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Circulation of *Mycobacterium tuberculosis* strains of the Beijing Central Asian Outbreak genotype in the Kemerovo region — Kuzbass in 2018–2022

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Abstract

Introduction. The Kemerovo region — Kuzbass is characterized by a high prevalence of multidrug-resistant (MDR) tuberculosis (TB), including coinfection with HIV (HIV/TB). A previously unknown in Russia relationship between MDR and the Beijing Central Asian Outbreak (CAO) subtype has been discovered, which updates studies of *Mycobacterium tuberculosis* taking into account this resistant variant.

Objective: to study the molecular genetic structure of the *M. tuberculosis* population, to assess the prevalence and possible routes of emergence of Beijing CAO strains in the Kemerovo region — Kuzbass.

Materials and methods. A total of 325 *M. tuberculosis* strains were studied in 2018–2022 using spoligotyping, MIRU-VNTR 24 and SNP typing. Whole genome sequencing and bioinformatics analysis were performed for seven Beijing CAO strains.

Results. Primary MDR and pre-extensive drug resistance (pre-XDR) were detected in 39.4% and 11.5% of strains, respectively. In the total sample, MDR was 43.4%, pre-XDR — 19.7%. In the structure of the *M. tuberculosis* population, the Beijing genotype prevailed (78.8%), with its subtypes Central Asian Russian (40.9%) and B0/W148 (32.6%). The Euro-American lineage (27.3%) was represented by the genotypes T (6.5%), LAM (5.8%), Ural (4.9%), H (0.9%); one strain CAS1-Delhi was detected, the genotype of 2.8% of strains was not identified. The proportion of Beijing CAO was 12.6% of the total sample; this subtype was significantly more often detected among HIV/TB (20.6%) than in HIV-negative TB patients (9.1%; $p = 0.005$). The results of the Beijing CAO genome analysis from the Kemerovo region indicate the absence of a direct chain of transmission between these TB cases. A hypothesis has been put forward about the introduction of Beijing CAO to the Kemerovo region from Central Asia and its endemic circulation in the region.

Conclusion. A high level of MDR and pre-XDR was detected in Beijing genotype strains in the *M. tuberculosis* population of the Kemerovo region — Kuzbass, especially the B0/W148 (97.2%) and CAO (87.5%) subtypes. Beijing CAO strains, detected mainly in newly diagnosed HIV/TB patients, require further monitoring and control of their spreading.

Keywords: *Mycobacterium tuberculosis, Beijing Central Asian Outbreak, Beijing B0/W148, multidrug resistance, Tuberculosis, HIV infection*

Ethics approval. The study was conducted with the informed consent of the patients.The research protocol was approved by the Ethics Committee of the Scientific Centre for Family Health and Human Reproduction Problem (protocol No. 4, April 12, 2023) and Ethics Committee of the Kemerovo State Medical University (protocol No. 255/к, November 11, 2020).

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Оригинальное исследование
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Циркуляция штаммов *Mycobacterium tuberculosis* Beijing Central Asian Outbreak в Кемеровской области — Кузбассе в 2018–2022 годах

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Аннотация

Введение. Кемеровская область — Кузбасс характеризуется распространённостью туберкулёза (ТБ) с множественной лекарственной устойчивостью (МЛУ), в том числе сочетанного с ВИЧ-инфекцией (ВИЧ/ТБ). Обнаружена высокая частота МЛУ среди штаммов Beijing, в том числе субтипа Central Asian Outbreak (CAO), что актуализирует исследования возбудителя с учётом этого резистентного варианта.
Цель исследования: изучить молекулярно-генетическую структуру популяции *Mycobacterium tuberculosis*, оценить распространённость и возможные пути появления штаммов Beijing CAO в Кемеровской области — Кузбассе.
Материалы и методы. Изучено 325 штаммов *M. tuberculosis*, выявленых за 2018–2022 гг., методами сполиготипирования, MIRU-VNTR 24 и SNP-типирования. Для 7 штаммов Beijing CAO проведены полногеномное секвенирование и биоинформатический анализ.
Результаты. Первичная МЛУ и преширокая лекарственная устойчивость (пре-ШЛУ) обнаружены у 39,4 и 11,5% штаммов соответственно. В общей выборке МЛУ составила 43,4%, пре-ШЛУ — 19,7%. В структуре популяции *M. tuberculosis* преобладал генотип Beijing (78,8%), его субтипы Central Asian Russian (40,9%) и B0/W148 (32,6%). Евро-американская линия (27,3%) представлена генотипами T (6,5%), LAM (5,8%), Ural (4,9%), H (0,9%); обнаружен 1 штамм CAS1-Delhi; 2,8% штаммов не идентифицированы. Доля Beijing CAO составляла 12,6% общей выборки, данный субтип значимо чаще обнаруживали среди ВИЧ/ТБ (20,6%), чем у ВИЧ-негативных больных ТБ (9,1%; p = 0,005). Результаты анализа геномов Beijing CAO из Кемеровской области свидетельствуют об отсутствии цепи передачи между этими случаями ТБ. Выдвинута гипотеза о заносе Beijing CAO из Центральной Азии и его эндемичной циркуляции в Кемеровской области.
Заключение. В популяции *M. tuberculosis* выявлен высокий уровень МЛУ и пре-ШЛУ у штаммов Beijing, в особенности субтипов B0/W148 (97,2%) и CAO (87,5%). Штаммы Beijing CAO, выявленные преимущественно у впервые выявленных больных ВИЧ/ТБ, требуют дальнейшего наблюдения и контроля их распространения.

Ключевые слова: *Mycobacterium tuberculosis, Beijing Central Asian Outbreak, Beijing B0/W148, множественная лекарственная устойчивость, туберкулёз, ВИЧ-инфекция*

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Introduction

Kemerovo region – Kuzbass, despite the decrease trends, maintains high levels of tuberculosis (TB) incidence and prevalence. The region is also characterized by high rates of HIV infection. In 2021, TB incidence was 63.07 per 100,000, which is more than 2 times the national level (31.1 per 100,000), prevalence — 138.0 per 100,000 [1]. During the same period, HIV incidence (1274.03 per 100,000) was 1.62 times higher than the national average (782.0)[1]

HIV infection increases not only the risk of active TB, but also gives low treatment efficacy.[2] The widespread of drug-resistant strains of *Mycobacterium tuberculosis* is also among the main causes of high TB incidence.

Therefore, the study of the features of modern strains of M. tuberculosis is of absolute relevant. Previously, a number of molecular genetic studies of *M. tuberculosis* were conducted in the Kemerovo region and the associations of multidrug resistance (MDR) with strains of the Beijing genotype were revealed [2–4]. However, the prevalence of Beijing strains of the Central Asian Outbreak (CAO) subtype frequently characterized by MDR [5] has not been evaluated, although they were present in collections from other West Siberian regions [3,6]. The **aim** of the study: to investigate the molecular genetic structure of *M. tuberculosis*, to assess the prevalence and possible pathways of emergence of Beijing SAO strains in the Kemerovo Region – Kuzbass.

