Russian Journal of Infection and Immunity = Infektsiya i immunitet
2023, vol. 13, no. 5, pp. 909–922
Инфекция и иммунитет
2023, Т. 13, № 5, с. 909–922

EPIDEMIC STATUS IN RUSSIA'S NORTHWESTERN FEDERAL DISTRICT: TICK-BORNE ENCEPHALITIS AND IXODES TICK-BORNE BORRELIOSIS (LYME DISEASE), 2002–2021

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Abstract. The study's objective was to reveal trends in tick-borne encephalitis (TBE) and Ixodes tick-borne borreliosis (ITBB) epidemic processes in Russia's Northwestern Federal District (NWFD) in 2002–2021. In the NWFD during the analyzed period, more than 1.1 million patients sought medical help following tick bites (14% of all cases registered nationwide). The long-term average tick bite incidence rate in the NWFD exceeded the nation-wide value: 409.5 and 280.7, respectively. In the NWFD, the highest long-term average tick bite incidence rates were recorded in Vologda Oblast, Pskov Oblast, and Novgorod Oblast. The tick bite incidence rate tended to grow in the NWFD, as well as nationally. The growth in tick bite incidence was statistically significant in the Republic of Komi, Kaliningrad Oblast, and Arkhangelsk Oblast. In 2002–2021, more than 6000 TBE cases were registered in the NWFD (11% of all cases registered nationwide), and the TBE long-term average incidence rate in the NWFD exceeded the national value: 2.3 and 2.0, respectively. The Republic of Karelia, Arkhangelsk Oblast, and Vologda Oblast were three NWFD subjects with high TBE epidemical hazard. TBE incidence in the analyzed period tended to decrease, both in the NWFD and nationwide. A statistically significant decrease in TBE incidence was revealed in St. Petersburg, in the Republic of Karelia, in Novgorod Oblast, and in Leningrad Oblast. About 22 000 ITBB cases were reported in the NWFD during the analyzed period (15% of all ITBB cases in Russia). The ITBB long-term average incidence rate in the NWFD exceeded the national value: 7.9 and 4.9, respectively. Vologda Oblast, Kaliningrad Oblast, and Pskov Oblast were three NWFD subjects with high epidemical hazard in terms of ITBB. ITBB incidence during the analyzed period tended to decrease, both in the NWFD and nationwide. The decrease in ITBB incidence was statistically significant in Vologda, Kaliningrad, Novgorod, Leningrad and Pskov Oblasts, as well as in St. Petersburg. In the Republic of Komi, in contrast to other NWFD subjects or national data, there was an uptrend in both TBE and ITBB incidence.

Key words: *incidence, tick-borne encephalitis, ixodes tick-borne borreliosis, Lyme disease, tick bite incidence, prophylaxis, Northwestern Federal District of the Russian Federation.*

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Для цитирования:
Кармоков И.А., Рябико Е.Г., Блинова О.В., Колосовская Е.Н., Токаревич Н.К. Эпидемическая ситуация по клещевому энцефалиту и иксодовым клещевым боррелиозам (болезни Лайма) в Северо-Западном федеральном округе Российской Федерации в 2002–2021 гг. // Инфекция и иммунитет. 2023. Т. 13, № 5. С. 909–922. doi: 10.15789/2220-7619-TES-12118

Citation:
Karmokov I.A., Riabiko E.G., Blinova O.V., Kolosovskaya E.N., Tokarevich N.K. Epidemic status in Russia's Northwestern Federal District: tick-borne encephalitis and ixodes tick-borne borreliosis (Lyme disease), 2002–2021 // Russian Journal of Infection and Immunity = Infektsiya i immunitet, 2023, vol. 13, no. 5, pp. 909–922. doi: 10.15789/2220-7619-TES-12118

DOI: http://dx.doi.org/10.15789/2220-7619-TES-12118

ЭПИДЕМИЧЕСКАЯ СИТУАЦИЯ ПО КЛЕЩЕВОМУ ЭНЦЕФАЛИТУ И ИКСОДОВЫМ КЛЕЩЕВЫМ БОРРЕЛИОЗАМ (БОЛЕЗНИ ЛАЙМА) В СЕВЕРО-ЗАПАДНОМ ФЕДЕРАЛЬНОМ ОКРУГЕ РОССИЙСКОЙ ФЕДЕРАЦИИ В 2002–2021 гг.

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Резюме. Целью данной работы является выявление современных тенденций развития и особенностей течения эпидемического процесса клещевого энцефалита (КЭ) и иксодовых клещевых боррелиозов (ИКБ) на территории Северо-Западного федерального округа Российской Федерации (СЗФО) в период с 2002 по 2021 гг. На территории СЗФО на протяжении анализируемого периода было зарегистрировано более 1,1 млн человек, обратившихся за медицинской помощью по поводу присасывания клещей (14% от всех зарегистрированных случаев обращения на территории РФ). Среднемноголетний показатель обращаемости населения за медицинской помощью по поводу присасывания клещей (далее обращаемости) за данный период на территории СЗФО превышает общероссийский (409,5 и 280,7 соответственно). Наиболее высокие уровни среднемноголетнего показателя обращаемости на территории СЗФО были зафиксированы в Вологодской, Псковской и Новгородской областях. Показатель обращаемости в СЗФО, как и в России в целом, имеет тенденцию к росту. Статистически значимый рост показателя обращаемости выявлен в Республике Коми, Калининградской и Архангельской областях. На территории СЗФО за период с 2002 по 2021 гг. было зарегистрировано более 6 тыс. случаев КЭ (11% всех случаев, зарегистрированных на территории РФ). Среднемноголетний показатель заболеваемости КЭ за анализируемый период на территории СЗФО выше, чем общероссийский (2,3 и 2,0 соответственно). К субъектам СЗФО с высоким уровнем эпидемической опасности по КЭ были отнесены Республика Карелия, Архангельская и Вологодская области. Показатель заболеваемости КЭ на протяжении анализируемого периода имеет тенденцию к снижению как в СЗФО, так и в России в целом. Статистически значимое снижение показателя заболеваемости КЭ выявлено в Санкт-Петербурге, Республике Карелия, Новгородской и Ленинградской областях. На территории СЗФО за анализируемый период было зарегистрировано около 22 тыс. случаев ИКБ (15% всех случаев, зарегистрированных на территории РФ). Среднемноголетний показатель заболеваемости ИКБ за данный период на территории СЗФО выше, чем общероссийский (7,9 и 4,9 соответственно). К субъектам с высоким уровнем эпидемической опасности по ИКБ были отнесены Вологодская, Калининградская и Псковская области. Показатель заболеваемости ИКБ на протяжении анализируемого периода имеет тенденцию к снижению как в СЗФО, так и в России в целом. Статистически значимое снижение показателя заболеваемости ИКБ выявлено в Вологодской, Калининградской, Новгородской, Ленинградской и Псковской областях, а также в Санкт-Петербурге. В Республике Коми, в отличие от других субъектов СЗФО и общероссийских показателей, на протяжении анализируемого периода наблюдалась тенденция к росту заболеваемости КЭ и ИКБ.

