemic process (confirmed disease cases and deaths) over 2020–2023 at the national (the RF) and regional (RF regions) levels relying on open information sources⁴ as well as departmental statistical reports issued by Rospotrebnadzor. We analyzed indicators that

² WHO Coronavirus (COVID-19) Dashboard. Geneva, World Health Organization, 2020. Available at: <https://covid19.who.int/> (April 20, 2023).

³ Virusolog Chepurnov predupredil o nastuplenii novoi volny koronavirusa [Chepurnov, a virologist, warns a new coronavirus wave is possible]. *URA.RU: Informatsionnoe agentstvo [Information Agency]*. Available at: <https://ura.news/news/1052624187> (April 20, 2023) (in Russian).

⁴ Daily new confirmed COVID-19 cases per million people. *Our World In Data: COVID-19 Data Explorer*. Available at: <https://ourworldindata.org/explorers/coronavirus-data-explorer?zoomToSelection=true&time=2020-03-01..latest&facet=none&country=~RUS&pickerSort=asc&pickerMetric=location&Metric=Confirmed+cases&Interval=7-day+rolling+average&Relative+to+Population=true&Color+by+test+positivity=false> (April 20, 2023).

were directly associated with the epidemic process, namely, the results of sequencing of COVID-19 genetic samples. Our information sources were open data taken from the *Our World In Data*⁴, a web-site specializing in aggregating official statistical data provided by different countries. Our analysis of regional data on the COVID-19 incidence and mortality over 2021–2022 relied on using the Federal Statistical Report Forms No.2 Data on Infectious and Parasitic Diseases⁵.

In this study, we have taken on a concept that describes the COVID-19 epidemiological process in dynamics of consistent interchanges between epidemiological waves. The term ‘wave’ means a period when a certain strain circulating among infected people accounted for more than 50 % in sequenced biomaterial samples; each wave usually involves a rise in incidence and / or mortality. Intra-wave dynamics of COVID-19 incidence as per specific RF regions was analyzed by establishing incidence peaks in weekly averaging and calculating a number of weeks necessary to reach them. RF regions were divided into separate groups relative to the mode value of the number of weeks necessary to reach an incidence peak within the analyzed wave at the regional level (in specific regions). RF regions where the number of weeks necessary to reach a peak in incidence was below the mode value were considered areas with ‘extensive’ (rapid) growth in incidence; in case this number was above the mode value, a region was considered an area with ‘slowed’ growth in incidence. RF regions where this number was equal to the mode value were considered areas with

‘steady’ growth in incidence. RF regions were divided into separate groups during the second wave, which involved two sequential rises in COVID-19 incidence, on the basis of specific dynamics of these two rises: regions with a plateau-like curve of the first rise, regions where the first rise in incidence was higher than the second one, and regions where the second rise was higher than the first one. Intensive indicators were calculated using data on population numbers provided by the RF Federal State Statistics Service.

This study did not require any approval by a committee on biomedical ethics (the study used only open population data taken from official statistical reports).

Results and discussion. According to available data^{4,5,6} over 2020–2022, in general, the COVID-19 (ICD-10 code U07.1) incidence grew in the RF by 282.4 % (from 2,157.1 cases to 8,248.7 cases per 100 thousand people); the COVID-19 mortality also grew by 59.0 % (from 0.39 cases to 0.62 cases per 1 thousand people) (Table 1). Among the first diagnosed diseases, COVID-19 accounted for 2.8 % in 2020 and for 7.2 % in 2021; the disease accounted for 2.7 % in 2020, 9.9 % in 2021 and 4.8 % in 2022 in the all-cause mortality in the country,

In 2021–2022, the highest incidence of the first diagnosed COVID-19 was in Saint Petersburg (12,821.8 cases and 17,341.2 cases per 100 thousand people); the highest mortality due to COVID-19 in 2021 was in the Tver region (427 cases per 100 thousand people), and in 2022 in the Arkhangelsk region (350.9 cases per 100 thousand people) (Figure 1, 2).

⁵ Ob utverzhdenii form federal'nogo statisticheskogo nablyudeniya s ukazaniyami po ikh zapolneniyu dlya organizatsii Federal'noi sluzhboi po nadzoru v sfere zashchity prav potrebiteli i blagopoluchiya cheloveka federal'nogo statisticheskogo nablyudeniya za sanitarnym sostoyaniem sub"ekta Rossiiskoi Federatsii: Prikaz Rosstata ot 30.12.2020 № 867 [On Approval of federal statistical report forms with recommendations on how to fill in them to facilitate federal statistical monitoring of the sanitary situation in RF regions by the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing: the Order by Rosstat issued on December 30, 2020 No. 867]. *KODEKS: electronic fund for legal and reference documentation*. Available at: <https://docs.cntd.ru/document/573324768> (April 21, 2023) (in Russian).

⁶ Demografiya [Demography]. *Federal State Statistics Service*. Available at: <https://rosstat.gov.ru/folder/12781> (April 19, 2023) (in Russian); Raspredelenie umershih po polu, vozrastnym gruppam i prichinam smerti: Statisticheskaya forma № 5 (tablitsa 51) [Distribution of the deceased as per sex, age groups and causes of death: Statistical Form No. 5 (Table 51)] (in Russian); Zabolevaemost' vsego naseleniya Rossii s diaznozom, ustanovlennym v pervye v zhizni: statisticheskie materialy za 2019–2021 gg. [Incidence of the first diagnosed diseases among the whole RF population: statistical data collected in 2019–2021]. Moscow, the RF Ministry of Health (in Russian).

Table 1

Some statistical indicators of public health in the Russian Federation in 2019–2022

Indicator / Year	2019	2020	2021	2022
Average annual population of the RF ⁶ , abs.	146,764,655	146,459,795	146,575,531	146,713,743
Deceased due to all causes, total ⁷ , abs.	1,798,307	2,138,86	2,441,594	1,905,778*
The number of patients with the first diagnosed diseases as per all the nosologies ⁸ , abs.	114,512,153	111,294,314	125,022,382	–**
All-cause mortality among the whole population, cases per 1 thousand people	12.25	14.6	16.7	12.9
The first diagnosed diseases among the whole population as per all the nosologies, cases per 100 thousand people	78,024.3	75,989.7	85,295.5	–**
The number of infected ⁹ with COVID-19, abs.	–	3,159,297** *	9,054,041	12,102,028
The number of deceased ⁹ due to COVID-19, abs.	–	57,019***	240,586	90,836
COVID-19 Incidence, cases per 100 thousand people	–	2,157.1 (2.8 %)**	6,177.1 (7.2 %)	8,248.7 (–)
COVID-19-caused mortality, cases per 1 thousand people	–	0.39 (2.7 %)	1.64 (9.9 %)	0.62 (4.8 %)

Note: * preliminary data provided by Rosstat; ** data unavailable; *** according to the web-site *Our World In Data*; **** the share in the total incidence / mortality is given in brackets.