Materials and methods

Clinical isolates and drug sensitivity testing

We examined 325 clinical isolates of *M. tuberculosis* from TB patients from the Kemerovo region – Kuzbass: from 2 screening studies in 2020–2021 (n = 86) and 2022 (n = 163); from the 2018–2019 cryo-collection (n = 76) of the Novosibirsk Research Institute of Tuberculosis, which is a reference center for TB control in Siberia and the Russian Far East (**Fig. 1**).

Bacterial isolates were characterized by standard bacteriological and biochemical methods. Drug susceptibility testing (DST) was performed by the method of proportions on the Loewenstein-Jensen medium (and/or modified proportion method on Middelbrook 7H9 liquid nutrient medium using a Bactec MGIT 960 bacteriological analyzer) [3, 4].

The terminology of drug resistance according to the Clinical Guidelines "Tuberculosis in adults, 2022" was used:

- mono-resistance is resistance of *M. tuberculosis* to only one antiturberculosis drug;
- poly-resistance is resistance of *M. tuberculosis* to 2 or more antiturberculosis drugs, except for simultaneous resistance to isoniazid and rifampicin;
- MDR is resistance of *M. tuberculosis* to isoniazid and rifampicin simultaneously, regardless of resistance to other antiturberculosis drugs;
- pre-extensive drug resistance (pre-XDR) is resistance of *M. tuberculosis* to rifampicin with or without resistance to isoniazid, combined with resistance to any fluoroquinolone.

Genotypic identification

DNA was extracted using previously described methods [3]. Isolates were first differentiated into Beijing and non-Beijing genotypes [3]. Beijing strains were divided into two major groups known to be prevalent in Russia (subtypes B0/W148 and Central Asian Russian) by testing specific SNP markers [3, 4]. Beijing Central Asian Russian strains were genotyped for Central Asian Outbreak (CAO) markers [6] by the authors' previously reported real time PCR test for a specific SNP in the pks *8 gene* (pos.1884305) [7]. All non-Beijing strains were subjected to spoligotyping [3] and MIRU-VNTR 24 loci typing [4].

Whole-genome sequencing, bioinformatics and statistical analysis

Genomic libraries were prepared using the DNA Flex kit (Illumina). Whole-genome sequencing (WGS) of samples was performed on a NextSeq 550 sequencer (Illumina) using the reagent kit v2.5 and a flow cell (High output) of 300 cycles. The 33O, 59Kem, 145O, 155c genomes have been deposited at NCBI (bioproject PRJNA1139960). A total of 229 complete *M. tuberculosis* Lineage 2 CAO genomes [5] were retrieved from the online WGS Short Read Archive (NCBI), being part of the following bioprojects: PRJEB2138, PRJEB21922, PRJEB6273, PRJEB7281, PRJEB9680, PRJNA980215. Primary data processing involved removing short reads of poor quality ($Q < 20$) and cutting out technical sequences using the CutAdapt program [8]. Next, the short reads were mapped to the NC_000962 reference genome with single nucleotide position determination [9]. As a result of data validation and normalization, the concatenated sequence of nucleotide sequences of the 3568 bp genome data array was used for phylogenetic analysis. Antiturberculosis drug resistance genes, their promoters, and genes with high variability (PP, PE, PPE) were excluded from the sequence. The genome of the Beijing family belonging to the ancient variant (Asian Ancestral 1), which was isolated in Omsk (bioproject PRJNA489691), as well as the closest ancestors of Beijing CAO – Beijing Central Asian genomes (bioproject PRJEB9680) were used as

[1] ВИЧ-инфекция за 2021 г. Бюллетень № 47. URL: http://www.hivrussia.info/wp-content/uploads/2023/05/Byulleten-47-VICH-infektsiya-za-2021-g.pdf (date of access: March 20, 2024).

[2] World Health Organization. Global Tuberculosis Report 2022. URL: https://iris.who.int/bitstream/handle/10665/363752/9789240061729-eng.pdf?sequence=1 (date of access: March 20, 2024).

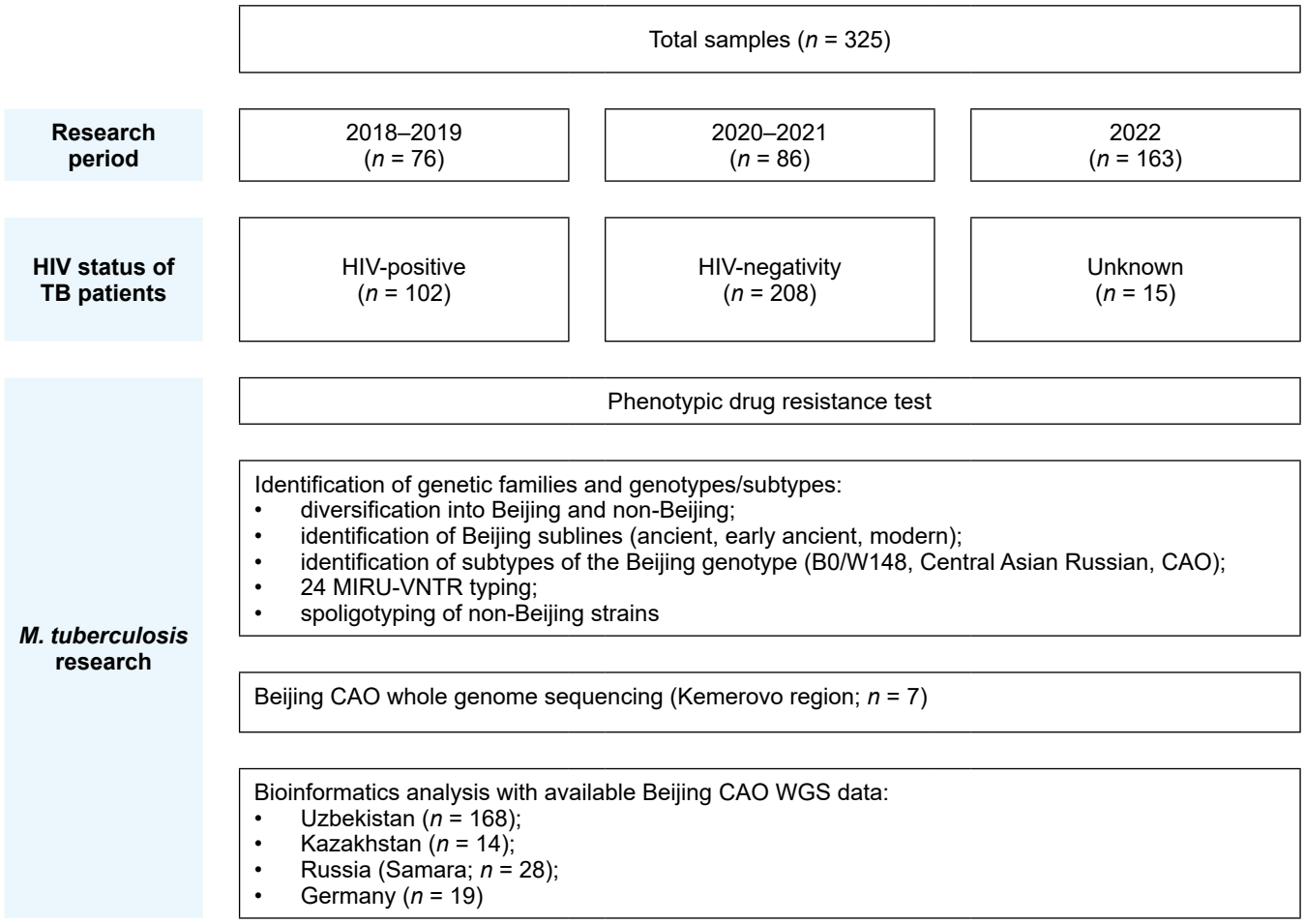

Fig. 1. Study design.

