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EPIDEMIOLOGICAL MANIFESTATIONS OF HEPATITIS C IN THE REPUBLIC OF SAKHA (YAKUTIA) DURING THE GLOBAL INFECTION ELIMINATION PROGRAM IN THE RUSSIAN FEDERATION

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The Republic of Sakha (Yakutia) is the largest administrative-territorial unit in the world, more than 40% of its territory is located beyond the Arctic Circle. At the same time, the population of the republic is the lowest among all subjects of the Russian Federation (0.32 people/km2). All this together significantly distinguishes this region from other territories of Russia. The purpose of this study: to assess the main manifestations of the epidemic process of chronic hepatitis C on the territory of the Republic of Sakha (Yakutia) at the stage of implementation of the national program for the elimination of viral hepatitis. Materials and methods. An epidemiological analysis of chronic hepatitis C and liver cancer was carried out for the period from 2000 to 2019. The incidence of liver cancer was assessed according to ICD-10, in which malignant neoplasms of the liver and intrahepatic bile ducts are summarized under code C22. Statistical analysis was carried out in the application package R. The study of differences in the distribution of incidence rates of chronic hepatitis C and malignant liver diseases between the Russian Federation and the Republic of Sakha (Yakutia) was carried out using the method of nonparametric assessment of the weighted average median of the Mann-Whitney test. Results and discussion. The decrease in the intensity of the incidence of acute and chronic hepatitis C in Russia was unidirectional in nature with a fairly close manifestation of their long-term movement. In contrast, in the Republic of Sakha (Yakutia) there was a significantly less pronounced decrease in the incidence of acute hepatitis C (4.9 times, rate of increase -6.2%), and the incidence of chronic hepatitis C in general for the entire analyzed period was cyclical and had a pronounced upward trend (2.4 times growth, rate of increase +2.6%). It was shown that there are statistically significant differences ($p<0.01$) between the median incidence rates of chronic hepatitis C and malignant liver diseases between the Russian Federation and the Republic of Sakha (Yakutia). Conclusion. To achieve the appropriate targets for hepatitis C elimination in the country, it is necessary to take into account the specific natural, climatic, social and ethnic characteristics of the Republic of Sakha (Yakutia).

Keywords: epidemiology, morbidity; hepatitis C; liver cancer; The Republic of Sakha (Yakutia).

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Introduction. Parenteral viral hepatitis B and C are a global medical and social problem, and therefore in May 2016, at the 69th World Health Assembly, the first global strategy to combat these diseases was adopted, and in September 2016, a similar long-term the action plan was approved by the WHO Regional Office for Europe [8]. In the Russian Federation, work on organizing and implementing regional programs to reduce the burden of hepatitis B and C in the format of WHO documents has only recently intensified. The systematic measures taken in recent years in the Russian Federation to combat parenteral viral hepatitis have contributed to a decrease in the intensity of epidemic processes for both nosological forms, which was especially clearly manifested in hepatitis B. In the Russian Federation for 2000-2020. the incidence of acute hepatitis B decreased by 121 times, and chronic hepatitis B by 3.3 times. In hepatitis C, the decrease in these indicators was much less pronounced and amounted to 32 and 1.3 times, respectively [2].

The President of the Russian Federation, in his message to the Federal Assembly dated April 21, 2021, clearly identified long-term tasks in this direction. “Hepatitis C also claims many young lives. Solutions are needed here that will allow us to minimize this danger to the health of the nation within a decade,” the President said. The subsequent decree of the Government of the Russian Federation dated November 2, 2022 No. 3306 determined a phased plan for the implementation of measures aimed at combating hepatitis C until 2030.

Obtaining adequate responses to ongoing activities (epidemiological control) is achieved mainly under homogeneous conditions, under which the development of epidemic processes of infectious diseases manifests itself in different territories. In this regard, it should be noted that the Russian Federation is the largest state entity on our planet, which determines a variety of natural, climatic and

social conditions in its individual territorial units. This, in turn, can contribute to various manifestations of epidemic processes of diseases that are similar in their pathogenetic properties and/or even with a single etiological agent causing them [5]. It is clear that these conditions must be taken into account when organizing regional programs.