Ключевые слова: *показатель заболеваемости, клещевой энцефалит, иксодовые клещевые боррелиозы, болезнь Лайма, показатель обращаемости, профилактика, Северо-Западный федеральный округ Российской Федерации.*

Introduction

Tick-borne encephalitis (TBE) and Ixodes tick-borne borreliosis (ITBB, Lyme disease) are natural focal diseases widespread in the Russian Federation, including the subjects of Russia's Northwestern Federal District (NWFD). The need for research on these infections stems from their high prevalence, degraded quality of life in chronic disease patients, development of persistent complications and disability, lack of specific methods for ITBB prevention, and frequent occurrence of lethal outcomes in the absence of specific treatment for TBE.

TBE is a vital issue in most Russian areas. It is endemic in seven out of eight Federal Districts, including 48 federal subjects ("List of administrative territories of the constituent entities of the Russian Federation endemic for tick-borne viral encephalitis in 2021" attached to the letter No. 02/2510-2022-32 of Rospotrebnadzor dated February 4, 2022 [https://www.rospotrebnadzor.ru/documents/details.php?ELEMENT_ID = 21225]). In addition, TBE foci are currently expanding and increasing in activity in Russia [4], Northern Europe and Eastern Europe [30, 32, 34, 39]. The growth in TBE incidence, and the expansion of TBE foci in Europe, are associated with climate change, increases in both tick and host populations, bird migration, as well as insufficient preventive vaccination in most European countries [30].

Both TBE and ITBB are of great socioeconomic importance. In the Russian Federation in 2011, the annual TBE-associated socioeconomic burden was estimated to be 1.26 billion rubles, while relevant DALYs totaled 4177 [3]. The highest ITBB incidence rates are recorded in Northeastern and Central Europe. ITBB incidence rates in excess of 100 are annually recorded in some districts of Sweden, Norway, Estonia, Lithuania, Poland, Germany, Austria, Slovenia, and Switzerland, while somewhat lower values (20–90) are registered in Finland, Belgium and France [33].

ITBB cases are annually reported in 67 subjects of the Russian Federation [25]. In 2011, the annual ITBB-associated socioeconomic burden in the Russian Federation was estimated to be 782.9 million rubles, while relevant DALYs totaled 16 370 [23]. The significance of TBE and ITBB highlights the need for research over time on both: disease incidence rates; and tick bite incidence rates (TBIR). These can provide a basis for improving appropriate preventive measures. The study's objective was to identify current developmental trends and features of the TBE and ITBB epidemic processes in the NWFD in 2002–2021.

Geographic and demographic data

The NWFD is located in Russia's European North and Northwest regions. The district is 1687.0 thousand square kilometers, representing 9.9% of Russia's total area. It shares land borders with a number of European countries: Norway and Finland to the northwest; as well as Estonia, Latvia and the Republic of Belarus to the west. The district includes Kaliningrad Oblast which borders Lithuania (north and east) and Poland (to the south). The NWFD borders the Ural Federal District in the east as well as Russia's Central and Volga Federal Districts in the south (Fig. 1).

The NWFD consists of eleven subjects: Arkhangelsk Oblast, Vologda Oblast, Kaliningrad Oblast, Leningrad Oblast, Murmansk Oblast, Novgorod Oblast, Pskov Oblast, Nenets Autonomous Okrug, the Republic of Karelia, the Republic of Komi, and the federal city of St. Petersburg (hereafter "St. Petersburg"). St. Petersburg is the center of the NWFD. The climate in the NWFD is mostly temperate (Atlantic-continental), with the exception of the north of Murmansk Oblast and the entire Nenets Autonomous Okrug, where the climate is subarctic (marine). The climate is temperate (marine) in the south of Murmansk Oblast and throughout Kaliningrad Oblast. The total population of the NWFD (as of January 1, 2022) was 13 901 100 [24]. The urban population represents 85%. The population density is 8.2 per km^2.

Materials and methods

We analyzed official data on TBE and ITBB incidence in those eleven subjects, as well as corresponding TBIRs, as published by Federal Service for Supervision of Consumer Rights Protection and Human Welfare (Rospotrebnadzor) branches in Arkhangelsk Oblast [8], Vologda Oblast [9], Kaliningrad Oblast [10], Leningrad Oblast [11], Murmansk Oblast [12], Nenets Autonomous Okrug [13], Novgorod Oblast [14], Pskov Oblast [15], the Republic of Karelia [16], the Republic of Komi [17], and St. Petersburg [19].

To break down NWFD subjects into groups of low, medium or high epidemical hazard, we calculated a 95% confidence interval (CI) for long-term average incidence rate (LTAIR). Subjects with LTAIRs less

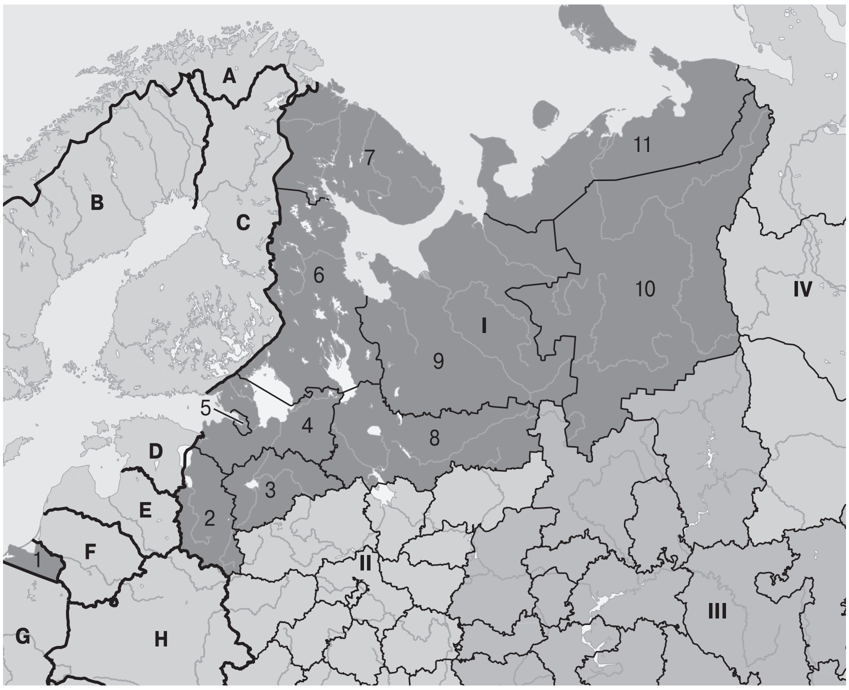

Figure 1. The Northwestern Federal District and adjacent territories
Note. A — Norway, B — Sweden, C — Finland, D — Estonia, E — Latvia, F — Lithuania, G — Poland, H — the Republic of Belarus. Federal Districts (FD): I — Northwestern FD, II — Central FD, III — Volga FD, IV — Ural FD. Regions (oblasts): 1 — Kaliningrad Oblast, 2 — Pskov Oblast, 3 — Novgorod Oblast, 4 — Leningrad Oblast, 5 — St. Petersburg, 6 — the Republic of Karelia, 7 — Murmansk Oblast, 8 — Vologda Oblast, 9 — Arkhangelsk Oblast, 10 — the Republic of Komi, 11 — Nenets Autonomous Okrug.