an outgroup. The phylogenetic tree was constructed using the IQ-TREE2 program by the maximum likelihood method; the phylogenetic tree was visualized using the FigTree program [9]. The reliability of the tree topology was evaluated based on bootstrap analysis with 1000 iterations. Transversion Substitution Model was chosen as the nucleotide substitution model because it had the best Akaike values calculated using IQ-TREE Model Finder. Evolutionary rate and tree topology were analyzed using the Total Recovery Time Substitution Model with gamma-distributed substitution rate at each site and 4 rate categories.

Statistical analysis was performed using the web resource http://www.medcalc.org/calc/odds_ratio.php, calculating Fisher's exact criterion values and odds ratios. Differences between groups were identified by the χ^2 test, and significance was confirmed at $p < 0.05$.

Results

General characterization and drug resistance of M. tuberculosis

In a sample of 325 clinical isolates, specimens from patients with infiltrative (30.8%), disseminated (31.1%), and fibrotic cavernous forms of pulmonary TB (20.6%) predominated, followed by tuberculomas (10.5%). Disseminated TB was significantly more common in HIV-infected patients (48.0%; 49/102) than in HIV-negative patients (22.6%; 47/208; $p < 0.0001$), while fibrotic cavernous TB and tuberculomas, on the contrary, had higher rates in HIV-negative patients, thus reflecting the clinical manifestations of TB characteristic of coinfection. A total of 226 69.5% isolates were obtained from patients with new TB cases (**Table 1**). New TB cases accounted for a significantly higher proportion of new TB cases in the HIV-infected group (84.4%; 84/102) than in the HIV-negative group (64.4%; 134/208; $p = 0.002$).

The results of the drug sensitivity test revealed a high prevalence of *M. tuberculosis* clinical isolates with drug resistance (75.7%; 246/325) to antituberculosis drugs (**Table 2**). 63.1% (205/325) of isolates were resistant to the main first-line antibiotics — rifampicin and isoniazid. Among them, 19.7% (64/325) cases were also accompanied by resistance to fluoroquinolones, which defined them as pre-XDR strains; their number was expectedly higher among previously treated TB patients than among new cases (44.6% vs. 11.5%; $p < 0.001$). The proportion of MDR (non-pre-XDR) strains among first-time cases was 39.4% and 43.4%

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Table 1. Demographic and clinical data of TB patients, *n* (%)

Characteristic	Total *n* = 325	New cases *n* = 226	Previously treated *n* = 99	χ^2; *p*
Gender				
female	102 (31,4)	69 (30,5)	33 (33,3)	0,251; *p* = 0,616
male	223 (68,6)	157 (69,5)	66 (66,7)	
Age, years				
19–45	241 (74,2)	159 (70,4)	82 (71,1)	5,589; *p* = 0,018
≥ 46	84 (25,8)	67 (29,6)	17 (28,9)	
HIV status*				
HIV-positive	102 (32,9)	84 (38,5)	18 (19,6)	10,54; *p* = 0,0012
HIV-negative	208 (67,1)	134 (61,5)	74 (80,4)	
TB clinical forms				
infiltrative	100 (30,8)	89(39,4)	11 (11,1)	25,827; *p* = 0,007
disseminated	101 (31,1)	82 (36,3)	19 (19,2)	9,389; *p* = 0,002
fibrous-cavernous	67 (20,6)	20 (8,8)	47 (47,5)	62,759; *p* < 0,001
focal	5 (1,6)	5 (2,2)	0	1,004; *p* = 0,316
tuberculomas	34 (10,5)	19 (8,4)	15 (15,2)	3,343; *p* = 0,068
caseous pneumonia	11 (3,4)	5 (2,7)	6 (5,1)	0,587; *p* = 0,444
intrathoracic	3 (1,0)	3 (1,3)	0	0,272; *p* = 0,602
TB meningitis	1 (0,3)	1 (0,4)	0	0,439; *p* = 0,602
TB pleurisy	1 (0,3)	1 (0,4)	0	0,439; *p* = 0,602

Note. *HIV status of 15 patients was not indicated; absolute data and percentage calculations are given for 310 patients (218 newly diagnosed and 92 previously treated).

in the total sample. MDR+pre-XDR levels were not significantly different between HIV-negative patients (62.0%; 129/208) and HIV/TB patients (57.8%; 59/102; $p = 0.480$).

Five isolates with drug resistance to bedaquiline were identified, 4 of which were characterized by mono- and poly-resistance and 1 by MDR. Drug sensitivity to linezolid was assessed for 163 isolates from a sample of 2022, when this test was included in routine bacteriologic studies in the Kemerovo region; all isolates remained sensitive to linezolid. The proportion of pre-XDR isolates was significantly lower in HIV/TB coinfected patients (12.7%; 13/102) than in HIV-negative patients (24.0%; 50/208; $p = 0.022$), as the latter group had significantly more previously treated TB cases.

Genotypic structure of M. tuberculosis

The Beijing genotype was detected in 256 (78.8%) of 325 *M. tuberculosis* isolates. Two isolates were attributed to the early ancient sublineage (intact NTF and RD 181 [10]), while the other 254 isolates belonged to the modern Beijing sublineage. The proportion of Beijing strains was significantly higher in the previously treated group (90.9%) than in the group of newly diagnosed TB patients (73.5%; $p < 0.001$; **Table 3**), with no significant difference in HIV-negative TB and HIV/TB patients (80.3%; vs. 75.5%; $p = 0.940$). The most abundant Beijing genetic groups were B0/W148 (32.9%) and Central Asian Russian, including the CAO subtype (41.5%; 134/325). The CAO subtype accounted for 12.6% of the total sample (15.6% of Beijing), and did not differ significantly between newly diagnosed (11.9%) and previously treated (13.1%) TB patients. However, among new cases, CAO strains were detected more frequently in the HIV/TB group (21.4%) than in HIV-negative cases (6.7%; $p = 0.005$). Overall, the proportion of Beijing CAO strains was higher in the HIV/TB group (20.6%; 21/102) than in HIV-negatives (9.1%; 19/208; $p = 0.005$).