A convincing example of the stated thesis is the position that the Russian Federation is essentially a northern country, since more than half of its territory consists of the regions of the so-called Far North. This definition (Far North) is a collective historical concept to designate the most distant northern territories of the Russian Federation, which are harsh in nature and climate, usually located beyond the Arctic Circle [7]. The main representative of this territory is the Republic of Sakha (Yakutia), the area of which is almost comparable to the entire European part of the country. The Republic of Sakha (Yakutia) is part of the Far Eastern Federal District and is not only the largest subject of the Russian Federation, but also the largest administrative-territorial unit in the world, more than 40% of its territory is located beyond the Arctic Circle. At the same time, the population of the republic, according to Federal state statistics service of Russia (2023), is 996,243 people, which determines one of the lowest population densities among all subjects of the Russian Federation (0.32 people/km^2). The Yakuts in the national structure of the population of the Republic make up half of the population with the number of urban residents as of 2022 being 67.1%. All this, together with the natural, climatic and social living conditions of the population, significantly distinguishes this region from other territories of the Russian Federation.

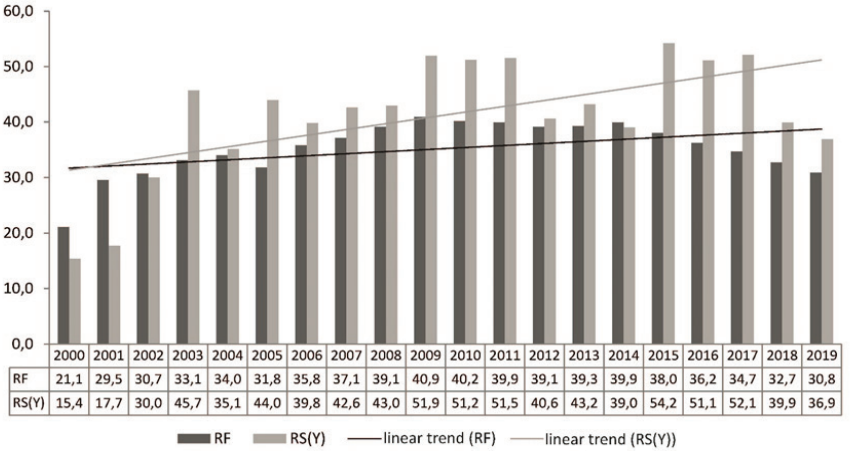
The purpose of this study is to assess the main manifestations of the epidemic process of chronic viral hepatitis C on the territory of the Republic of Sakha (Yakutia) at the stage of implementation of the national program for the elimination of viral hepatitis.

Materials and methods. The epidemiological analysis was carried out mainly for the period from 2000 to 2019. The choice of the final point of the study was determined by subsequent violations of anti-epidemic measures in 2019 associated with the COVID-19 pandemic, which, according to V. Isakov, D. Nikityuk, (2022), leads to a distortion of statistical indicators when assessing the manifestations of the epidemic process of chronic hepatitis C (CHC) [11]. One of the unfavorable outcomes of CHC is hepatocellular carcinoma (HCC). Considering that there are no specific statistics on HCC, the incidence of this nosological form was assessed using ICD-10, in which malignant neoplasms of the liver and intrahepatic bile ducts are summarized under code C22. The acceptability of this approach is due to the fact that 95% of all liver cancer cases are represented by HCC, which allows the use of official statistical reporting with a small degree of error.

Statistical analysis was carried out in the application package R. The study of differences in the distribution of morbidity rates between the Russian Federation and the Republic of Sakha (Yakutia) was carried out using the method of nonparametric assessment of the weighted average median of the Mann-Whitney test.