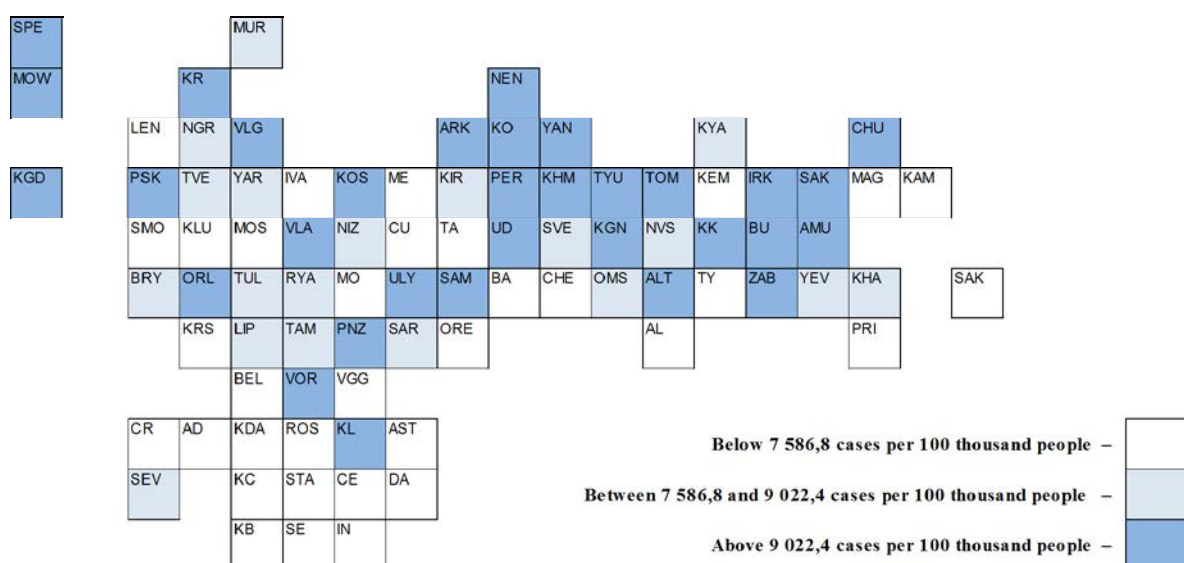


Figure 1. Spatial distribution of COVID-19 incidence among the RF regions in 2021, cases per 100 thousand people

⁷ Raspreделение umershih po polu, vozrastnym gruppam i prichinam smerti: Statisticheskaya forma № 5 (tablitsa 51) [Distribution of the deceased as per sex, age groups and causes of death: Statistical Form No. 5 (Table 51)] (in Russian).

⁸ Zabolevaemost' vsego naseleniya Rossii s diaznozom, ustanovlennym v pervye v zhizni: statisticheskie materialy za 2019–2021 gg. [Incidence of the first diagnosed diseases among the whole RF population: statistical data collected in 2019–2021]. Moscow, the RF Ministry of Health (in Russian).

⁹ Daily new confirmed COVID-19 cases per million people. *Our World In Data: COVID-19 Data Explorer*. Available at: <https://ourworldindata.org/explorers/coronavirus-data-explorer?zoomToSelection=true&time=2020-03-01..latest&facet=none&country=~RUS&pickerSort=asc&pickerMetric=location&Metric=Confirmed+cases&Interval=7-day+rolling+average&Relative+to+Population=true&Color+by+test+positivity=false> (April 20, 2023).

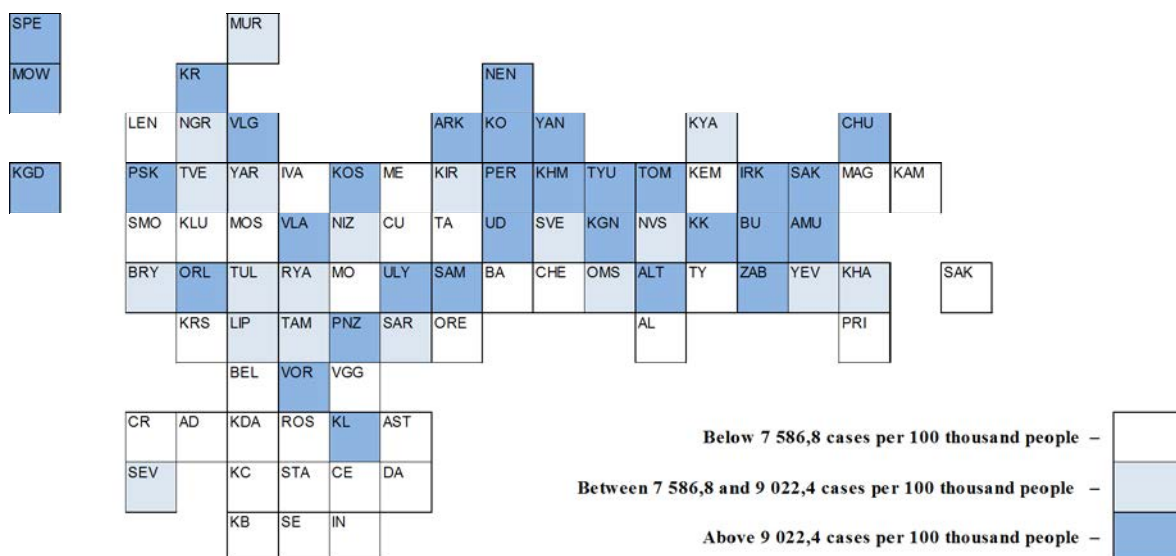


Figure 2. Spatial distribution of COVID-19 incidence among the RF regions in 2022, cases per 100 thousand people

Dynamics of the COVID-19 incidence and mortality varied within substantial ranges at the regional level in 2021–2022: between -54.5 % (growth rates) in Dagestan to 222.2 % in the Novosibirsk region for incidence (the regional average is 43.4 %); between -98.9 % in the Nenets Autonomous Area and 168.2 % in the Nizhniy Novgorod region (the regional average is -57.1 %) for mortality.

In the RF as a whole, children (≤ 17 years) accounted for 10.1 % among all the infected in 2021 and 15.7 % in 2022; at the regional level, the share of children in the total infected population ranged between 1.8 % (Tatarstan) and 22.5 % (Buryatia) in 2021, the regional average was 10.5 %; in 2022, the share ranged between 8.3 % (the Belgorod region) and 30.0 % (the Yamal Nenets Autonomous Area), the regional average was 16.2 %.

