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ALZHEIMER'S DISEASE IN THE REPUBLIC OF SAKHA (YAKUTIA): REALITIES AND EXPECTATIONS

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Introduction. Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized by cognitive decline, primarily loss of memory for recent events. Despite the widespread prevalence of AD in the world, in Russia there is a high level of deficiency in diagnosing the disease. The Republic of Sakha (Yakutia) is a large subject of the Russian Federation; at the beginning of 2023, the population of the Republic was 997,565 people, and over the past 20 years, the share of elderly people (60 years and older) has increased 1.86 times (from 8.3% to 15.5%). The **aim of the research:** to assess the level of diagnosis of Alzheimer's disease and predict the likely number of patients in the Republic of Sakha (Yakutia). **Materials and methods:** to estimate the number of patients with AD, reports from neurologists of the Republic of Sakha (Yakutia) and official data on the disease provided by the Yakut Republican Medical Information and Analytical Center were analyzed (YRMIAC). To predict the number of patients in the city of Yakutsk and the regions of the Republic of Sakha (Yakutia) for each age group of the population, the maximum and minimum proportions of people who could potentially suffer from AD were calculated. Based on various epidemiological studies, three forecast scripts have been identified: "Chinese", "Japanese" and "American". **Results and discussion.** According to official data, 45 patients diagnosed with AD are registered in the Republic of Sakha (Yakutia), of which 36 (80%) people live in Yakutsk. According to reports from neurologists for 2022, only 7 people are registered at the dispensary with a diagnosis of Alzheimer's disease. If we extrapolate world data for the Republic Sakha (Yakutia), then the minimum number of patients with Alzheimer's disease should be 4,166.4 people and observed under the "Chinese" script, and the maximum number of patients – 8,428.5 people – under the "American" script. The largest number of patients is predicted in the industrial districts of the republic (Neryungri, Mirny and Aldan). The smallest number of patients with Alzheimer's disease is predicted in the Arctic and Northern districts, especially in Eveno-Bytantaysky and Anabarsky. **Conclusion.** Alzheimer's disease is one of the leading medical and social problems of the modern world. At this stage in the Republic of Sakha (Yakutia), improved diagnosis of the disease is required for the timely initiation of symptomatic therapy. The predicted number of patients determined by us in the city of Yakutsk and the districts of the Republic can serve as a guideline when screening patients for cognitive impairment.

Keywords: dementia, Alzheimer's disease, cognitive impairment, mind.

Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized by cognitive decline, primarily loss of memory for recent events [9]. AD is not only the leading cause of dementia, but also leads to significant mortality in the population. According to the 2023 Alzheimer's Disease Facts and Figures, the number of deaths from AD increased 145.2% from 2000 to 2019, making the disease the sixth leading cause of death among older adults in USA [8].

AD is based on the earlier extracellular accumulation of beta-amyloid and the later intracellular accumulation of tau protein, with amyloid plaques disrupting interneuronal communication at synapses, and intracellular tau protein blocks the transport of nutrients for the normal functioning of the neuron [3, 11, 21].

According to leading neurologists, in Russia there is an extremely low detection rate of Alzheimer's disease: only 9 thousand patients are officially registered, while the expected number of patients is about 1.2 million people [1, 4, 6]. The disease is detected mainly only at the stage of severe dementia [2].

Age is one of the key risk factors for the disease. In the United States, 5.3% of people aged 65-74 years, 13.8% of people aged 75-84 years, and 34.6% of people over 85 years old have dementia due to Alzheimer's disease [17]. With regard to early-onset Alzheimer's disease, a large meta-analysis estimated that the prevalence of Alzheimer's disease among persons 35-64 years of age was 41.1 per 100,000 population, much higher in Europe than in the United States (54.1 vs. 31.8 for 100,000). In the age groups 35-39 years, 40-44 years, 45-49 years, the prevalence is only 0.1 for 100,000 people, while in the groups 50-54 years, 55-59 years, 60-64 years it increases and equals 1.5; 6.9 and 24.8 for 100,000 people, respectively [14].

Ethnicity is also likely to play a role in the development of Alzheimer's disease. Study of 10,342 participants from the United States showed that 18.6% of African Americans, 14.0% of Hispanic Americans and 10% of Caucasian Americans suffered from Alzheimer's disease [17]. According to another study, the lowest

prevalence of dementia is found in Japanese Americans - 6.3% among people 65 years of age and older [15]. Almost similar data were obtained during a 10-year follow-up of 2034 people in Japan itself: the proportion of patients with AD dementia among people 65 years of age and older was 7.2% [24]. According to a meta-analysis, a high prevalence of AD is observed in China. Thus, among people 65-69 years old it occurs in 12.7%, and among people 95-99 years old – 48.2% [13].