Table. Trends in the development of the epidemic process (TBE, ITBB) and TBIR, 2002–2021

NWFD subject	Arkhangelsk Oblast	Vologda Oblast	Kaliningrad Oblast	The Republic of Karelia	The Republic of Komi	Leningrad Oblast	Novgorod Oblast	Pskov Oblast	St. Petersburg	NWFD	Russian Federation
LTATBIR in 2002–2021	460.1	1231.9	365.8	589.0	173.5	358.1	584.1	611.0	261.0	409.5	280.7
95% CI	398.0–522.2	1070.2–1393.6	286.7–444.9	532.2–645.8	127.0–220.0	315.3–400.9	505.9–662.3	489.2–732.8	229.9–292.1	366.8–452.2	239.2–322.2
Rincr/Rdecr in 2002–2021, %	5.6	0.4	6.3	–0.4	15.2	–1.2	–0.9	2.2	2.3	1.6	3.2
R^2, %	60.62	1.04	49.91	19.47	75.28	2.13	2.24	2.91	8.64	6.42	58.99
p	< 0.01	0.67	< 0.01	0.05	< 0.01	0.54	0.53	0.47	0.21	0.28	< 0.01
LTAIR of TBE in 2002–2021	5.5	5.5	1.3	6.3	1.3	1.9	1.6	2.1	1.2	2.3	2.0
95% CI	4.4–6.6	4.5–6.5	0.9–1.7	4.8–7.8	0.9–1.7	1.3–2.5	0.8–2.4	1.2–3.0	0.9–1.5	1.9–2.7	1.6–2.4
Rincr/Rdecr in 2002–2021, %	–1.0	–6.0	–9.0	–7.1	11.4	–13.9	–9.4	–1.5	–6.3	–5.7	–8.3
R^2, %	12.22	13.33	12.35	64.09	29.69	32.42	45.86	17.83	44.91	51.84	91.32
p	0.13	0.11	0.13	< 0.01	0.01	0.01	< 0.01	0.06	< 0.01	< 0.01	< 0.01
LTAIR of ITBB in 2002–2021	4.7	24.7	11.6	6.8	0.8	5.8	8.0	10.0	7.4	7.9	4.9
95% CI	3.7–5.7	19.9–29.5	8.8–14.4	5.6–8.0	0.5–1.1	4.0–7.6	6.0–10.0	6.0–14.0	6.1–8.7	6.4–9.4	4.4–5.4
Rincr/Rdecr in 2002–2021, %	–2.9	–6.1	–3.8	–0.9	11.9	–13.9	–9.3	–17.1	–4.1	–5.3	–3.3
R^2, %	16.47	36.63	45.56	11.14	21.75	46.42	40.89	60.13	35.63	50.77	27.03
p	0.08	< 0.01	< 0.01	0.15	0.04	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	0.02

than the lower CI limit were classified as "low epidemical hazard", those with LTAIRs within the CI boundaries were assigned to the group "medium epidemical hazard", and those with LTAIRs exceeding the CI upper limit were assigned to the group "high epidemical hazard".

According to epidemical hazard, NWFD subjects were ranked as follows. For TBE: low epidemical hazard corresponded to LTAIRs < 1.9; medium epidemical hazard corresponded to 1.9 < LTAIRs < 2.7, while high epidemical hazard corresponded to LTAIRs > 2.7. For ITBB: low epidemical hazard corresponded to LTAIRs < 6.4; medium epidemical hazard corresponded to 6.4 < LTAIRs < 9.4; and high epidemical hazard corresponded to LTAIRs > 9.4.

Ranking of NWFD regions according to relevant LTAIR (TBE, ITBB), and according to TBIR, was performed using the Power BI Desktop program. Results were processed by standard methods of variation statistics using the Microsoft Excel 2016 and R-studio application packages. Trends in epidemic process development were analyzed by the method of linear regression with calculation of the coefficient of determination (R^2) and testing the significance of the regression line slope using p-value (significance level $\alpha = 0.05$).

Trends in TBIR and incidence (TBE, ITBB) during the analyzed period were interpreted as: "pronounced" with an average annual rate of growth (Rincr)/average annual rate of decrease (Rdecr) ≥ 5%; «moderate» at Rincr/Rdecr = 4.9–1.1%; or "insignificant" at Rincr/Rdecr ≤ 1%.

Results

In 2002–2021 according to official statistics, the number of medical care encounters in Russia as a consequence of tick bites exceeded 8 million [18], of which more than 1.1 million occurred in the NWFD (14% of all registered cases) [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 29]. For 2002–2021, the long-term average tick bite incidence rate (LTATBIR) in Russia was 280.7 (95% CI: 239.2–322.2) [18], with a moderate uptrend in TBIR values (Table, Fig. 2). Rincr for TBIR was 3.2%.

In the entire NWFD during the analyzed period, the LTATBIR was 409.5 (366.8–452.2) [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 29]. Statistically significant variations in TBIR were not seen (Table, Fig. 3).