In the RF, incidence was 1.5–1.8 times higher in urban areas than in rural ones both in 2021 (6,759.8 cases and 4,448.6 cases per 100 thousand people accordingly) and in 2022 (9,264.3 cases and 5,225.8 cases per 100 thousand people accordingly). At the national level (RF), cases of carrying the COVID-19 infectious agent equaled 6.8 % in 2021 and 6.9 % in 2022; the share of COVID-19-induced pneumonia went down considerably over the same period, from 18.3 to 3.7 %.

It is difficult to analyze the COVID-19 incidence and mortality within one year due to the epidemic process being rather short, anti-epidemic activities being distributed unevenly both in the world and in the country, and frequent interchanges between dominant strains. That is, social, natural and biological factors are not stable and this does not make it possible to discuss any seasonality within one year and even more so any long-term cyclicity. Still, we were able to establish incidence and mortality levels higher than the annual average in October – December 2020–2021, as well as in July – September 2021 and January – March 2022 due to more virulent (*Delta*) and contagious (*Omicron*) strains circulating at that moment (Figure 3).

We assessed monthly dynamics of the COVID-19 incidence in the RF regions in 2021; as a result, levels of this incidence higher than the national annual average (considering two standard errors $M + 2m$) were identified in all the months except from March and April (Figure 4a); in 2022, except from the periods April – July and October – December (Figure 4b). The greatest number of the RF regions where the COVID-19 incidence was higher than the national annual average (considering two standard errors $M + 2m$) was established in October (51 regions), November (68), and December (51) 2021 and February (82 regions) 2022.

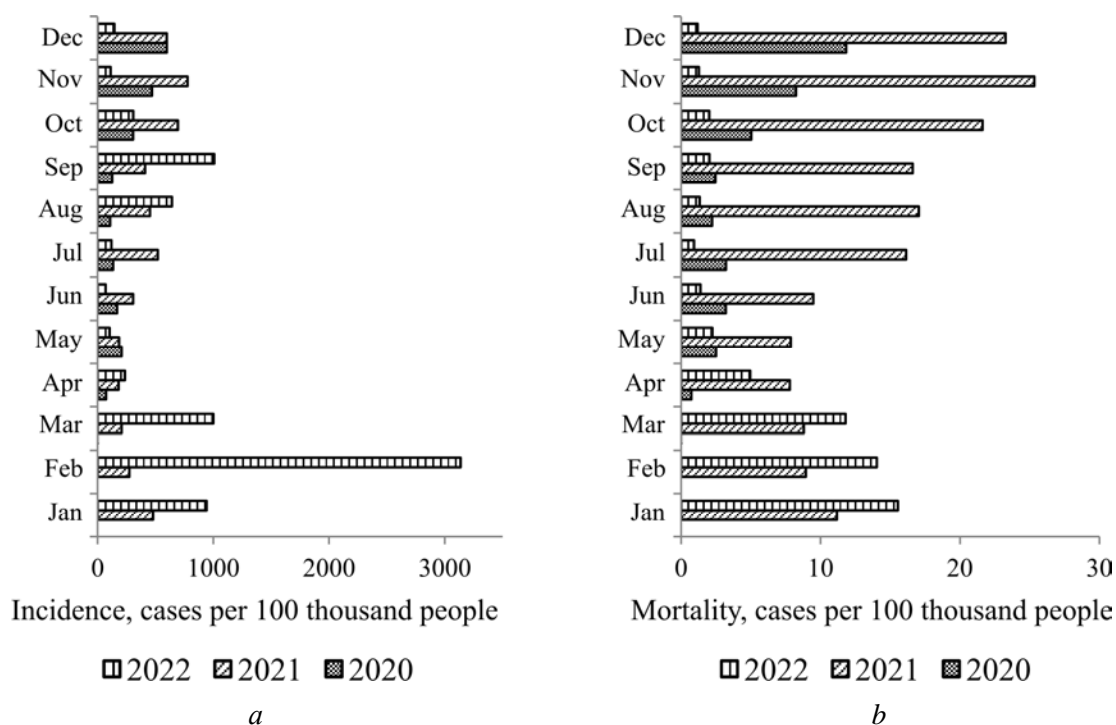


Figure 3. Monthly dynamics of the COVID-19 incidence (a) and mortality (b) in 2020–2022 in the RF, cases per 100 thousand of the total population

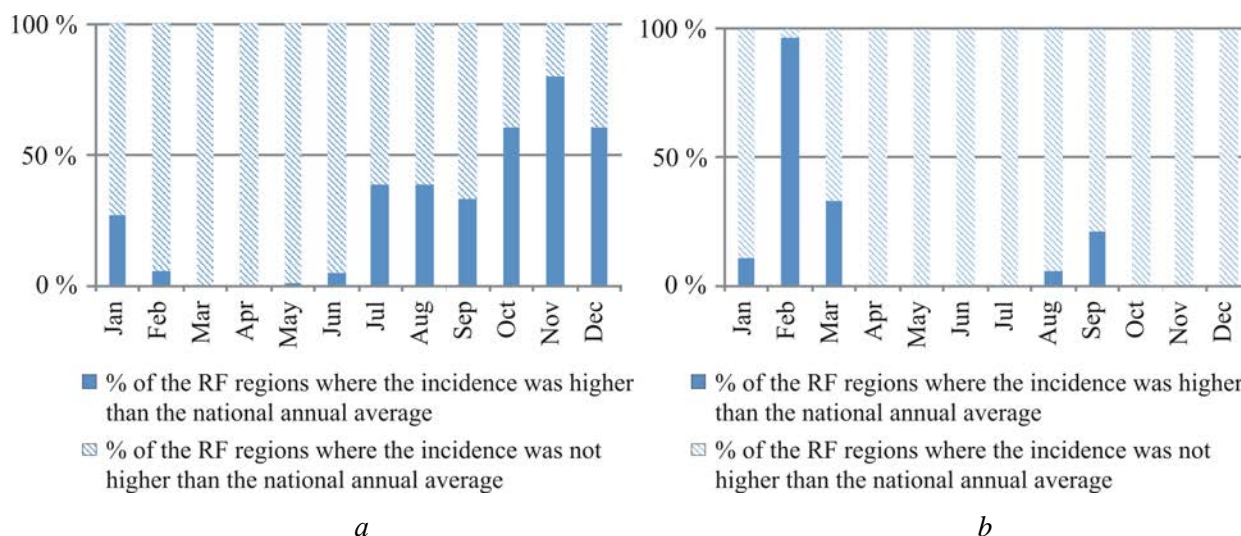


Figure 4. The share of the RF regions with the COVID-19 incidence being higher than the national annual average in 2021 (a) and 2022 (b), %

According to the concept of epidemiological waves accepted in this study and based on the analyzed data, we established five ‘waves’ of the COVID-19 epidemic process that sequentially changed one another over 2020–2023. These waves are characterized by a change in prevalence of the most contagious SARS-CoV-2 strains with relevant rises in the COVID-19 incidence (Figure 5).