Isolates of B0/W148 Beijing subtype was detected more frequently among previously treated TB patients than in new cases (45.5% vs. 27.0%, respectively; $p = 0.001$). No statistically significant differences between 'B0/W148 strains were found when the association by HIV status, treatment history of TB patients with other Beijing subtypes were analyzed.

All Beijing CAO strains from the Kemerovo region shared a common MIRU-VNTR 94-32 profile. Information to assess the association between cases was insufficient, but analysis of available data on 27 out of 40 Beijing CAO cases indicates that there was no association between these patients by place of residence. Only 8 cases of TB with Beijing CAO were among residents of different districts of Kemerovo, the rest of the

Table 2. Drug resistance of *M. tuberculosis* isolates, *n* (%)

Genotypes, subtypes	Total *n* = 325	New cases			Previously treated		
		all *n* = 226	TB *n* = 134	HIV/TB *n* = 84	all *n* = 99	TB *n* = 74	HIV/TB *n* = 18
Susceptible	79 (24,3)	74 (32,7)	45 (33,6)	27 (32,1)	5 (5,1)	3 (4,1)	1 (5,6)
Monoresistant	17 (5,2)	16 (7,1)	10 (7,5)	5 (6,0)	1 (1,0)	0	1 (5,6)
Polyresistant	24 (7,4)	21 (9,3)	12 (9,0)	9 (10,7)	3 (3,0)	3 (4,1)	0
MDR not XDR	141 (43,4)	89 (39,4)	50 (37,3)	35 (41,7)	52 (52,5)	35 (47,3)	11 (61,1)
pre-XDR	64 (19,7)	26 (11,5)	17 (12,7)	8 (9,5)	38 (38,4)	33 (44,6)	5 (27,8)

diseases were detected in 10 industrial cities of Kuzbass, distant from the regional center by 27–90 km.

Non-Beijing isolates belonged to Lineage 4 (Euro-American lineage) and Lineage 3 (CAS1-Delhi) spoligotypes. Spoligotyping of 69 non-Beijing isolates identified 31 spoligotypes. Apart from one Lineage 3 isolate, the rest represented 4 Lineage 4 genetic families: LAM, T, Ural and H (60 isolates) and 9 unclassified strains. Isolates belonging to the Euro-American lineage were identified in 23 spoligotypes; of these, 7 were represented by clusters of 2 to 10 isolates: SIT53/T, 10 isolates; SIT42 and SIT254/ LAM, 8 isolates each; SIT35/ Ural, 7 isolates; SIT262/Ural, 6 isolates; SIT1480/ Ural and SIT2128/ T, 2 isolates each.

Drug resistance and genotypes

The proportion of rifampicin- and isoniazid-resistant Beijing genotype strains was 74.6% (191/256), which was significantly higher than among non-Beijing strains, 17.4% (12/69; $p < 0.001$). The frequency of MDR+pre-XDR detection of Beijing genotype strains among previously treated cases (82.8%; 82/99) was more pronounced than among new TB cases (48.2%; 109/226; $p < 0.001$). Because of the small number of strains of other genetic families (non-Beijing), no significant differences in MDR frequency could be detected. Non-Beijing strains unclustered by spoligoprofile possessed MDR in 26.9% (7/26) of cases, while those combined by a single spoligotype possessed MDR in 11.6% (5/43; $p = 0.194$).

The highest MDR+pre-XDR frequencies were found in Beijing isolates of subtypes B0/W148 (97.2%; 103/106) and CAO (87.5%; 35/40). The proportions of MDR+pre-XDR isolates of Central Asian Russian and Beijing (other, including early ancient sublineage) were 46.8% (44/94) and 68.8% (11/16), respectively (**Fig. 2**).

Bioinformatic analysis showed that 7 Beijing CAO isolates whose full genomic data are presented in this study (kem 59, 33O, 155c, 145c, IM117-8c, IM115-6c, IM134-53c), isolated from 5 HIV-infected and 2 TB patients without HIV infection, belonged to 4 different clusters. It is noteworthy that one of them

Table 3. Genotypes and subtypes of *M. tuberculosis* isolates, *n* (%)

Genotypes, subtypes	Total *n* = 325	New cases			Previously treated		
		all *n* = 226	TB *n* = 134	HIV/TB *n* = 84	all *n* = 99	TB *n* = 74	HIV/TB *n* = 18
Beijing total	256 (78,8)	166 (73,5)	99 (73,9)	61 (72,6)	90 (90,9)	68 (91,9)	16 (88,9)
Beijing B0/W148	106 (32,9)	61 (27,0)	38 (28,4)	19 (22,6)	45 (45,5)	35 (47,3)	7 (38,9)
Beijing Central Asian Russian non-CAO	94 (28,9)	68 (30,1)	46 (34,3)	20 (23,8)	26 (26,3)	19 (25,7)	5 (27,8)
Beijing CAO	40 (12,6)	27 (11,9)	9 (6,7)	18 (21,4)	13 (13,1)	10 (13,5)	3 (16,7)
Beijing other	16 (4,9)	10 (4,4)	6 (4,5)	4 (4,8)	6 (6,1)	4 (5,4)	1 (5,6)
Non-Beijing total	69 (21,2)	60 (26,5)	35 (26,1)	23 (27,4)	9 (9,1)	6 (8,1)	2 (11,2)
T	21 (6,5)	19 (8,4)	14 (10,4)	4 (4,8)	2 (2,0)	1 (1,4)	0
LAM	19 (5,8)	15 (6,6)	6 (4,5)	9 (10,7)	4 (4,0)	3 (4,1)	1 (5,6)
Ural	16 (4,9)	15 (6,6)	9 (6,7)	6 (7,1)	1 (1,0)	0	1 (5,6)
H	3 (0,9)	3 (1,3)	0	2 (2,4)	0	0	0
Unknown	9 (2,8)	7 (3,1)	6 (4,5)	1 (1,2)	2 (2,0)	2 (2,7)	0
CAS1-Delhi	1 (0,3)	1 (0,4)	0	1 (1,2)	0	0	0

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was phylogenetically close to strains from Uzbekistan, suggesting the probability of origin of this strain outside the Kemerovo region (**Fig. 3**, highlight 1). Six others were included in 3 separate groups on the most recent highly resolved branches (bootstrap from 87% to 100%) among modern strains from Kazakhstan and Europe (Germany). This arrangement of the Kemerovo samples on the tree confirms the absence of a direct chain of transmission between these TB cases (**Fig. 3**, highlights 2–4).

Discussion

A study of a modern sample of *M. tuberculosis* strains from the Kemerovo region shows that the overall genotype structure is typical for the Asian part of Russia, where the dominant genotype Beijing (78.8%) is represented mainly by two subtypes: Central Asian Russian (41.2%) and B0/W148 (32.9%) [11–14]. However, a marked predominance of Beijing was found among previously treated TB cases (90.9%), and primarily due to a significant increase in the proportion of B0/W148 (from 27.0 to 45.5%). The increase in the proportion of Beijing B0/W148 was seen among both HIV-negative and HIV-infected TB patients. This unidirectional accumulation in both groups reflects the properties of this epidemic subtype, which in most cases carries primary MDR. Overall, its qualities reduce the efficacy of treatment of new TB cases and likely reduce adherence to MDR-TB therapy in repeated courses of treatment.