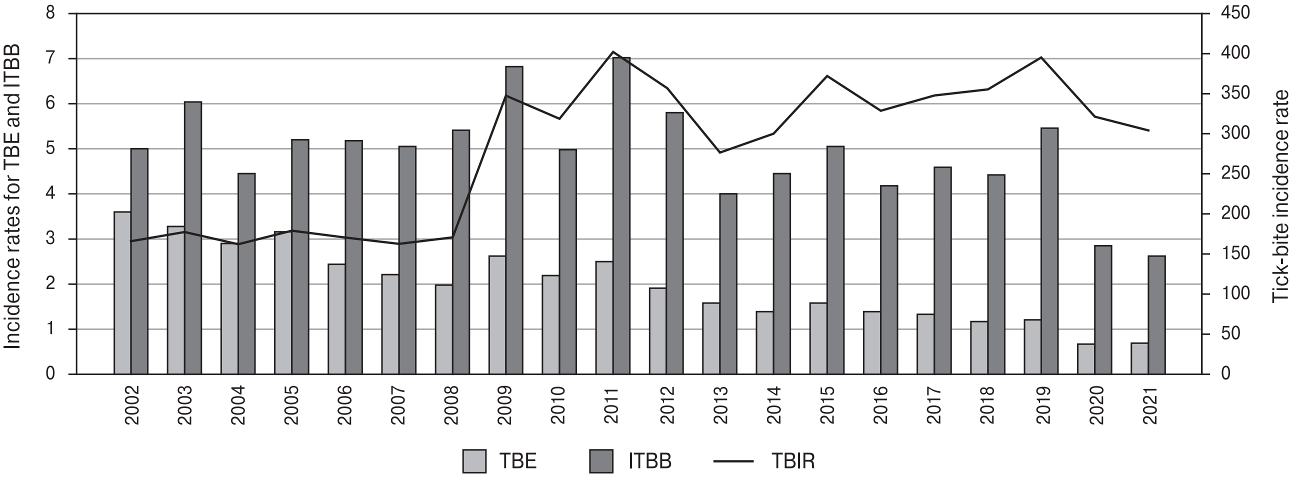

Figure 2. Incidence dynamics (TBIR, TBE, ITBB) in Russia, 2002–2021

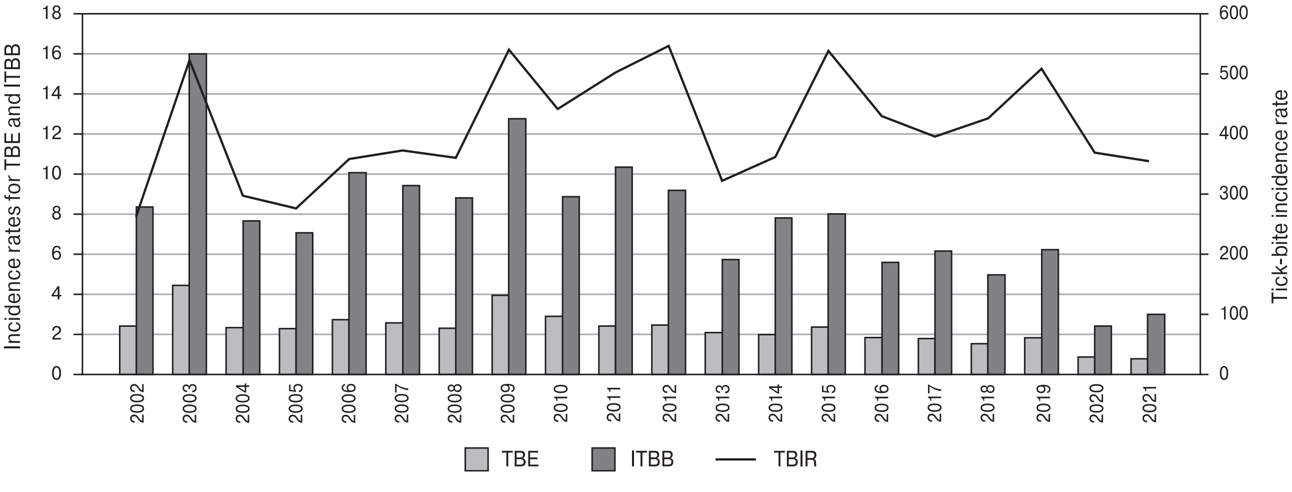

Figure 3. Incidence dynamics (TBIR, TBE, ITBB) in the Northwestern Federal District, 2002–2021

The highest TBIRs were reported in Vologda Oblast, Pskov Oblast, Novgorod Oblast, and in the Republic of Karelia (Table, Fig. 4) [9, 14, 15, 16]. A pronounced uptrend in TBIR was revealed in the Republic of Komi, Kaliningrad Oblast, and Arkhangelsk Oblast. For the other NWFD subjects, no statistically significant TBIR variation was noted during the study period.

Numerous medical care encounters caused by tick bites had taken place in all NWFD subjects. The shares of each subject in tick bite incidence (NWFD) were as follows: Vologda Oblast 26%, St. Petersburg 23%, Leningrad Oblast 11%, Arkhangelsk Oblast 10%, the Republic of Karelia 7%, Novgorod Oblast 7%, Pskov Oblast 7%, Kaliningrad Oblast 6%, the Republic of Komi 2%, and Murmansk Oblast plus Nenets Autonomous Okrug (together 1%).

In some NWFD subjects, LTATBIRs in children (below 17) exceeded those in adults. For example, in Vologda Oblast, LTATBIR in children (below 17) amounted to 1705.2 (1446.2–1965.2), while in adults it was 1100.5 (960.5–1240.5). In the Republic of Karelia, those figures were 630.4 (548.8–669.9) and 553.9 (506.6–613.1), respectively [9, 16].

In the NWFD, *I. ricinus* and *I. persulcatus* ticks are the major vectors of both TBE virus and *B. burgdorferi sensu lato*. Seasonal factors determine the activity of ticks and therefore play a significant role in the infection of humans with TBE and ITBB. Hence, both diseases show pronounced spring-summer seasonality. As a rule, in the analyzed period, adult ticks began to be found in March-April. The maximal tick abundance was recorded in May [2, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 27, 28, 29].

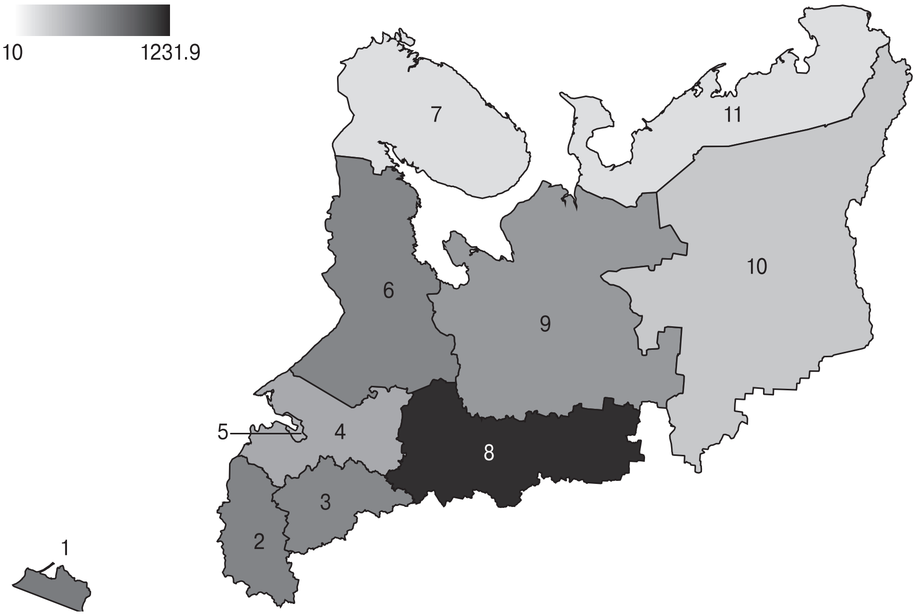

Figure 4. Distribution of NWFD subjects by LTATBIR in 2002–2021

Note. 1 — Kaliningrad Oblast, 2 — Pskov Oblast, 3 — Novgorod Oblast, 4 — Leningrad Oblast, Figure 5 — St. Petersburg, 6 — the Republic of Karelia, 7 — Murmansk Oblast, 8 — Vologda Oblast, 9 — Arkhangelsk Oblast, 10 — the Republic of Komi, 11 — Nenets Autonomous Okrug.