The first wave was 73-week long; it started in the first decade of March 2020 and ended in late May 2021. It was accompanied with genetic diversity of the virus, wide prevalence (up to 30 %) of the *Alpha* strain at the end (Figure 5, 6). The second wave was 32-week long, from late May 2021 and till the beginning of January 2022; it was characterized with the dominating *Delta* strain (Figure 5, 6).

This wave had the highest weekly COVID-19 mortality levels (up to 6 ‰) among the total (Figure 6). The third wave lasted 24 weeks, from early January 2022 till early June 2022, and was characterized with two dominant sub-variants of the *Omicron* strain changing each other, *BA.1* and *BA.2* (Figures 5, 6). The *BA.1* sub-variant of the *Omicron* strain induced a ‘drastic’ growth in the COVID-19 incidence and the beginning of a decline in the COVID-19 mortality (Figures 5, 6). The fourth COVID-19 wave lasted from early June 2022 till the beginning of January 2023, 27 weeks overall (Figures 5, 6). During this wave, the prevailing *BA.5* sub-variant of the *Omicron* strain induced another rise in the weekly COVID-19 incidence (up to 240 ‰) together with a slight growth in the COVID-19 mortality (up to 0.5 ‰). The fifth wave started after one of the *Omicron* strain variants, *XBB*, had become prevalent. It has been lasting from middle January 2023 up to now (April 2023) and is characterized with rela-

tively low levels of the COVID-19 incidence and mortality due to the prevailing strain being even less contagious and virulent (Figure 5, 6).

The epidemic process had its peculiarities in different RF regions within the aforementioned waves. We analyzed Rospotrebnadzor’s department statistical reports on the weekly incidence in the RF regions (starting from September 2020). As a result, three different groups of the RF regions were identified; the maximum COVID-19 incidence was reached with a different speed during the **first** wave: regions with slowly growing incidence (18 regions); regions with steadily growing incidence (19 regions); regions with extensively growing incidence (47 regions) (Figure 7). There were some regions in all three groups where the COVID-19 incidence was not higher than the national average (12, 21 and 16 regions accordingly). The maximum incidence was identified on the 52nd week (late December) of 2020, 136.4 cases per 100 thousand people.

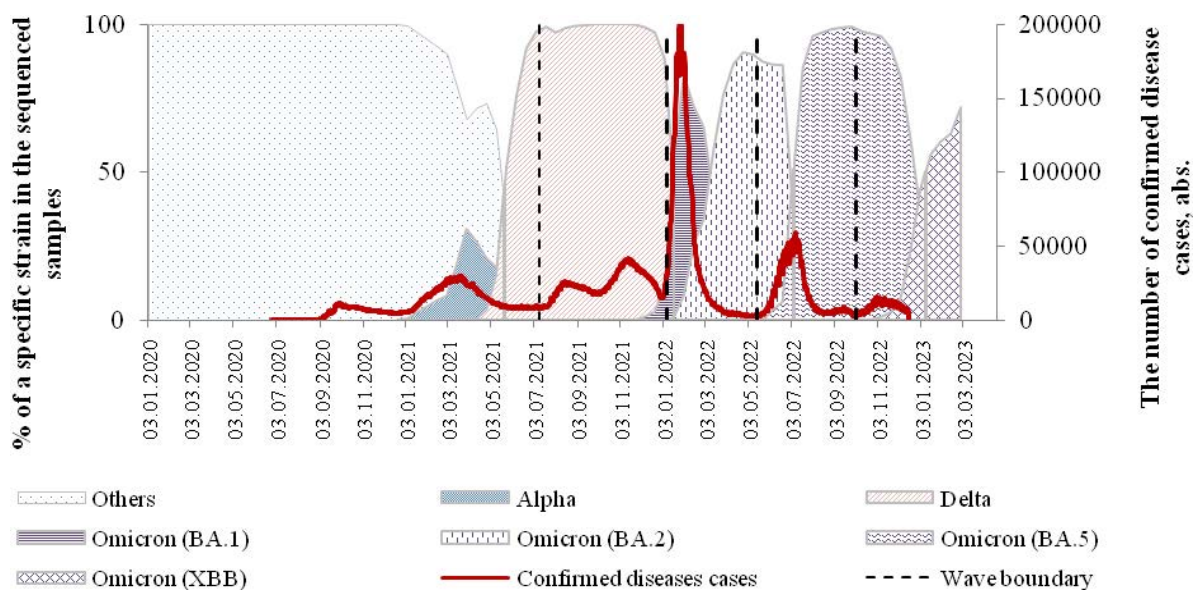


Figure 5. Dynamics of the confirmed COVID-19 cases¹⁰ and the share of dominant SARS-CoV-2 strains among the sequenced¹¹ samples in 2020–2023

¹⁰ Daily new confirmed COVID-19 cases per million people. *Our World In Data: COVID-19 Data Explorer*. Available at: <https://ourworldindata.org/explorers/coronavirus-data-explorer?zoomToSelection=true&time=2020-03-01..latest&facet=none&country=~RUS&pickerSort=asc&pickerMetric=location&Metric=Confirmed+cases&Interval=7-day+rolling+average&Relative+to+Population=true&Color+by+test+positivity=false> (April 20, 2023).

¹¹ SARS-CoV-2 sequences by variant, Russia, Apr 24, 2023. *Our World In Data: COVID-19 Data Explorer*. Available at: <https://ourworldindata.org/explorers/coronavirus-data-explorer?zoomToSelection=true&time=2020-03-01..latest&facet=none&country=~RUS&pickerSort=asc&pickerMetric=location&Metric=Variants&Interval=7-day+rolling+average&Relative+to+Population=true&Color+by+test+positivity=false> (April 20, 2023).