Results and discussion. An analysis of the incidence of infectious diseases in the Russian Federation over the first two decades of the 21st century revealed a unidirectional downward trend in this indicator for the vast majority of all major infectious diseases. An increase in long-term morbidity was detected only for infections caused by the human immunodeficiency virus and a group of acute respiratory viral infections [2]. At the same time, for acute respiratory viral infections, this increase was due mainly to their joint recording in 2020 with a new coronavirus infection, which began to be separately recorded in the relevant forms only in 2021.

As noted above, from the group of parenteral viral hepatitis, its most unfavorable component is CHC due to the signifi-



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
RF	21,1	29,5	30,7	33,1	34,0	31,8	35,8	37,1	39,1	40,9	40,2	39,9	39,1	39,3	39,9	38,0	36,2	34,7	32,7	30,8
RS(Y)	15,4	17,7	30,0	45,7	35,1	44,0	39,8	42,6	43,0	51,9	51,2	51,5	40,6	43,2	39,0	54,2	51,1	52,1	39,9	36,9

Fig. 1. CHC incidence rates in the Russian Federation (RF) and the Republic of Sakha (Yakutia) (RS (Y)) in 2000-2019, according to official registration (per 100,000 population)

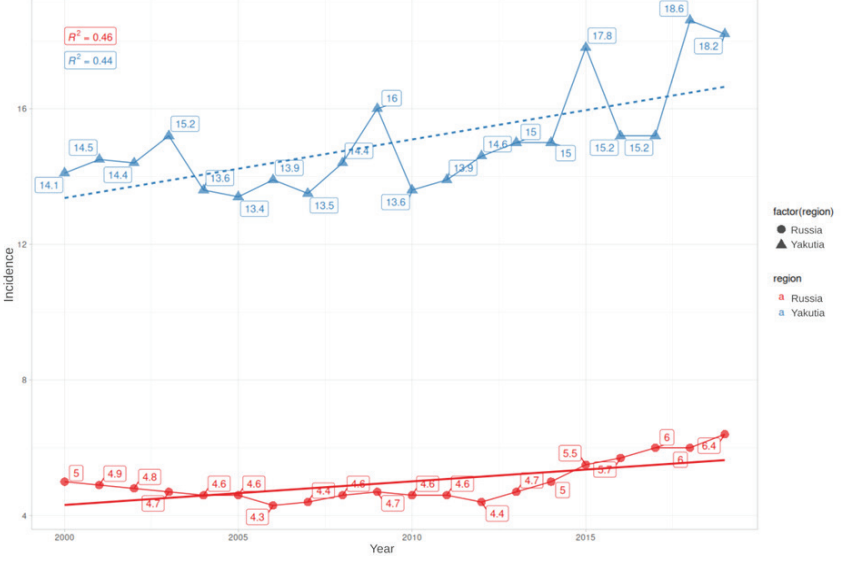


Fig. 2. Long-term dynamics of the incidence of malignant neoplasms of the liver and intrahepatic bile ducts in the Republic of Sakha (Yakutia) and the Russian Federation

cantly lower efficiency of epidemiological control in this disease. Consequently, despite significant advances in the creation of effective methods of treating hepatitis C, it still continues to be one of the leading causes of HCC, which is causally related to mortality from CHC [1].

It should also be noted that current studies indicate that the clinical manifestations of both CHC and HCC associated with HCV infection have not revealed any differences in the ethnic groups of Caucasians, Mongoloids and the Turkic-speaking population of Northeast Asia [3]. As for the epidemiological manifestations of the epidemic process of CHC in the territory of the Russian Federation and the Republic of Sakha (Yakutia), there are significant differences when comparing territorial indicators of the movement of the incidence of this infection [9].