The Beijing genotype, which occurred equally frequently in TB patients with different HIV status, revealed higher MDR and pre-XDR levels in both groups: no significant association of MDR-TB with HIV infection was found. Thus, the previously found excess MDR-TB frequency among TB/HIV patients in Russian studies [13, 15–17] and their association with MDR strains was not confirmed in the present study.

The main distinctive feature of the *M. tuberculosis* population in Kemerovo region was the detection of about 30% (40/134) of CAO subtype strains in the structure of Beijing Central Asian Russian. According to our study, MDR frequency among Beijing Central Asian Russian strains was second only to Beijing B0/W148 (95.3%): about 60% of strains were MDR+pre-XDR (79 out of 134). This subtype, which unites a heterogeneous group of strains, in the Kemerovo region showed not only an exceptionally high presence of Beijing CAO (12.9% of the total collection) compared to other regions of Russia (**Table 4**), but also extremely high levels of MDR+pre-XDR (87.5%; 35/40). In turn, exclusion of CAO samples from the Central Asian Russian group leads to a decrease in the proportion of strains with MDR to 48.6% (44 out of 94), which corresponds to the average for the Beijing genotype (49.1% MDR; 53/108) without considering B0/W148 in this group. Importantly, Beijing CAO was significantly more frequently detected among HIV-infected people (20.6%). Thus, not only B0/W148 but also strains of the CAO subtype were the most successful among Beijing strains in the Kemerovo region — Kuzbass. The latter clearly benefited from the acquisition of MDR/pre-XDR, expressed in a wide spread among HIV-infected people in the region.

The cross-border route of transmission of TB caused by Beijing CAO from Central Asian countries to the population of the Kemerovo region can be considered as the most obvious one for the emerging of

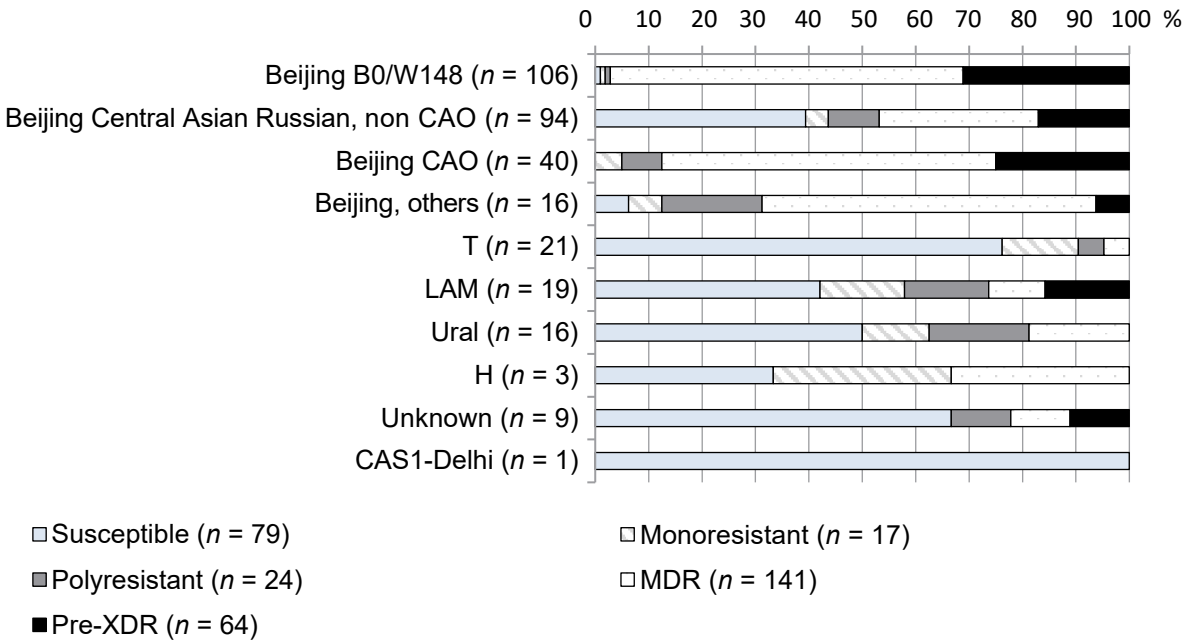

Fig. 2. Drug resistance of *M. tuberculosis* isolates in the Kemerovo region, %.

the first cases. An outbreak of CAO in Karakalpakstan (Uzbekistan) described by M. Merker et al., evaluated on strains from 2001–2005 [5], and then the detection of accumulation since 2015 and the significant presence of Beijing SAO in modern samples in Kazakhstan [21–23] indicate its successful spread outside Uzbekistan and the setting up of conditions for endemic circulation. All Beijing CAOs detected in the Kemerovo collection belonged to the MIRU-VNTR 94-32 supercluster [6], although other MIRU-VNTR profiles of CAOs in Russian regions have also been described [10, 22], emphasizing their current evolution due to the origin from 94-32 [6].

It is highly probable that transmission could have been carried out by labor migrants from Central Asia, whose regular influx to the Kemerovo region has been observed over the past 30 years [23]. Despite the fact that the registered incidence of TB in the Kemerovo region among migrants from Central Asia is estimated to be low (less than 1 case per 100,000 migrants) [24],