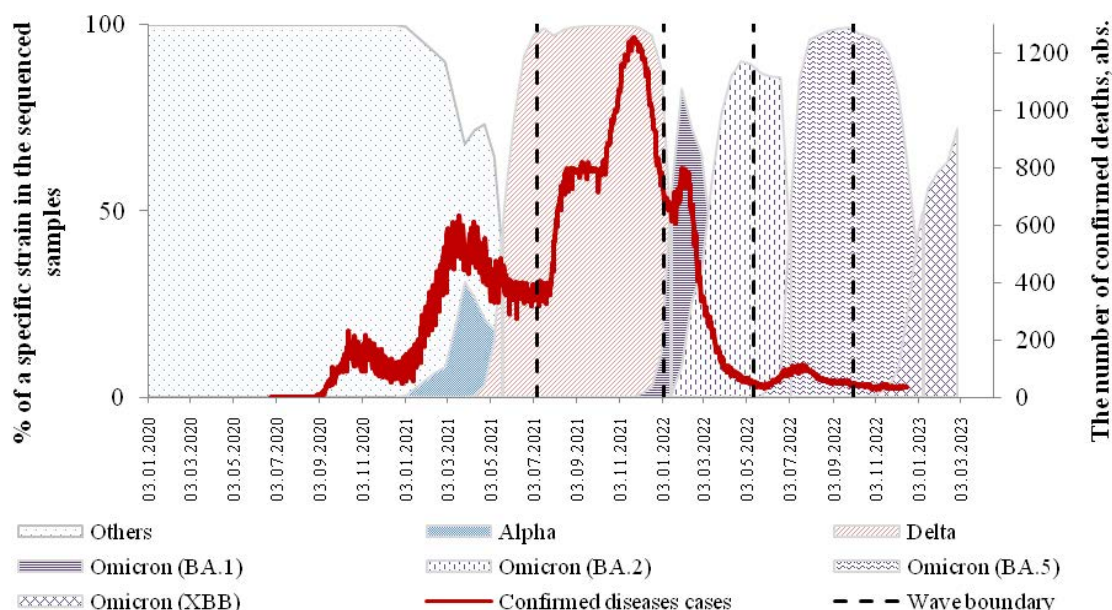


Figure 6. Dynamics of the confirmed COVID-19 deaths and the share of dominant SARS-CoV-2 strains among the sequenced¹¹ samples in 2020–2023

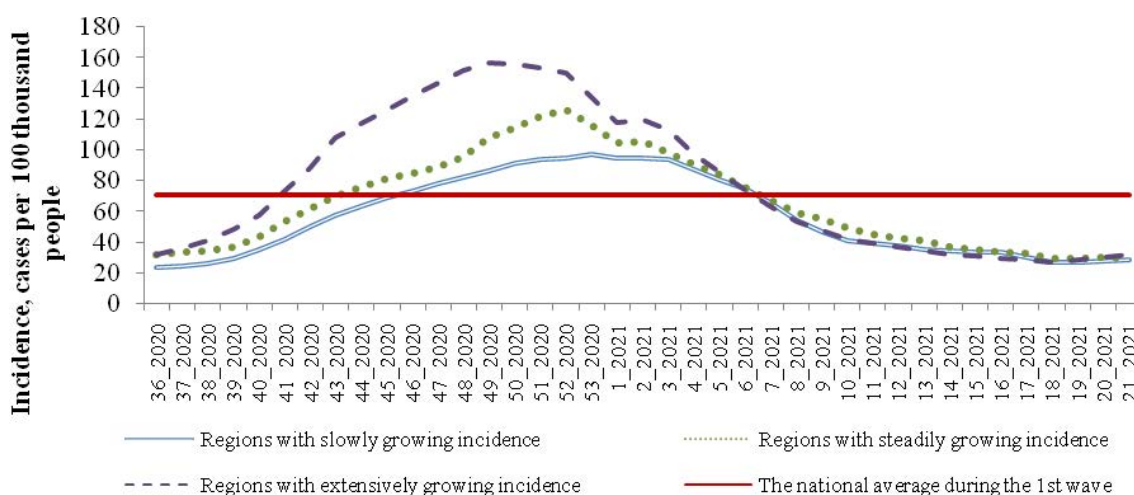


Figure 7. Dynamics of the weekly COVID-19 incidence in three groups of the RF regions during the first wave

The second COVID-19 epidemiological wave had two subsequent rises in incidence caused by the *Delta* strain (Figure 8). Differentiated analysis of the period also made it possible to identify three groups of the RF regions as per the character of the incidence growth during its first rise: regions with a plateau-like curve during the first rise in incidence (52 regions); regions with a fast growth and decline in the incidence with its level not exceeding the second rise (21 regions); regions with rapidly growing and declining incidence with its level

being higher during the first rise than the second one (12 regions). There were some regions in all three groups where the COVID-19 incidence was not higher than the national average during the second wave (32, 9 and 3 regions accordingly). The highest incidence for the *Delta* strain prevalence was identified on the 44th week of 2021 (early November) when it equaled 191.0 cases per 100 thousand people.

The *Omicron* strain prevailed during the **third** wave with the highest incidence and its most rapid growth. We did not identify any ap-

parent asynchronicity among the RF regions as regards reaching the incidence peak during this wave. It had a rather short (6 weeks) period during which the incidence was higher than the national average and the incidence peak was achieved quite rapidly during this wave (6–7 weeks) in most RF regions (68). The third wave was characterized with apparent differences between the RF regions as per the value by which a regional incidence level was higher than the national average (Figure 9). The maximum incidence in the third wave was identified on the 6th week of 2022 (middle February) and was equal to 907.6 cases per 100 thousand people.

The fourth COVID-19 wave occurred due to the BA.5 sub-variant of the *Omicron*

strain; it involved relatively higher incidence than the first two waves but at the same time mortality was relatively low during it (Figures 5, 6). This wave was similar to the first one as per the epidemic process during it since there was similar asynchronicity in the speed at which different RF regions reached the incidence peak (Figure 10). Within the wave, three different groups of the RF regions were identified: regions with slowly growing incidence (5 regions); regions with steadily growing incidence (52 regions); regions with extensively growing incidence (28 regions). During this wave, the incidence peak was reached on the 37th week of 2022 (late September), 253.1 cases per 100 thousand people.