The decrease in the intensity of the incidence of acute and chronic hepatitis C in Russia was unidirectional and the manifestation of their long-term movement was quite close. In contrast, in the Republic of Sakha (Yakutia) there was a significantly less pronounced decrease in the incidence of acute hepatitis C (4.9 times, growth rate -6.2%), and the incidence of CHC in general for the entire analyzed period was cyclical in nature and had a pronounced upward trend (2.4 times growth, growth rate +2.6%). The minimum value occurred in 2000 (15.4 per 100,000 population), and the maximum was noted in 2015 (54.2 per 100,000 population), with a long-term average of 41.2$^{0}/_{0000}$ (Fig. 1).

Currently, HCC is in second place among cancer causes of death [10]. The main etiological causes of HCC are hepatitis B and C viruses, and due to effective vaccine prevention of hepatitis B, the emphasis in etiological significance in recent years has shifted towards hepatitis C. In this regard, as a rule, the incidence of HCC is more correlated with the prevalence of CHC than with other risk factors.

To determine the incidence rates between CHC and malignant neoplasms of the liver and intrahepatic bile ducts in the Russian Federation and the Republic of Sakha (Yakutia), the Mann-Whitney criteria were used. The long-term dynamics of incidence in these territories followed a general trend, but with more factorial trends in the territory of the Republic of Sakha (Yakutia) (Fig. 2). It was found that there are additional statistically significant differences between the median incidence rates of CHC (p=0.0043) and liver cancer (p<0.00001) in comparable regions (Fig. 3). At the same time, if the incidence rate of CHC according to the

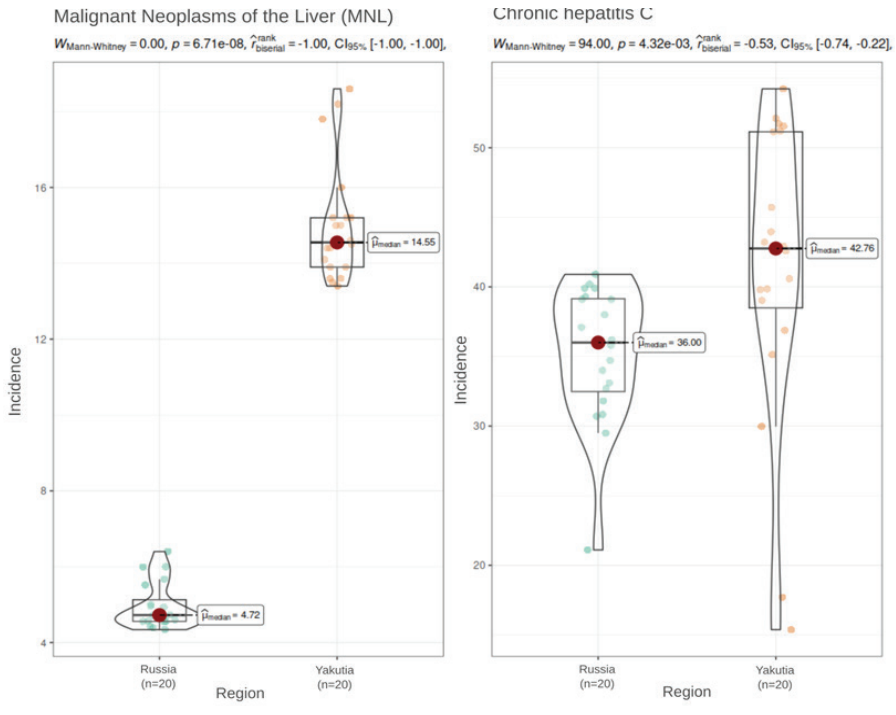


Fig. 3. Comparative level of long-term incidence of malignant neoplasms of the liver and intrahepatic bile ducts and CHC according to the weighted median of the Mann-Whitney test in the Republic of Sakha (Yakutia) and the Russian Federation

median in the Republic of Sakha (Yakutia) is 1.2 times higher according to observations with signs in the Russian Federation, then for malignant neoplasms of the liver and intrahepatic bile ducts in the Republic of Sakha (Yakutia) there is a 3-fold excess of the average long-term indicators federal estimates. Significant differences in the incidence of malignant neoplasms of the liver and intrahepatic bile ducts may be significant with the presence of additional risk factors in the Republic of Sakha (Yakutia). These include the widespread prevalence of hepatitis D virus in the republic, co-infection with hepatotropic viruses, diabetes mellitus, and metabolic syndrome [6].