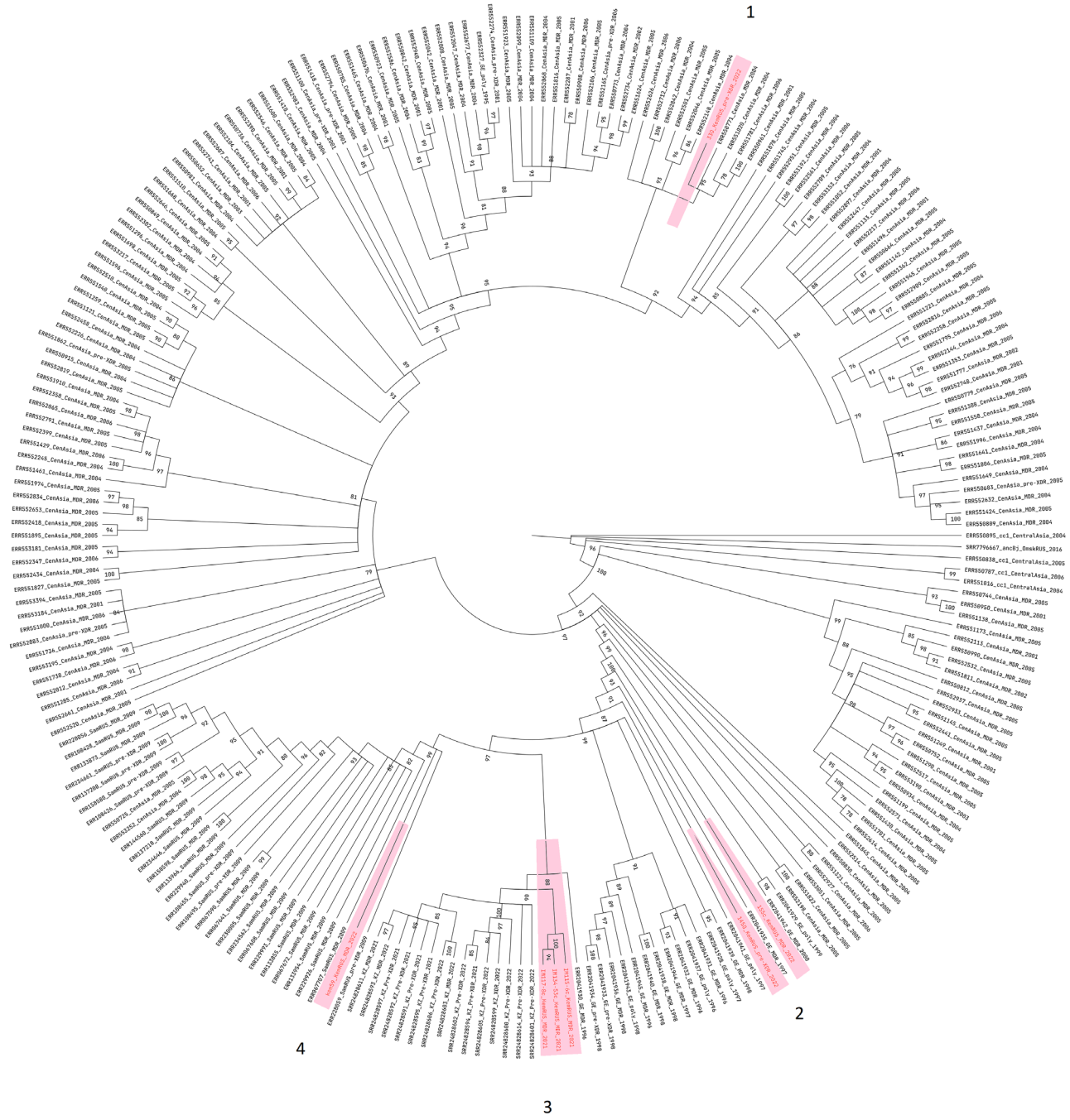

Fig. 3. Maximum-likelihood phylogenetic tree for sequences of 241 clinical isolates of Beijing CAO *M. tuberculosis*.

The genomes from the Kemerovo region are marked; numbers 1–4 mark their groups; sequences from other regions are marked in black with following designations: from Central Asia — Uzbekistan (CenAsia), Kazakhstan (KZ), Samara — Russia (SamRus), Germany (GE).

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Table 4. Beijing CAO of *M. tuberculosis* isolates from Central Asian countries and Russia, *n* (%)

Countries (total number of isolates)	*n*	Number of isolates, % of total			Source
		Beijing total	Beijing Central Asian Russian	Beijing CAO	
Central Asia					
Uzbekistan	235	136 (57,9)	58 (24,7)	–	[18]
Uzbekistan	277	237 (85,5)	174 (62,8)	173 (62,5)	[5]
Tajikistan	206	154 (78,4)	49 (23,8)	–	[18]
Kyrgyzstan	166	121 (72,9)	38 (22,9)	–	[18]
Kazakhstan	701	538 (76,7)	314 (51,7)	116 (16,5)	[19]
Kazakhstan	29	24 (82,8)	20 (69,0)	15 (51,7)	[20]
Russia					
Komi	130	73 (56,2)	45 (34,6)	2 (1,5)	[10]
Vologda	82	51 (62,2)	41 (50,0)	7 (8,5)	[16]
Kaliningrad	73	46 (63,0)	21 (28,8)	4 (5,5)	[10]
Karelia	67	36 (53,7)	18 (26,9)	3 (4,5)	[10]
Murmansk	67	35 (52,2)	23 (34,3)	1 (1,5)	[10]
Pskov	78	45 (57,7)	28 (35,9)	2 (2,6)	[10]
Samara	428	354 (82,7)	214 (50,9)	28 (6,5)	[5]
Omsk	131	93 (71,0)	51 (38,9)	5 (9,8)	[6]

Note. Dash indicated the absence of data.

the possibility of transmission of the *M. tuberculosis* to the local communities. This is consistent with the data from the neighboring Novosibirsk region, where TB cases among migrants were registered among citizens of Uzbekistan, Tajikistan, Kyrgyzstan and Kazakhstan, which prevail in seasonal labor migration in Siberia [25]. In the Kemerovo region, more than 25 thousand people who come to work every year are officially registered. Labor migrants are employed in construction, manufacturing industry, wholesale and retail trade, although they account for no more than 1% of the region's employed population [23].

In the present study, the fact that Beijing CAO strains were detected in 40 TB cases among the local population of the Kemerovo region, in particular, in 20.6% — HIV/TB, suggests the presence of conditions of endemic circulation of Beijing CAO in local setting.

Kuzbass is a highly urbanized industrial region [23] with an epidemic level of HIV infection. Despite the downward trends in the total number of registered HIV-infected persons since 2016, high levels of new cases remain [26]. In 2021, the all-Russian incidence rate was 41.7 per 100,000 population, and in the Kemerovo region — 83.23. The role of HIV-infected people in the setting up of condition for circulation of successful variants of *M. tuberculosis* in local area cannot be excluded. The risks of developing bacillary forms of TB in HIV-infected people against the background of insufficient efficacy of MDR-TB chemotherapy are in favor of some increase in the infectiousness of HIV-infected people [27]. Furthermore, a recent study shows that among coinfected people, the probability of recent TB transmission is more than 2 times higher than in the general population of TB patients. Moreover, endemic strains had a higher chance of being responsible for recent transmission among HIV-positive patients [28]. In the present study sample, Beijing CAO subtype was identified among new cases significantly more frequently in HIV/TB (17/84) than in HIV-negative TB patients, which may also be a consequence of their recent infection.

Phylogenetic reconstruction using WGS data confirms that the spread of CAO strains in the Kemerovo region is most likely the result of the expansion of Beijing isolates of this subtype into Russia from Uzbekistan. Previously, M. Merker et al. reconstructed the evolutionary history of CAO strains obtained in 2001-2006 as a result of an outbreak in Uzbekistan and showed the appearance of the first strains in the mid-1970s [5]. Phylogeography of CAO strains shows that the expansion from Uzbekistan is directed not only to different regions of Russia (Table 4), but also to European countries, as evidenced by the CAO strains from Germany and Kazakhstan presented in the tree (Fig. 3), among which 6 isolates from Kemerovo are clustered. The presence of one Kemerovo isolate in the cluster of CAOs from Uzbekistan indicates the possibility of recent transboundary transmission of this subtype from Central Asia to the Kemerovo region.