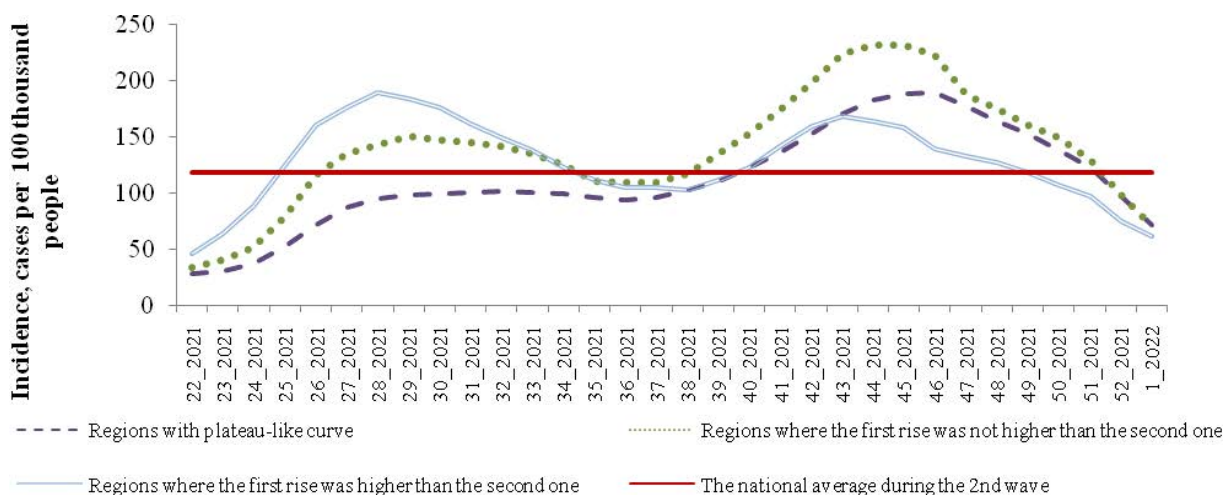


Figure 8. Dynamics of the weekly COVID-19 incidence in three groups of the RF regions during the second wave

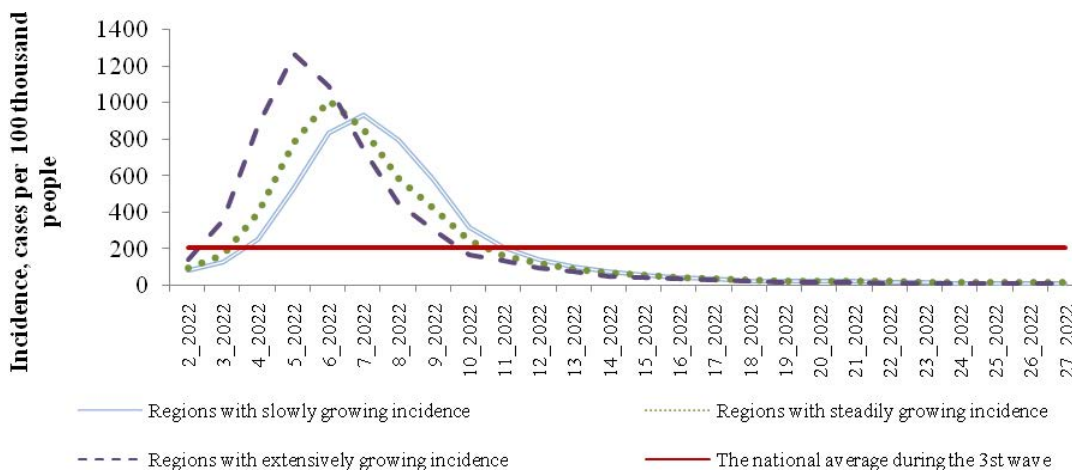


Figure 9. Dynamics of the weekly COVID-19 incidence in three groups of the RF regions during the third wave

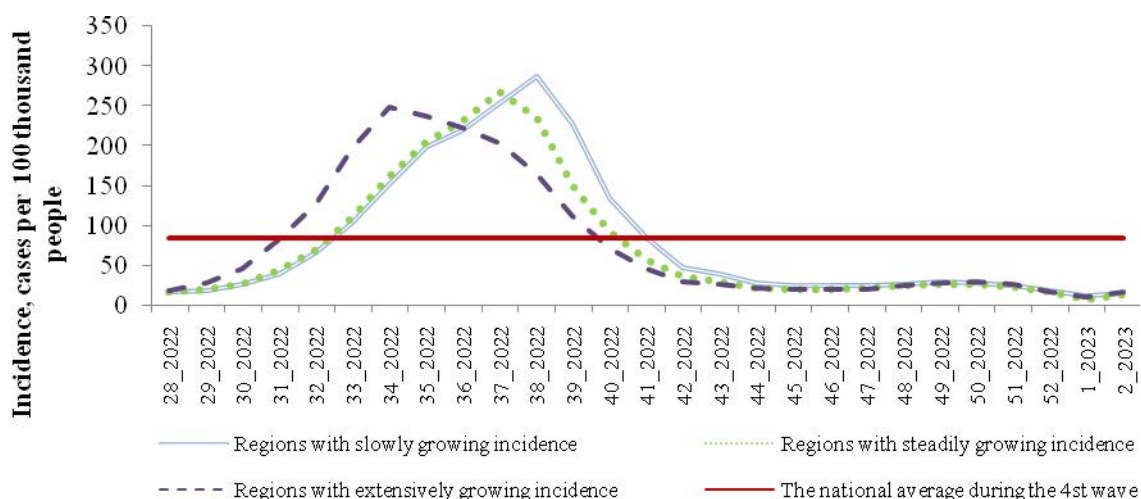


Figure 10. Dynamics of the weekly COVID-19 incidence in three groups of the RF regions during the fourth wave

It was hardly advisable to have full-scale analysis of the **fifth** COVID-19 epidemiological wave at the moment this study was being conducted (April 2023). Although we can see an obviously prevailing strain (*Omicron* sub-variant *XBB*) and an already reached peak in the incidence, the epidemic process is still ongoing.

Therefore, we have established spatial-dynamic heterogeneity of the epidemic process over the whole pandemic period. This indicates that intensity of the process depends not only on unstable biological factors (strains changing each other) and introduced restrictive measures but also on initial socioeconomic conditions and medical-demographic features of the RF regions. Some studies have established that levels of the COVID-19 incidence tend to differ depending on age and sex structure of population and socioeconomic conditions. This also includes differences identified between different epidemiological waves of incidence accompanied with implemented non-medical activities that could be also different in their intensity [18, 19].

Initially, working age population and elderly people prevailed among COVID-19-infected people in the RF regions; however, the COVID-19 incidence among children started to grow gradually over 2021–2022 and in 2022 its share reached 16 % in the total COVID-19 incidence. These changes in the structure of incidence are possibly due to a

change in prevailing *SARS-CoV-2* strains with better ability to ‘escape’ an immune response of the human body [3, 4, 20].

When it comes down to territorial differences, the COVID-19 incidence was 1.5–1.8 times (2021–2022) higher among urban residents than among rural population over the whole epidemiological process observed up to the present moment. Some studies report that such factors as high population density, frequent social contacts, and available tourist attractions are more typical for urban areas and they can make the COVID-19 epidemic process more intense regardless of any introduced restrictions [21–24].