Thus, at present, the manifestations of the epidemic process of CHC and malignant neoplasms of the liver and intrahepatic bile ducts in the Republic of Sakha (Yakutia) have pronounced unfavorable epidemiological differences compared to similar long-term indicators in the Russian Federation. These data indicate the need to apply proactive anti-epidemic measures to combat hepatitis C in the territory of the Republic of Sakha (Yakutia). These measures should include active efforts to identify new cases of HCC and prevent infection, improve the health care delivery system, and increase the coverage of patients in need of antiviral therapy and early diagnosis of HCC. Only in this case can we achieve target indicators and fit into the general trend of hepatitis C elimination in the country.

Conclusion. To assess the effectiveness of state programs for the elimination of hepatitis C in the Russian Federation, a comparative analytical assessment of the development of the epidemic process in certain territories of the country is necessary with mandatory consideration of natural, climatic, social and ethnic factors characteristic of a particular region. This approach is a necessary condition for obtaining reliable conclusions about the successful implementation and effectiveness of anti-epidemic measures in various territorial entities of the Russian Federation. Reducing the incidence of CHC in the Republic of Sakha (Yakutia) is a necessary, but not sufficient condition for reducing the incidence of malignant liver tumors. In this regard, attention to other risk factors of an infectious and constitutional nature should become an important element in a comprehensive strategy to combat diseases associated with viral hepatitis [4, 6].

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ANALYSIS OF THE MEDICAL AND DEMOGRAPHIC SITUATION IN THE REPUBLIC OF SAKHA (YAKUTIA) IN THE CONTEXT OF HEALTH THREATS DUE TO THE COVID-19 PANDEMIC

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The analysis of fertility, morbidity (primary and general) and mortality in the Republic of Sakha (Yakutia), in dynamics, over a 10-year period (2013-2022). Differences in the structure of morbidity in the Republic of Sakha (Yakutia) and in the Russian Federation as a whole were revealed. The peak of mortality rates of the urban and rural population of the Republic of Sakha (Yakutia), caused by the COVID-19 pandemic, has been determined. Problematic aspects of rural health care have been identified, as well as diseases complicated by the pandemic that require rehabilitation. The results of the study should be taken into account by health authorities and institutions for management decisions on countering challenges and threats to the health of the population of the Republic of Sakha (Yakutia) caused by a new coronavirus infection.

Keywords: Republic of Sakha (Yakutia), health threats, morbidity of the population, rural health, COVID-19.

Introduction. The geopolitical and demographic situation in Russia and its territories necessitates the development of a promising model of medical and demographic policy [8, 9, 11, 13].

Inequality in the provision of medical care to the population of Russia is associated with geographic, climatic and national characteristics, as well as the territorial accessibility of medical care to rural residents [5]. The Republic of Sakha (Yakutia) (RS(Y)) is part of the Far Eastern Federal District (FEFD), which is the largest in the Asia-Pacific region [6, 12]. The COVID-19 pandemic has worsened the medical and demographic situation in the Russian Federation and its regions, including the Far Eastern Federal District and the Republic of Sakha (Yakutia) [1, 2, 4, 7].

The purpose of the study: to provide an analysis of the medical and demographic situation and newly identified morbidity among the population, including rural ones, in the Republic of Sakha (Yakutia) during the COVID-19 pandemic and to develop proposals for management decisions in healthcare at the regional and municipal levels.

Materials and methods of research: statistical and analytical. Materials from Rosstat, data from official state statistics of the Ministry of Health of Russia and the Republic of Sakha (Yakutia) were used.