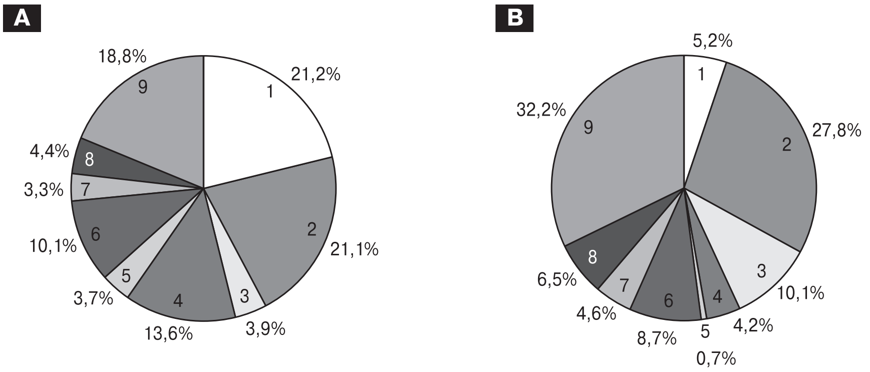

Figure 5. Contribution of each NWFD subject to total TBE (A) and ITBB (B) incidence,%

Note. 1 — Arkhangelsk Oblast, 2 — Vologda Oblast, 3 — Kaliningrad Oblast, 4 — the Republic of Karelia, 5 — the Republic of Komi, 6 — Leningrad Oblast, 7 — Novgorod Oblast, 8 — Pskov Oblast, 9 — St. Petersburg.

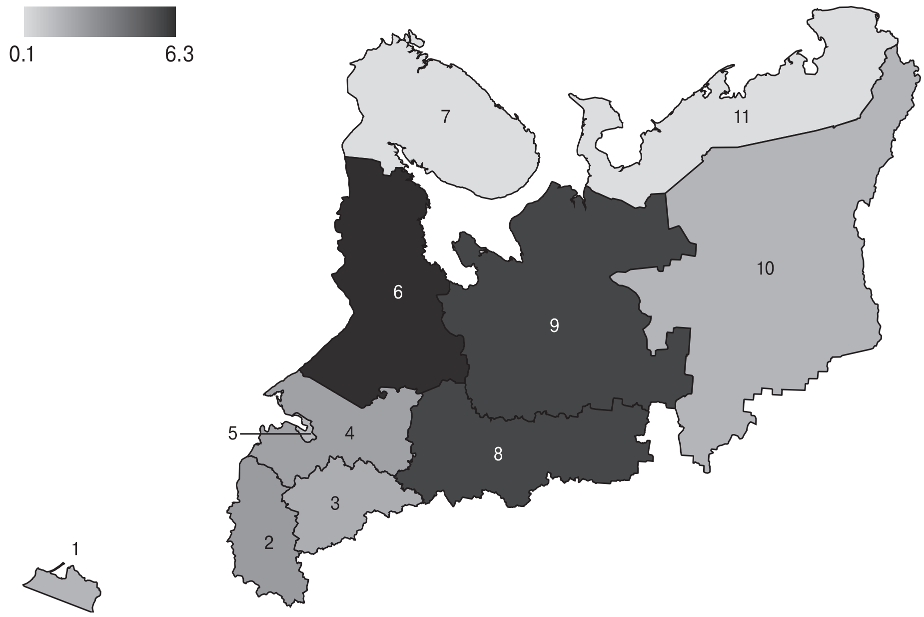

Figure 6. Distribution of NWFD subjects according to TBE LTAIR, 2002–2021
Note. 1 — Kaliningrad Oblast, 2 — Pskov Oblast, 3 — Novgorod Oblast, 4 — Leningrad Oblast, 5 — St. Petersburg, 6 — the Republic of Karelia, 7 — Murmansk Oblast, 8 — Vologda Oblast, 9 — Arkhangelsk Oblast, 10 — the Republic of Komi, 11 — Nenets Autonomous Okrug.

TBE incidence and trends in epidemic process development

More than 57,000 TBE cases were reported in Russia in 2002–2021 [18], with a pronounced downtrend in TBE incidence (Table, Fig. 2). Rdecr was 8.3%. In the NWFD during the same time period, more than 6,000 TBE cases were registered (i.e., 11% of all cases registered in Russia) [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 29]. Only a few imported cases of TBE and ITBB were reported in Murmansk Oblast and Nenets Autonomous Okrug. Therefore, those two subjects were not taken into account in our further calculations. In the NWFD during the analyzed period, there was a pronounced downtrend in TBE incidence (Fig. 3) with Rdecr = 5.7%. TBE incidence in the NWFD varied significantly during the studied period. Its maximal value was 4.5 (in 2003), while the minimum was 0.8 (in 2021) [8, 9, 10, 11, 14, 15, 16, 17, 19, 29].

The largest TBE incidence values were reported in: Arkhangelsk and Vologda Oblasts (more than 1300 cases in each, i.e. 21% of all TBE cases in the NWFD); St. Petersburg (about 1,200 cases, 19%); and the Republic of Karelia (more than 850 cases, 14%) [8, 9, 16, 19]. The contribution of each NWFD subject to total TBE incidence is shown in Fig. 5A.

NWFD subjects with high TBE epidemical hazard were the Republic of Karelia, Arkhangelsk Oblast, and Vologda Oblast. Subjects with a medium level were Pskov Oblast and Leningrad Oblast. Subjects with a low level were Novgorod Oblast, Kaliningrad Oblast, the Republic of Komi, and St. Petersburg (Table, Fig. 6).