The COVID-19 incidence and mortality had the greatest influence on public health indicators (the total incidence and mortality) at the end of 2021 and the beginning of 2022 despite all the introduced restrictive measures and high vaccination scales. The prevailing *Delta* and *Omicron* strains had high infectivity and virulence [20] and easily promoted wide spread of the infection all over the country. In addition, the highest share of COVID-19-induced pneumonia among all the infected people (18.3 %) was also identified in 2021 and this confirms high virulence of the *Delta* strain [25]. Still, the number of cases of carrying the COVID-19 infectious agent was approximately the same both in 2021 and 2022, about 7.0 %.

We have not been able to establish any apparent regularities of the incidence within one year due to the epidemic process being relatively short, anti-epidemic activities being distributed unevenly and different in different regions, and frequent changes between dominant strains. At the same time, the research results allow tracing some trends of elevated incidence levels in autumn and winter. Thus, the greatest number with the RF regions where the COVID-19 incidence was higher than the national average was established in October (51 region), November (68 regions), and December (51 region) 2021 and February (82 regions) 2022, that is, during a period with autumn-winter weather, which meant lower air temperatures, and a growth in seasonal incidence of other airborne infections [23, 26].

In literature, analysis of COVID-19 epidemiological waves frequently relies on using compartmental models that are run with ordinary differential equations to describe how fast people move between groups participating in an epidemic process (susceptible, infected, and recovered) [5, 27]. In the present study, regional peculiarities of the COVID-19 epidemic process were established with retrospective assessments of incidence growth rates within the established time boundaries of the beginning and end of each epidemiological wave together with analyzing prevalence of this or that particular strain.

Limitations of the study. Among limitations of the present study, we should mention the statistical data used in it as regards results of sequencing and the graphs showing how the prevailing coronavirus strains replaced each other that were built on their basis. The actual

structure of strain prevalence could be distorted either by volumes of conducted sequencing when laboratory diagnostics was focusing on specific strains during certain periods or by sensitivity of test-systems applied in the process. Some uncertainty also occurs due to the concept of a ‘wave’ upon which epidemiologists and healthcare experts have not reached a consensus yet. Given that, the waves that are investigated in this study are rather tentative and this might have influenced the ultimate results of assessing incidence growth rates in the RF regions. To get a better insight into differences in the epidemic process among RF regions, in future it would be necessary to perform additional assessment of influence exerted by various factors on registered incidence and mortality.

Conclusion. This study has made it possible to identify some regional peculiarities of the COVID-19 epidemic process among the RF regions over 2020–2023. We have established that peaks of the COVID-19 incidence were reached at different speed in different RF regions within each epidemic wave; this might be due to heterogeneity of environmental factors that influence the epidemic process. The identified territorial differences in the COVID-19 epidemic process should be considered when developing optimal regulatory impacts including those aimed at predicting probable emergent infections.

Funding. The research was not granted any sponsor support.

Competing interests. The authors declare no competing interests.

References

1. Konings F., Perkins M.D., Kuhn J.H., Pallen M.J., Alm E.J., Archer B.N., Barakat A., Bedford T. [et al.]. SARS-CoV-2 Variants of Interest and Concern naming scheme conducive for global discourse. *Nat. Microbiol.*, 2021, vol. 6, no. 7, pp. 821–823. DOI: 10.1038/s41564-021-00932-w
2. XBB.1.5 Updated Risk Assessment, 24 February 2023. *WHO*. Available at: https://www.who.int/docs/default-source/coronaviruse/22022024xbb.1.5ra.pdf?sfvrsn=7a92619e_3 (April 20, 2023).
3. XBB.1.16 Initial Risk Assessment, 17 April 2023. *WHO*. Available at: https://www.who.int/docs/default-source/coronaviruse/21042023xbb.1.16ra-v2.pdf?sfvrsn=84577350_1 (April 20, 2023).
4. Zhang S.X., Arroyo Marioli F., Gao R., Wang S. A Second Wave? What Do People Mean by COVID Waves? – A Working Definition of Epidemic Waves. *Risk Manag. Healthc. Policy*, 2021, vol. 14, pp. 3775–3782. DOI: 10.2147/RMHP.S326051