The Republic of Sakha (Yakutia) is the largest subject of the Russian Federation, located in the North-West of the Far East, the area is 3102.2 thousand km². If in 1990 the population of the Republic was 1,111,480 people, then in subsequent years there was a population decline, reaching a minimum number in 2003 - 948,636 people. Since 2004, there has been a slight annual increase in population and at the beginning of 2023 the population of the Republic was 997,565 people, incl. 48.3% are men and 51.7% are women. Yakutia has a unique multinational composition: more than half of the population (55.3%) are Yakuts, 32.6% are Russians, the remaining share (12.1%) is made up of Evenks, Evens, Kyrgyz, Ukrainians and other nationalities. As for the age structure, over the past 20 years the proportion of elderly people (60 years and older) has increased by 1.86 times (from 8.3% to 15.5%) (Fig. 1) [7].

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The **aim of the research** is to assess the level of diagnosis of Alzheimer's disease and predict the likely number of patients in the Republic of Sakha (Yakutia).

Materials and methods. The study was conducted at the Department of Neurology and Psychiatry of the Medical Institute of the North-Eastern Federal University named after M.K. Ammosov and the Laboratory of Neurodegenerative Diseases of the Yakut Scientific Center for Complex Medical Problems. To estimate the number of patients with Alzheimer's disease, reports from neurologists of the Republic of Sakha (Yakutia) for 2022 and official data on the disease provided by the Yakut Republican Medical Information and Analytical Center (YRMIAC) were analyzed. To predict the number of patients in the city of Yakutsk and districts of the Republic of Sakha (Yakutia) for each age group of the population, the maximum and minimum proportions of people who could potentially suffer from Alzheimer's disease were calculated. Age groups of the population were formed from open data of the Territorial Authority of the Federal State Statistics Service for the Republic of Sakha (Yakutia) [7]. Based on various epidemiological studies [13,15,17], three forecast scripts have been identified: "Chinese", "Japanese" and "American".

Results. According to official data from YRMIAC for 2022, 45 patients diagnosed with Alzheimer's disease are registered in the Republic of Sakha (Yakutia), of which 36 (80%) people live in Yakutsk, the rest in the central districts and in the Vilyui group of districts. Of the Arctic regions, only one patient was registered in the Abyisky district.

The results of the analysis of reports from neurologists are radically different from the YRMIAC data. According to reports from neurologists for 2022, only 7 people are registered at the dispensary with a diagnosis of Alzheimer's disease: three patients in Yakutsk, two patients in the Tattinsky district and one patient each in the Verkhnevilyuysky and Nyurbinsky districts.

Table 1 shows the forecast for the number of patients with Alzheimer's disease among people 65 years of age and older in the city of Yakutsk and regions of the Republic of Sakha (Yakutia).

Based on Table 1, the minimum number of patients with Alzheimer's disease in the Republic of Sakha (Yakutia) should be 4,166.4 people. and be observed under the "Chinese" script, and the maximum number of patients is 8,428.5 people. – in the "American" script. The largest number of patients is predicted

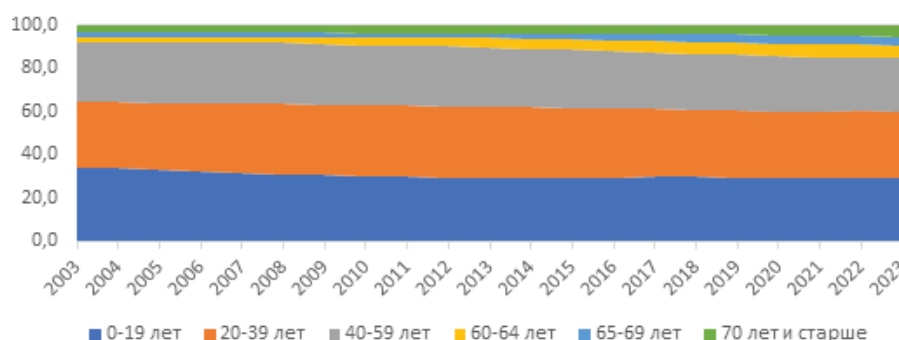


Fig. 1. Age structure of the population of the Republic of Sakha (Yakutia) from 2003 to 2023.