A pronounced downtrend in TBE incidence during this period was revealed in St. Petersburg, the Republic of Karelia, Novgorod Oblast, and Leningrad Oblast. In contrast, a pronounced upward trend in TBE incidence was revealed in the Republic of Komi (Rincr = 11.4%, $p = 0.01$). For the other NWFD subjects, there were no significant trends in TBE incidence during the analyzed period.

The LTAIR of TBE in children (below 17) in the studied period was lower than that in adults. In the Republic of Karelia, the share of children among all registered TBE cases was about 9%. The corresponding LTAIR was 2.3 (1.0–3.5), while in adults it was 5.0 (4.0–6.1). In St. Petersburg, the share of children was about 11%. The corresponding LTAIR was 0.9 (0.5–1.2) in children, while in adults it was 1.2 (1.0–1.4) [16, 19].

Febrile and meningeal TBE dominate among all other clinical forms [8, 9, 10, 11, 14, 15, 16, 17, 19, 29]. In Leningrad Oblast, 63% of patients had febrile TBE, while 35% manifested meningeal forms. In St. Petersburg, the shares were 35% and 40%, respectively [11, 19]. Mixed infections (TBE plus ITBB) were also reported. In Leningrad Oblast, the share of mixed forms reached 18% [11]. Despite the strong predominance of the tick-bite route of transmission, alimentary-acquired TBE has also been reported (e.g., a number of cases in St. Petersburg, Leningrad Oblast and Pskov Oblast) [11, 15, 19].

ITBB incidence and trends in epidemic process development

About 142 000 ITBB cases were reported in Russia in 2002–2021 [18], with a moderate downward trend in incidence (Table, Fig. 2). The corresponding Rdecr was 3.3%. In the NWFD during the same time

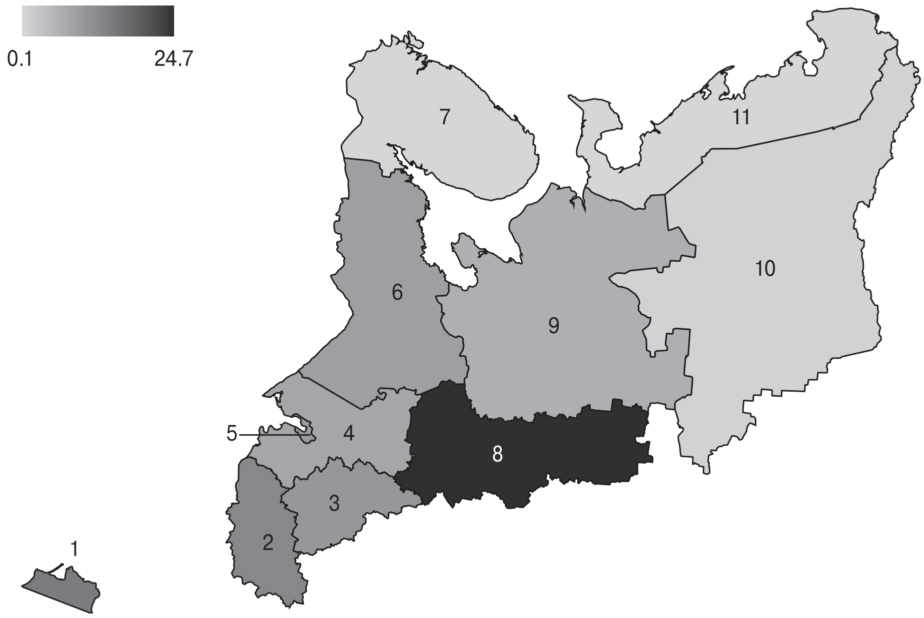

Figure 7. Distribution of NWFD subjects according to ITBB LTAIR, 2002–2021
Note. 1 — Kaliningrad Oblast, 2 — Pskov Oblast, 3 — Novgorod Oblast, 4 — Leningrad Oblast, 5 — St. Petersburg, 6 — the Republic of Karelia, 7 — Murmansk Oblast, 8 — Vologda Oblast, 9 — Arkhangelsk Oblast, 10 — the Republic of Komi, 11 — Nenets Autonomous Okrug.

period, about 22 000 ITBB cases were reported (i.e., 15% of all ITBB cases in Russia) [8, 9, 10, 11, 14, 15, 16, 17, 19, 29]. In the NWFD as a whole during the analyzed period, there was a pronounced downtrend in ITBB incidence (Fig. 3) with Rdecr = 5.3%.

ITBB incidence in the NWFD varied significantly during the studied period. Its maximal value was 16.0 (in 2003), while the minimum was 2.4 (in 2020) [8, 9, 10, 11, 14, 15, 16, 17, 19, 29]. St. Petersburg ranked first in terms of ITBB incidence in the NWFD in 2002–2021: about 7000 cases (i.e., 32% of all ITBB cases reported). Vologda Oblast reported 6000 cases (28%), and Kaliningrad Oblast reported 2200 cases (10%) [9, 10, 19]. The contribution of NWFD subjects to ITBB incidence is shown in Figure 5B.

In terms of the ITBB LTAIR in 2002–2021, the following classifications apply. Three NWFD subjects (Vologda Oblast, Kaliningrad Oblast, Pskov Oblast) fell into the group "high epidemical hazard". Novgorod Oblast, St. Petersburg, and the Republic of Karelia fell into the group "medium epidemical hazard". Leningrad Oblast, Arkhangelsk Oblast, and the Republic of Komi fell into the group "low epidemical hazard" (Table, Fig. 7).

A pronounced downtrend in ITBB incidence over this twenty-year period was revealed in Vologda Oblast, Novgorod Oblast, Leningrad Oblast, and Pskov Oblast. A moderate downtrend was seen in St. Petersburg and Kaliningrad Oblast. In contrast, a pronounced uptrend was revealed in the Republic of Komi (Rincr = 11.9%, p = 0.04). For the remaining NWFD subjects, no statistically significant trends in ITBB incidence were seen.

The urban population prevails in the structure of ITBB patients. Thus, in 2002–2021 among all reported ITBB cases in Vologda Oblast, urban residents accounted for 68%, while the rural population accounted for 32% [9]. However, in terms of LTAIR, the ratio is different. For example, in Vologda Oblast, the ITBB LTAIR was 23.1 (15.2–30.9) in the rural population, while 19.6 (13.4–25.8) in the urban population [9].

The ITBB LTAIR in children (below 17) was less than that in adults. In Kaliningrad Oblast during the studied period, about 7% of all ITBB patients were children under 17. The corresponding LTAIR was 3.6 (2.0–5.2), while for adults it was 11.7 (8.4–14.9). In contrast, in St. Petersburg where children under 17 accounted for about 14% of all ITBB cases, the LTAIR for children was 6.0 (4.9–7.1), i.e. quite close to that of adults, 6.9 (5.6–8.1) [10, 19].