[3] ВИЧ-инфекция за 2021 г. Бюллетень № 47. URL: http://www.hivrussia.info/wp-content/uploads/2023/05/Byulleten-47-VICH-infektsiya-za-2021-g.pdf (date of access: March 20, 2024).

Thus, in the Kemerovo region, a significant distribution of strains of not only highly transmissible subtype B0/W148 (31.9%), but also of Beijing CAO subtype (12.6%), which is rarely found in Siberia, was revealed, carrying MDR and pre-XDR in most cases. The hypothesis of Beijing CAO emergence in Kuzbass as a result of repeated introductions from Uzbekistan directly or indirectly through neighboring countries is presented. The phenomenon of Beijing CAO anchoring in Kuzbass as well as the endemic circulation of these strains among HIV-infected people requires further study using WGS.

СПИСОК ИСТОЧНИКОВ | REFERENCES

1. Санников А.Л., Заглубоцкая А.С., Пономаренко М.А. и др. Эпидемиологический анализ проблемы туберкулёза в территориях Сибирского федерального округа. *Международный научно-исследовательский журнал.* 2023;(12). Sannikov A.L., Zaglubotskaya A.S., Ponomarenko M.A. An epidemiological analysis of the tuberculosis problem in the territories of the Siberian Federal District. *International Research Journal.* 2023;(12). DOI: https://doi.org/10.23670/IRJ.2023.138.128 EDN: https://elibrary.ru/ppkvwp
2. Dymova M.A., Kinsht V.N., Cherednichenko A.G., et al. Highest prevalence of the *Mycobacterium tuberculosis* Beijing genotype isolates in patients newly diagnosed with tuberculosis in the Novosibirsk oblast, Russian Federation. *J. Med. Microbiol*. 2011;60(Pt. 7):1003–9. DOI: https://doi.org/10.1099/jmm.0.027995-0
3. Vyazovaya A., Felker I., Schwartz Y., Mokrousov I. Population structure of Mycobacterium tuberculosis from referral clinics in Western Siberia. Russia: before and during the COVID-19 pandemic. *Infect. Genet. Evol.* 2022;103:105343. DOI: https://doi.org/10.1016/j.meegid.2022
4. Лебедева И.Б., Жданова С.Н., Кондратов И.Г. и др. Генетическая структура и лекарственная устойчивость популяции *Mycobacterium tuberculosis* в Кемеровской области – Кузбассе. *Журнал микробиологии, эпидемиологии и иммунобиологии.* 2023;100(6):428–41. Lebedeva I.B., Zhdanova S.N., Kondratov I.G., et al. Genetic structure and drug resistance of *Mycobacterium tuberculosis* strains in the Kemerovo Region – Kuzbass. *Journal of Microbiology, Epidemiology, Immunobiology.* 2023;100(6):428–41. DOI: https://doi.org/10.36233/0372-9311-449 EDN: https://elibrary.ru/uwbzwm
5. Merker M., Barbier M., Cox H., et al. Compensatory evolution drives multidrug-resistant tuberculosis in Central Asia. *Elife*. 2018;7:e38200. DOI: https://doi.org/10.7554/eLife.38200
6. Shitikov E., Vyazovaya A., Malakhova M., et al. Simple assay for detection of the Central Asia outbreak clade of the *Mycobacterium tuberculosis* Beijing genotype. *J. Clin. Microbiol.* 2019;57(7):e00215-19. DOI: https://doi.org/10.1128/JCM.00215-19
7. Хромова П.А., Огарков О.Б., Жданова С.Н. и др. Выявление высокотрансмиссивных генотипов возбудителя в клиническом материале для прогноза неблагоприятного течения туберкулёза. *Клиническая лабораторная диагностика.* 2017;62(10):622–7. Khromova P.A., Ogarkov O.B., Zhdanova S.N., et al. The detection of highly-transmissible genotypes of agent in clinical samples for prognosis of unfavorable course of tuberculosis. *Clinical Laboratory Diagnostics.* 2017;62(10):622–7. DOI: https://doi.org/10.18821/0869-2084-2017-62-10-622-627 EDN: https://elibrary.ru/zoladv
8. Martin M. Cutadapt removes adapter sequences from high-throughput sequencing reads. *EMBnet.journal.* 2011;17(1):10–2. DOI: https://doi.org/10.14806/ej.17.1.200
9. Хромова П.А., Синьков В.В., Савилов Е.Д. и др. Распространение эндемичных субклонов Beijing B0/W148 *M. tuberculosis* на территориях Сибирского и Дальневосточного федеральных округов по результатам полногеномного секвенирования. *Эпидемиология и вакцинопрофилактика.* 2020;19(3):41–5. Khromova P.A., Sinkov V.V., Savilov E.D., et al. Dispersal of Beijing B0/W148 *M. tuberculosis* endemic subclones in territories of the Siberia and Far Eastern Federal District by whole genome study. *Epidemiology and Vaccinal Prevention.* 2020;19(3):41–5. DOI: https://doi.org/10.31631/2073-3046-2020-19-3-41-45
10. Vyazovaya A., Gerasimova A., Mudarisova R., et al. Genetic diversity and primary drug resistance of *Mycobacterium tuberculosis* Beijing genotype strains in Northwestern Russia. *Microorganisms*. 2023;11(2):255. DOI: https://doi.org/10.3390/microorganisms11020255
11. Zhdanova S., Mokrousov I., Orlova E., et al. Transborder molecular analysis of drug-resistant tuberculosis in Mongolia and Eastern Siberia, Russia. *Transbound. Emerg. Dis.* 2022;69(5):e1800–14. DOI: https://doi.org/10.1111/tbed.14515
12. Жданова С.Н., Огарков О.Б., Алексеева Г.И. и др. Генетическое разнообразие изолятов микобактерий туберкулеза из Республики Саха (Якутия), Россия. *Молекулярная генетика, микробиология и вирусология.* 2016;34(2):43–8. Zhdanova S.N., Ogarkov O.B., Sinkov V.V., et al. Genetic diversity of *Mycobacterium tuberculosis* isolates in the Republic of Sakha (Yakutia), Russia. *Molecular Genetics, Microbiology and Virology.* 2016;31(2):51–7. DOI: https://doi.org/10.3103/S0891416816020105 EDN: https://elibrary.ru/xfjfst
13. Умпелева Т.В., Белоусова К.В., Голубева Л.А. и др. Генетический полиморфизм возбудителя туберкулеза на территории города с ограниченной миграцией населения и высоким уровнем заболеваемости ВИЧ-инфекцией. *Туберкулез и болезни легких.* 2019;97(3):40–5. Umpeleva T.V., Belousova K.V., Golubeva L.A., et al. Genetic polymorphism of tuberculosis mycobacteria in the city with limited population migration and high incidence of HIV infection. *Tuberculosis and Lung Diseases.* 2019;97(3):40–5. DOI: https://doi.org/10.21292/2075-1230-2019-97-3-40-45 EDN: https://elibrary.ru/ewwuwz
14. Жданова С.Н., Огарков О.Б., Савилов Е.Д., Кондратов И.Г. Применение молекулярно-генетических инструментов для оценки трансграничной передачи туберкулеза в Иркутской области. *Эпидемиология и вакцинопрофилактика.* 2022;21(2):59–65. Zhdanova S.N., Ogarkov O.B., Savilov E.D., Kondratov I.G. Application of new molecular genetic strategies for transborder transmission analysis of tuberculosis in Irkutsk region. *Epidemiology and Vaccinal Prevention.* 2022;21(2):59–65. DOI: https://doi.org/10.31631/2073-3046-2022-21-2-59-65 EDN: https://elibrary.ru/ymgdfc
15. Микова О.Е., Жданова С.Н., Сергевнин В.И. и др. Высокая распространённость генотипа B0/W148 *Mycobacterium tuberculosis* у больных ВИЧ-инфекцией, сочетанной с туберкулёзом, в Пермском крае и Иркутской области. *Бюллетень Восточно-Сибирского научного центра Сибирского отделения Российской академии медицинских наук.* 2016;1(5):142–5. Mikova O.E., Zhdanova S.N., Sergevnin V.I., et al. High prevalence of genotype B0/W148 of *Mycobacterium tuberculosis* among HIV-TB patients in Perm Krai and Irkutsk region. *Bulletin of the East Siberian Scientific Center SBRAMS.* 2016;1(5):142–5. DOI: https://doi.org/10.12737/23412 EDN: https://elibrary.ru/wxbrvf
16. Вязовая А.А., Лебедева И.А., Ушакова Н.Б. и др. Молекулярно-генетический анализ популяции *Mycobacterium tuberculosis* в Вологодской области — регионе с низкой заболеваемостью туберкулезом. *Инфекция и иммунитет.* 2021;11(3):497–505. Vyazovaya A.A., Lebedeva I.A., Ushakova N.B., et al. Molecular and genetic analysis of *Mycobacterium tuberculosis* population in the Vologda Region with low tuberculosis incidence. *Russian Journal of Infection and Immunity.* 2021;11(3):497–505. DOI: https://doi.org/10.15789/2220-7619-MAG-1545 EDN: https://elibrary.ru/tmhefj
17. Panova A.E., Vinokurov A.S., Shemetova A.A., et al. Molecular characteristics of *Mycobacterium tuberculosis* drug-resistant isolates from HIV- and HIV+ tuberculosis patients in Russia. *BMC Microbiol.* 2022;22(1):138. DOI: https://doi.org/10.1186/s12866-022-02553-7
18. Engström A., Antonenka U., Kadyrov A., et al. Population structure of drug-resistant *Mycobacterium tuberculosis* in