Table 1

Projected number of patients with Alzheimer's disease in the Republic of Sakha (Yakutia) among persons 65 years of age and older

	Сценарий		
	"Chinese" script	"Japanese" script	"American" script
Population of the Republic of Sakha (Yakutia), human.	992 115		
Population of the Republic of Sakha (Yakutia) aged 65 years and older, people.(%)	94 470 (9.52%)		
Predicted number of patients in the Republic of Sakha (Yakutia), people.	4 166.4	5 951.6	8 428.5
Predicted number of patients in Yakutsk, people.	1 499.4	1 947.1	2 908

in the industrial districts of the republic: Neryungri (302.0-671.1 people), Mirny (196.2-429.6 people) and Aldan (173.3-365.9 people). In the central (Khanga-lassky, Namsky, Gorny) and trans-river districts (Ust-Aldansky, Churapchinsky, Tattinsky, Amginsky, Ust-Maisky) the projected number of patients with Alzheimer's disease ranges from 45.8 to 249.9 people, in the Vilyui group of districts (Vilyuysky, Verkhnevilyuysky, Nyurbinsky, Suntarsky) - from 74.5 to 167.6 people. The smallest number of patients with Alzheimer's disease is predicted in the Arctic and Northern districts, especially in Eveno-Bytantai (6.9-11.1 people) and Anabar (4.8-10.5 people) (Fig. 1).

Discussion. According to the results of our study, it follows that there is an extremely high level of underdiagnosis of Alzheimer's disease in the Republic of Sakha (Yakutia). The diagnostic deficit is 99%! The reason for low diagnosis, in our opinion, may be:

1. failure to timely seek medical help in the early stages of AD;
2. insufficient awareness of primary care physicians about the early manifestations of AD;
3. misunderstanding of dementia only as complete functional dependence on others (in fact, severe dementia);
4. lack of routing of patients with AD;

5. lack of highly sensitive biomarkers available in clinical practice.

The population of the Republic of Sakha (Yakutia) is heterogeneous by age group, which will certainly affect the number of patients with Alzheimer's disease in different districts. In 2022, the share of the population aged 60 years and older in the Republic was 15.5% (among women - 18.4%, among men - 12.4%). In six northern districts, the proportion of people of this age is less than 10% (Oleneksky - 6.8%, Anabarsky - 6.8%, Eveno-Bytantaisky - 7.4%, Bulunsky - 8.7%, Zhigansky - 9.0%, Momsky - 9.3%). In three districts there is a large proportion

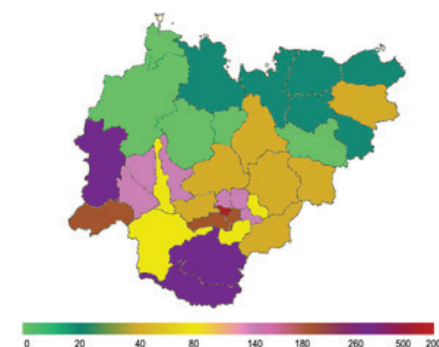


Fig. 2. Map of the projected number of patients with Alzheimer's disease in the city of Yakutsk and regions of the Republic of Sakha (Yakutia), abs.

Table 2

Characteristics of cognitive decline in Alzheimer's disease

MCI in Alzheimer's disease	There are biomarkers of Alzheimer's disease and subtle problems with memory, speech and thinking. These disturbances are noticeable to the patient, family members, friends, but not to others and do not interfere with daily activities.
Mild dementia	People are able to function independently in many areas, but require assistance with some activities (especially managing finances and paying bills). Patients can still drive, work, and do business on their own.
Moderate dementia	People experience even greater problems with memory and speech, there may be episodes of disorientation, and it is difficult to perform multi-step tasks (bathing, dressing). Urinary incontinence may occur at times, and personality and behavior changes may begin, including suspiciousness and agitation. There may be problems recognizing loved ones.
Severe dementia	Patients almost completely lose the ability to communicate, require round-the-clock monitoring, and are often bedridden. Possible complications such as thrombosis, skin infections, sepsis, dysphagia, aspiration pneumonia

of people aged 60 years and older (> 20%): Verkhnekolymsky - 20.3%, Tattinsky - 20.6%, Ust-Maysky - 20.8%. The proportion of elderly women was higher than the proportion of men in the corresponding group by an average of 6.0%, the largest difference was found in the Aldan (8.6%) and Khangalass (8.0%) districts, the smallest difference was in the Anabar district (0.5%).

Dementia in Alzheimer's disease does not develop acutely and, in its development, overcomes the stage of moderate cognitive impairment. According to a systematic review, the conversion rate of AD in MCI ranges from 10.6% to 37.8% over 5 years [16]. The importance of identifying MCI is dictated by the fact that at this stage of cognitive impairment, 53.4% may have an improvement in cognitive functions, although for the amnesic type of MCI the proportion of patients with improvement is only 6.3% [17]. MCI is detected in 6.7% of the population aged 60-64 years, this figure increases and in the group of 80-84 years old reaches 14.8% [18]. Table 2 shows the characteristics of patients with varying degrees of cognitive decline in AD [1].