In the structure of ITBB clinical forms, a predominance of erythematous forms over non-erythematous forms was revealed. In St. Petersburg, the share of erythematous ITBB was about 68% [19]. To reveal differences in epidemic process dynamics (TBE, ITBB) in NWFD subjects, the analyzed period was broken down into four equal intervals: I — 2002–2006; II — 2007–2011; III — 2012–2016; and IV — 2017–2021.

During the study period in some NWFD subjects, the rise in incidence was later followed by falling values for both TBE and ITBB. TBE incidence in Arkhangelsk Oblast was on the rise in 2002–2009. It was 8.6 in 2007, achieving 9.9 (maximum) in 2009, followed by a considerable decrease. In 2007–2011, the TBE LTAIR was 1.6-fold higher than in 2002–2006, but in 2012–2016 it decreased by 1.2-fold. ITBB incidence in Arkhangelsk Oblast also increased from 2002 to 2010. The maximum was achieved in 2009–2010 (8.0), and incidence began decreasing considerably after 2011. The ITBB LTAIR in 2007–2011 increased by 1.8-fold as compared to 2002–2006, but decreased by almost 2-fold in 2012–2016. Meanwhile, the TBIR was on rise till the end of the period under study [8].

Something similar was observed in Vologda Oblast and in the Republic of Komi. TBE incidence in Vologda Oblast was increasing after 2002 to reach its maximum (10.9) in 2009, followed by a decline. The TBE LTAIR in 2007–2011 increased by 1.2-fold as compared to 2002–2006, but decreased by 1.5-fold in 2012–2016. In Vologda Oblast, ITBB incidence increased from 28.7 in 2002 to 46.3 in 2003. It then it decreased markedly, but the decline was followed by a second rise from 2005 to 2009 (40.8 in 2009). Starting from 2012, ITBB incidence went into decline once more. The ITBB LTAIR in 2007–2011 increased by 1.2-fold as compared to 2002–2006, but decreased by 1.5-fold in 2012–2016 [9].

In the Republic of Komi during the analyzed period, two series of incidence rate rises and falls were observed for both for TBE and ITBB. For TBE, the first rise in incidence took place in 2002–2010 (3.3 in 2010). The second occurred in 2015–2019 (1.9 in 2019). The TBE LTAIR in 2007–2011 increased by 3.6-fold in comparison with 2002–2006, but decreased somewhat in 2012–2016. Regarding ITBB, the first rise in incidence occurred in 2002–2011 (2.2 in 2011). The second took place in 2015–2019 (1.8 in 2019). The ITBB LTAIR in 2007–2011 increased by 4.4-fold as compared with 2002–2006, but decreased somewhat in 2012–2016. In contrast, TBIR continued to grow until the end of the study period [17].

Discussion

The epidemic situation with TBE and ITBB in the NWFD has its own peculiarities. The LTATBIR during the analyzed period in the NWFD exceeded the national rate by 1.5-fold [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 29]. Although the significance of the TBIR is inevitably limited by incomplete registration of tick bites [2], long-term analysis of its values makes it possible to estimate epidemical hazards related to ticks, albeit indirectly. The pronounced uptrend in TBIR revealed in the Republic of Komi and Arkhangelsk Oblast, together with information on the regional distribution of tick bites [2, 36], proves the northward expansion of ticks in both NWFD subjects. In the view of some researchers, the habitat of ticks in the Republic of Komi, Arkhangelsk Oblast, and the Republic of Karelia has expanded northward by 150–200 km over the past decades [2, 27, 36].

There may be a variety of reasons for the growth of the TBIR registered. On the one hand, raising public awareness of the dangerous consequences of tick bites and improved availability of medical care likely plays a role. On the other hand, there are certain social changes that increase the risk of human exposure to ticks, such as: development of the woodworking industry [1]; land use for summer house construction in tick habitats [20]; climate changes that provide better living conditions for ixodid ticks in northern regions [37]; an increase in the number of ticks in natural habitats [7]; and others.

Of particular concern are LTATBIRs in children (below 17). In Vologda Oblast, they were 1.5-fold higher than in adults [9]. Both in the NWFD and nationwide, the TBIR trend line had the opposite direction compared to trend lines for TBE and ITBB incidence. TBE and ITBB incidence during the analyzed period tended to decrease both in the NWFD and nationally. Regarding TBE, the nationwide downtrend is even more apparent than that in the NWFD. It is probable that reductions in reported incidence rates (TBE, ITBB) in 2020–2021 were due to less attention to both those infections amid the COVID-19 pandemic, including decreased volumes of associated laboratory diagnostics required for detection. The decreases in reported TBE and ITBB incidence are probably associated with significant overloads of the healthcare system during that period, including significant redistribution of inpatient and outpatient medical care in favor of patients with COVID-19 [6, 25].

In the NWFD during the analyzed period, the TBE LTAIR was 1.2-fold higher than nationwide [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 29]. In Vologda Oblast, Arkhangelsk Oblast, and in the Republic of Komi, undulations in TBE and ITBB incidence rates were observed. In other NWFD subjects, those incidence rates decreased rather evenly. During the analyzed period in the Republic of Komi, there was a pronounced uptrend in incidence rates of both TBE and ITBB. This was unlike the nationwide trend and those of other NWFD subjects. A pronounced rise in the TBIR was observed both in the Republic of Komi and in Arkhangelsk Oblast.

The highest LTATBIR was reported in Vologda Oblast. In the Republic of Karelia, it was also rather high, albeit lower. Both are subjects with high TBE epidemical hazard. The Republic of Komi (in the northern part of the NWFD) is a subject with low epidemical hazard. However, the pronounced uptrend in local TBE incidence allows, in our opinion, one to consider this subject as an area that requires special attention in relation to this infection.

In some NWFD subjects, local LTATBIRs in children exceed those in adults, but TBE LTAIRs in children were lower. This may be thanks to closer attention to the health of children. The predominance of mild forms (febrile, meningeal) is typical for TBE clinical courses, both in the NWFD and in some countries of Northern and Eastern Europe [30, 39]. In the Far East, severe focal forms with a higher mortality rate are common [7].

The downtrend in TBE incidence in all NWFD subjects (except for an upward trend in the Republic of Komi) is possibly due to increased TBE vaccination. Long-term average (LTA) share of the population vaccinated against TBE in 2010–2021 amounted to: 0.41±0.08% (Rincr = 5.7%) in Pskov Oblast; 0.68±0.08% (Rincr = 2.5%) in St. Petersburg; 0.74±0.24% (Rincr = 13.1%) in Kaliningrad Oblast; 2.00±0.15% (Rincr = 1.2%) in the Republic of Karelia; 2.15±0.62% (Rincr = 15.2%) in Leningrad Oblast; 2.86±0.45% (Rincr = 5.6%) in Arkhangelsk Oblast; 3.44±0.99% (Rincr = 17.8%) in the Republic of Komi; and 7.92±0.66% (Rincr = 3.4%) in Vologda Oblast [8, 9, 10, 11, 14, 15, 16, 17, 19].