Central Asia. *BMC Infect. Dis.* 2019;19(1):908.
DOI: https://doi.org/10.1186/s12879-019-4480-7.
19. Klotoe B.J., Kacimi S., Costa-Conceicão E., et al. Genomic characterization of MDR/XDR-TB in Kazakhstan by a combination of high-throughput methods predominantly shows the ongoing transmission of L2/Beijing 94-32 central Asian/ Russian clusters. *BMC Infect. Dis.* 2019;19(1):553.
DOI: https://doi.org/10.1186/s12879-019-4201-2
20. Auganova D., Atavliyeva S., Amirgazin A., et al. Genomic characterization of drug-resistant *Mycobacterium tuberculosis* L2/Beijing isolates from Astana, Kazakhstan. *Antibiotics (Basel).* 2023;12(10):1523.
DOI: https://doi.org/10.3390/antibiotics12101523
21. Akhmetova A., Bismilda V., Chingissova L., et al. Prevalence of Beijing Central Asian/Russian cluster 94-32 among multidrug-resistant *M. tuberculosis* in Kazakhstan. *Antibiotics (Basel)*. 2024;13(1):9.
DOI: https://doi.org/10.3390/antibiotics13010009
22. Fursov M.V., Shitikov E.A., Bespyatykh J.A., et al. Genotyping, assessment of virulence and antibacterial resistance of the Rostov strain of *Mycobacterium tuberculosis* attributed to the Central Asia Outbreak clade. *Pathogens*. 2020;9(5):335.
DOI: https://doi.org/10.3390/pathogens9050335
23. Савинов Л.В., Варкентин А.В. Управление миграционными процессами в Кемеровской области. *Развитие территорий.* 2019;(1):33–8. Savinov L.V., Varkentin A.V. Management of migration processes in Kemerovo Region. *Territory Development.* 2019;(1):33–8.
DOI: https://doi.org/10.32324/2412-8945-2019-1-33-38
EDN: https://elibrary.ru/bpnbxl
24. Цыбикова Э.Б., Гадирова М.Э., Мидоренко Д.А. Заболеваемость туберкулезом среди трудовых мигрантов в России. *Туберкулез и болезни легких.* 2021;99(11):35–42. Tsybikova E.B., Gadirova M.E., Midorenko D.A. Tuberculosis incidence among migrant workers in Russia. *Tuberculosis and Lung Diseases.* 2021;99(11):35–42.
DOI: https://doi.org/10.21292/2075-1230-2021-99-11-35-41
EDN: https://elibrary.ru/hahkjb
25. Фелькер И.Г., Волик М.В., Джурабаева Г.К., Гордеева Е.И. Оценка своевременности выявления туберкулеза среди иностранных граждан Новосибирской области. *Туберкулёз и болезни лёгких.* 2022;100(8):18–24. Felker I.G., Volik M.V., Dzhurabaeva G.K., Gordeeva E.I. Assessment of timeliness of tuberculosis detection among foreign citizens in Novosibirsk Oblast. *Tuberculosis and Lung Diseases.*
DOI: https://doi.org/10.21292/2075-1230-2022-100-8-18-24
EDN: https://elibrary.ru/difpas
26. Савина А.А., Лукманов А.С., Землянова Е.В. Тенденции смертности от ВИЧ-инфекции в регионах Российской Федерации. *ВИЧ-инфекция и иммуносупрессии.* 2023;15(2):81–9. Savina A.A., Lukmanov A.S., Zemlyanova E.V. HIV-mortality trends in the regions of Russian Federation. *HIV Infection and Immunosuppressive Disorders.* 2023;15(2):81–9.
DOI: https://doi.org/10.22328/2077-9828-2023-15-2-81-89
EDN: https://elibrary.ru/natkib
27. Melsew Y.A., Doan T.N., Gambhir M., et al. Risk factors for infectiousness of patients with tuberculosis: a systematic review and meta-analysis. *Epidemiol. Infect.* 2018;146(3):345–53.
DOI: https://doi.org/10.1017/S0950268817003041
28. Saavedra Cervera B., López M.G., Chiner-Oms Á., et al. Fine-grain population structure and transmission patterns of *Mycobacterium tuberculosis* in southern Mozambique, a high TB/HIV burden area. *Microb. Genom.* 2022;8(7):mgen000844.
DOI: https://doi.org/10.1099/mgen.0.000844

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