Of the identified genes, the APOE4 gene has the greatest influence on the development of AD. The APOE4 protein is involved in cholesterol transport. The greatest risk is observed in patients with the $\epsilon 4/\epsilon 4$ genotype (8-12 times higher), while the $\epsilon 2/\epsilon 2$ genotype is associated with a reduced risk, and the $\epsilon 3/\epsilon 3$ genotype has a neutral effect [10]. According to a large meta-analysis that included studies from 1985 to 2010, the distribution of heterozygous and homozygous carriage of the APOE4 gene in patients with AD differs depending on geographic location. The lowest prevalence of carriage was found in Asia (heterozygotes $\epsilon 4$ - 41.9%, homozygotes $\epsilon 4/\epsilon 4$ - 7.7%)

and Southern Europe (heterozygotes $\epsilon 4$ - 40.5%, homozygotes $\epsilon 4/\epsilon 4$ - 4.6%); on the contrary, in Northern Europe there was the largest number of carrier patients (heterozygotes $\epsilon 4$ - 61.3%, homozygotes $\epsilon 4/\epsilon 4$ - 14.1%) [19].

Despite hereditary burden, modifiable risk factors play a role in the development of AD. A study of more than 22,000 people showed that the cognitive performance of people aged 40-79 years who did not have risk factors for dementia was similar to that of people 10-20 years younger who did have risk factors [22]. It was found that a high level of education reduces the relative chance of developing AD (odds ratio = 0.64, confidence interval = 0.56-0.74), and also delays the time of development of cognitive impairment (OR = 0.76, CI = 0.67 -0.85) [22]. This is explained by a higher level of cognitive reserve in people whose work is associated with continuous education and intellectual activity [5].

One of the protective effects among the indigenous population of the Republic of Sakha (Yakutia) may be bilingualism. In China, the effect of bilingualism on AD was studied in Cantonese and Mandarin monolinguals as well as bilinguals. Scientists have found that bilinguals have a later onset of AD (70.93 years versus 63.9 years and 63.4 years) and an initially high level of MMSE (16.43 points versus 12.25 points and 15.75 points) [23].

Conclusion. Thus, AD is one of the leading medical and social problems of the modern world. At this stage in the Republic of Sakha (Yakutia), improved diagnosis of the disease is required for the timely initiation of symptomatic therapy. The predicted number of patients determined by us in the city of Yakutsk and the regions of the Republic can serve as a guideline when screening patients for cognitive impairment.

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EMERGENCY SURGICAL AID TO PATIENTS WITH COLORECTAL CANCER IN THE REPUBLIC OF SAKHA (YAKUTIA)

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The article presents materials of the coloproctology department of the Republic hospital №2 - Emergency Medical Center for the last five years (2018-2022). Diagnosis and treatment of 399 patients with complicated colorectal cancer admitted by emergency indications were analyzed. 115 patients (28.8%) were delivered from the districts of the Republic by air ambulance. The remaining 284 patients (71.2%) were hospitalized from Yakutsk and its suburbs. 90% of patients were operated by emergency. The mortality rate after emergency surgical interventions amounted to 20.2%.

Keywords: neoplasms, colon, colorectal cancer, surgical treatment.

Introduction: Emergency surgical care in the Republic of Sakha (Yakutia) has its own peculiarities related to the vast territory, sparsely populated areas, transportation scheme and weather con-

ditions [3]. There is a certain number of patients with complicated colorectal cancer among emergency surgical patients, who are admitted urgently to the surgical departments, as well as to the coloproctology department of the Republic hospital №2 - Emergency Medical Center. Specialized oncological care in the Republic is provided by the State Budgetary Institution of the Republic of Sakha (Yakutia) "Yakutsk Republic Oncological Dispensary".

According to the researches [2], colorectal cancer ranks the 3rd position in the structure of oncologic morbidity in developed countries after lung cancer and gastric cancer, and accounts for 4-6% of the total oncopathology. There is an increase in the level of primary morbidity of malignant neoplasms by 13.4% according to the data of Yakutsk oncological dispensary for the last 10 years in the Republic of Sakha (Yakutia). 2506 cases of malignant neoplasms were detected

in 2021 in the Republic for the first time. It is established that the age of patients with first detected colorectal cancer is predominantly older than 50 years old, and women are 1.5 times more often than men. [6]. Colorectal and rectosigmoid cancer occupies leading positions in morbidity and mortality among other malignant tumors due to clinical statistics. 45277 new cases of colorectal cancer were registered in 2019 in Russia, 23593 patients died from this disease [1]. Colorectal cancer was 14.0 per 100 thousand population, and rectosigmoid-rectal cancer was 12.2 per 100 thousand population in the Republic of Sakha Yakutia in 2019 according to L.N.Afanasyeva and co-author study [2]. The mortality rate was 5.3 deaths per 100,000 population for colorectal cancer, and 3.0 per 100,000 population was for rectosigmoid-rectal cancer. The main problem in colorectal cancer is the occurrence of various complications in 8-30% of patients, first of all

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