Modern TBE vaccines protect 95–98% of persons bitten by infected ticks [21], and immunoprophylaxis prevents the development of manifest TBE forms in 79% of cases on average [22]. Strictly speaking, however, vaccination does not guarantee protection. In 2019, thirty-two cases of TBE were reported in vaccinated individuals in Russia (2.1%) [7].

Rises in natural immunization may also cause declines in TBE incidence. TBE virus seroprevalence in the unvaccinated population is rather high in some NWFD subjects [28, 36]. However, latent immunization of humans in TBE foci does not guarantee protection insofar as the acquired antibody prevalence decays significantly over a few months. Hence, humoral immunity may not provide resistance to infectious doses of TBE virus [5].

Another possible reason for TBE incidence declines within the studied period in some NWFD subjects was a decrease in TBE virus prevalence in ticks collected from vegetation or removed from victims. For example, the Rdecr of TBE virus prevalence in ticks removed from victims was: 12% (LTA = 2.6±0.9%) in the Republic of Karelia; 16% (LTA = 1.4±0.4%) in Kaliningrad Oblast; and 24% (LTA = 3.4±1.5%) in Pskov Oblast [10, 15, 16]. In the Republic of Karelia, the Rdecr of TBE virus prevalence in ticks collected from vegetation was 29% (LTA = 2.7±1.8%). In Leningrad Oblast, it was 17% (LTA = 1.7±1.5%) [11, 16].

However, TBE virus prevalence in ticks at the site of collection may differ from that of the region as whole. Moreover, according to some sources [5], the most informative indicator of potential epidemical hazard in a natural TBE focus is “the density of heavily infected ticks.” Those authors believe that clinically apparent disease develops only in patients who receive a high dose of the virus.

The pronounced uptrend in TBE and ITBB incidence in the Republic of Komi to a certain extent is possibly accounted for by expansion of ticks into the northern territories, where inhabitants are at increased risk of infection due to low natural immunity against those infections as well as insufficient vaccination against TBE [2].

Similar trends revealed for TBE and ITBB epidemic processes in some NWFD subjects also support the theory of tick northward distribution. This probably contributed to the increase in TBE incidence up until 2010, and ITBB incidence before 2011, in those locations. In the Republic of Komi, the process was probably developing further, as evidenced by the repeated rise in incidence rates (TBE, ITBB) from 2015 to 2019.

The trends in epidemic process development and TBE incidence in the NWFD feature peculiarities in compared with neighboring countries. TBE incidence rates in Lithuania, Latvia, Estonia, and Sweden exceeded those in the NWFD. TBE incidence rates in Finland, Norway, and Poland tended to increase, unlike that of the NWFD [31].

In Russia, TBE incidence rates recorded in the Siberian and Ural Federal Districts exceed that of the NWFD. In all Russian Federal Districts including the NWFD, there was either a downward trend in TBE incidence or no statistically significant changes [6].

During the analyzed period, the downtrend in ITBB incidence in the NWFD was even more pronounced than nationwide. At the same time, the ITBB LTAIR in the NWFD was 1.6-fold higher than that nationwide [8, 9, 10, 11, 14, 15, 16, 17, 18, 19]. The highest ITBB LTAIR was reported in Vologda Oblast. In the Republic of Komi, there was a pronounced uptrend in ITBB incidence that requires special consideration.

Regarding ITBB LTAIR, attention should also be paid to the fact that St. Petersburg is classified with subjects of medium epidemical hazard, while Leningrad Oblast (LO) is a subject with low epidemical hazard. However, about 70% of St. Petersburg inhabitants who sought medical help after tick bites had been bitten by ticks in Leningrad Oblast [19]. In our opinion, this indicates that there is some underdiagnosis of ITBB in LO.

ITBB incidence rates are rather high both in northeastern and central Europe, with noticeable reduction both to the west and south. An upward trend in ITBB incidence has been recorded in many European countries, especially in northern and central Europe [33, 35, 38].

Regarding Russia, the Siberian, Ural and Central Federal Districts have recorded local ITBB incidence rates exceeding that of the NWFD. However, unlike other Federal Districts (and Russia overall), there is a pronounced tendency towards an increase in ITBB incidence in the Central Federal District [26].

In the NWFD and nationwide in 2002–2021, ITBB LTAIRs exceeded those of TBE. However, in Arkhangelsk Oblast and the Republic of Komi, ITBB LTAIRs were less than those of TBE. This may be due to some underdiagnosis of ITBB in those two subjects. In some NWFD subjects, ITBB LTAIRs of the rural population exceed those of the urban population, possibly due to more frequent contacts of the rural population with natural ITBB foci. The predominance of erythematous forms over those non-erythematous in the overall structure of ITBB clinical forms may be due to underdiagnosis of this infection.

The decrease in ITBB incidence, recorded in the context of TBIR growth and an uptrend in B. burgdorferi sensu lato prevalence in ticks, may also be related to: underdiagnosis of ITBB due to an increase in the share of non-erythematous forms in the structure of ITBB clinical forms; and/or decreases in the volume of laboratory diagnostics with associated impacts on reported ITBB incidence. In Kaliningrad Oblast for example, B. burgdorferi sensu lato prevalence in ticks collected from vegetation increased from 5.4% in 2002 to 16.9% in 2021 (LTA = 9.5±1.5%, Rincr = 7%) [10]. In other NWFD subjects, Rincr was lower, but *B. burgdorferi sensu lato* prevalence in ticks was rather high. In St. Petersburg, the average long-term *B. burgdorferi sensu lato* prevalence in ticks was 19±3.5%. Other values were: 20±6.5% in Vologda Oblast; 32±6.4% in the Republic of Karelia; and 34±4.4% in Leningrad Oblast [9, 11, 16, 19].

It can also be assumed that incidence rates of TBE and ITBB are also influenced by yet incompletely studied biocenotic patterns that cause cyclic changes in natural foci loimopotential. Thus, the epidemical situation regarding TBE and ITBB in the NWFD continues to be tense. Its efficient control is only possible under the conditions of increased attention to diagnostic problems, as well as with improvements and increases in the volume of preventive measures. The northward expansion in range of ixodid ticks justifies the need for studies on the prevalence of tick-borne pathogens in those ticks as well as serological surveys of the local population in order to increase the effectiveness of preventive measures.

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Поступила в редакцию 28.05.2023
Принята к печати 03.11.2023

Received 28.05.2023
Accepted 03.11.2023