5. Xiang Y., Jia Y., Chen L., Guo L., Shu B., Long E. COVID-19 epidemic prediction and the impact of public health interventions: A review of COVID-19 epidemic models. *Infect. Dis. Model.*, 2021, vol. 6, pp. 324–342. DOI: 10.1016/j.idm.2021.01.001
6. Dutta A. COVID-19 waves: variant dynamics and control. *Sci. Rep.*, 2022, vol. 12, pp. 9332. DOI: 10.1038/s41598-022-13371-2
7. Amin R., Sohrabi M.-R., Zali A.-R., Hannani K. Five consecutive epidemiological waves of COVID-19: a population-based cross-sectional study on characteristics, policies, and health outcome. *BMC Infect. Dis.*, 2022, vol. 22, no. 1, pp. 906. DOI: 10.1186/s12879-022-07909-y
8. Popova T.E., Tikhonova O.G., Romanova A.N., Tappakhov A.A., Andreev M.E. Analysis of the epidemiological situation on COVID-19: a second wave. *Yakutskii meditsinskii zhurnal*, 2021, no. 1 (73), pp. 61–64. DOI: 10.25789/YMJ.2021.73.17 (in Russian).
9. Popova T.E., Tikhonova O.G., Romanova A.N., Tappakhov A.A., Andreev M.E., Konnikova E.E. Analysis of the epidemiological situation on COVID-19: third and fourth waves. *Yakutskii meditsinskii zhurnal*, 2021, no. 4 (76), pp. 72–75. DOI: 10.25789/YMJ.2021.76.17 (in Russian).
10. Karpova L.S., Stolyarov K.A., Popovtseva N.M., Stolyarova T.P., Danilenko D.M. Comparison of the first three waves of the COVID-19 pandemic in Russia in 2020–21. *Epidemiologiya i vaktsinoprofilaktika*, 2022, vol. 21, no. 2, pp. 4–16. DOI: 10.31631/2073-3046-2022-21-2-4-16 (in Russian).
11. Akimkin V.G., Kuzin S.N., Kolosovskaya E.N., Kudryavtceva E.N., Semenenko T.A., Ploskireva A.A., Dubodelov D.V., Tivanova E.V. [et al.]. Assessment of the COVID-19 epidemiological situation in St. Petersburg. *Zhurnal mikrobiologii, epidemiologii i immunobiologii*, 2021, vol. 98, no. 5, pp. 497–511. DOI: 10.36233/0372-9311-154 (in Russian).
12. Karpova L.S., Komissarov A.B., Stolyarov K.A., Popovtseva N.M., Stolyarova T.P., Pelikh M.Yu., Lioznov D.A. Features of the COVID-19 Epidemic Process in Each of the of the Five Waves of Morbidity in Russia. *Epidemiologiya i vaktsinoprofilaktika*, 2023, vol. 22, no. 2, pp. 23–36. DOI: 10.31631/2073-3046-2023-22-2-23-36 (in Russian).
13. Makhova V.V., Maletskaya O.V., Kulichenko A.N. Features of the epidemic process and epidemic risks of COVID-19 in the subjects of the Northern Caucasus. *Epidemiologiya i vaktsinoprofilaktika*, 2023, vol. 22, no. 1, pp. 74–81. DOI: 10.31631/2073-3046-2023-22-1-74-81 (in Russian).
14. Komissarov A.B., Fadeev A.V., Sergeeva M.V., Ivanova A.A., Danilenko D.M., Lioznov D., Safina K.R., Bazykin G.A. [et al.]. Genomic epidemiology of the early stages of the SARS-CoV-2 outbreak in Russia. *Nat. Commun.*, 2021, vol. 12, no. 1, pp. 649. DOI: 10.1038/s41467-020-20880-z
15. Gradoboeva E.A., Tyulko Zh.S., Fadeev A.V., Vasilenko A.G., Yakimenko V.V. Comparative analysis of the diversity of SARS-CoV-2 lines circulating in Omsk region in 2020–2022. *Epidemiologiya i vaktsinoprofilaktika*, 2022, vol. 21, no. 6, pp. 24–33. DOI: 10.31631/2073-3046-2022-6-24-33 (in Russian).
16. Alves A., Marques da Costa N., Morgado P., Marques da Costa E. Uncovering COVID-19 infection determinants in Portugal: towards an evidence-based spatial susceptibility index to support epidemiological containment policies. *Int. J. Health Geogr.*, 2023, vol. 22, pp. 8. DOI: 10.1186/s12942-023-00329-4
17. Zaitseva N.V., Popova A.Yu., Kleyn S.V., Letyushev A.N., Kiryanov D.A., Glukhikh M.V., Chigvintsev V.M. Modifying impact of environmental factors on the course of an epidemic process. *Gigiena i sanitariya*, 2022, vol. 101, no. 11, pp. 1274–1282. DOI: 10.47470/0016-9900-2022-101-11-1274-1282 (in Russian).
18. Mari-Dell'olmo M., Gotsens M., Pasarín M.I., Rodríguez-Sanz M., Artazcoz L., Garcia de Olalla P., Rius C., Borrell C. Socioeconomic inequalities in COVID-19 in a European urban area: Two waves, two patterns. *Int. J. Environ. Res. Public Health*, 2021, vol. 18, no. 3, pp. 1256. DOI: 10.3390/ijerph18031256
19. Khalatbari-Soltani S., Cumming R.C., Delpierre C., Kelly-Irving M. Importance of collecting data on socioeconomic determinants from the early stage of the COVID-19 outbreak onwards. *J. Epidemiol. Community Health*, 2020, vol. 74, no. 8, pp. 620–623. DOI: 10.1136/jech-2020-214297
20. Kumar S., Karuppanan K., Subramaniam G. Omicron (BA.1) and sub-variants (BA.1.1, BA.2, and BA.3) of SARS-CoV-2 spike infectivity and pathogenicity: A comparative sequence and structural-based computational assessment. *J. Med. Virol.*, 2022, vol. 94, no. 10, pp. 4780–4791. DOI: 10.1002/jmv.27927
21. Md Iderus N.H., Lakha Singh S.S., Mohd Ghazali S., Ling C.Y., Vei T.C., Md Zamri A.S.S., Jaafar N.A., Ruslan Q. [et al.]. Correlation between Population Density and COVID-19 Cases during the

Third Wave in Malaysia: Effect of the Delta Variant. *Int. J. Environ. Res. Public Health*, 2022, vol. 19, no. 12, pp. 7439. DOI: 10.3390/ijerph19127439

22. Sy K.T.L., White L.F., Nichols B.E. Population density and basic reproductive number of COVID-19 across United States counties. *PLoS One*, 2021, vol. 16, no. 4, pp. e0249271. DOI: 10.1371/journal.pone.0249271

23. Smith T.P., Flaxman S., Gallinat A.S., Kinoshian S.P., Stemkovski M., Unwin H.J.T., Watson O.J., Whittaker C. [et al.]. Temperature and population density influence SARS-CoV-2 transmission in the absence of nonpharmaceutical interventions. *Proc. Natl Acad. Sci. USA*, 2021, vol. 118, no. 25, pp. e2019284118. DOI: 10.1073/pnas.2019284118

24. Hamidi S., Hamidi I. Subway Ridership, Crowding, or Population Density: Determinants of COVID-19 Infection Rates in New York City. *Am. J. Prev. Med.*, 2021, vol. 60, no. 5, pp. 614–620. DOI: 10.1016/j.amepre.2020.11.016

25. Saito A., Irie T., Suzuki R., Maemura T., Nasser H., Uriu K., Kosugi Y., Shirakawa K. [et al.]. Enhanced fusogenicity and pathogenicity of SARS-CoV-2 Delta P681R mutation. *Nature*, 2022, vol. 602, no. 7896, pp. 300–306. DOI: 10.1038/s41586-021-04266-9

26. Liu M., Li Z., Liu M., Zhu Y., Liu Y., Nzoyoum Kuetche M.W., Wang J., Wang X. [et al.]. Association between temperature and COVID-19 transmission in 153 countries. *Environ. Sci. Pollut. Res. Int.*, 2022, vol. 29, no. 11, pp. 16017–16027. DOI: 10.1007/s11356-021-16666-5

27. de Lima Gianfelice P.R., Oyarzabal R., Cunha A. Jr., Vicensi Grzybowski J.M., da Conceição Batista F., Macau E.E.N. The starting dates of COVID-19 multiple waves. *Chaos*, 2022, vol. 32, no. 3, pp. e031101. DOI: 10.1063/5.0079904

Zaitseva N.V., Kleyn S.V., Glukhikh M.V. Spatial-dynamic heterogeneity of the COVID-19 epidemic process in the Russian Federation regions (2020–2023). Health Risk Analysis, 2023, no. 2, pp. 4–16. DOI: 10.21668/health.risk/2023.2.01.eng

Received: 25.04.2023

Approved: 20.06.2023

Accepted for publication: 25.06.2023