Original Article

Prevalence of liver cancer in Kazakhstan: a systematic review

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ABSTRACT

Background

The study aimed to study the relative and absolute indicators of liver cancer (C22) in Kazakhstan over 10 years in the prism of a trend indicator (moving average), coefficient of variation (Cv), accounting reliability index (Idi).In 2022, in Kazakhstan, the incidence of liver cancer (C22) was 5.1 per 100 thousand people, mortality was 2.9, respectively, the index of reliability of accounting was 0.2.The unified risk of morbidity of the population of Kazakhstan with liver cancer for the period 2013-2022 amounted to 28.6%, mortality - 33.5%, respectively.

Result

Over the period 2013-2022, newly diagnosed liver cancer in Kazakhstan increased by 31%, the rate of decrease in the number of newly diagnosed liver cancers varied unevenly over the years, which demonstrates a high rate and amplitude of change from 105 to -140, which significantly complicates the prediction of this pathology. ***Conclusion: For*** the period 2013-2022, posthumously registered liver cancer consistently occupied the first place in the structure of specific gravity among all malignant neoplasms in Kazakhstan.

Keywords

liver cancer; mortality; reliability index; malignant tumors; high-risk groups

INTRODUCTION

In 2020, liver cancer was not included in the top six cancers in terms of prevalence (among new cases), but liver cancer ranks third in the world in terms of causes of death (830,000 deaths) [1]. Drug resistance is the cause of most deaths associated with primary liver cancer [2-3].

Current liver cancer screenings are insufficient. In modern conditions, it is proposed to conduct screening in high-risk groups, including those with cirrhosis of the liver and viral hepatitis by the method of fragmetomic analysis of full-genome cell-free DNA. The use of this method gives a sensitivity for detecting liver cancer of 88% in the medium-risk population and up to 98% among high-risk individuals [4].

The accumulation of fibroblasts in the liver, whether in precancerous or malignant conditions, is a hallmark of liver cancer. However, this accumulation doesn't have therapeutic applications. Hepatocellular carcinoma primarily presents as a non-desmoplastic tumor, characterized by the accumulation of fibroblasts in the liver's precancerous fibrous tissue. These fibroblasts play a crucial role in regulating the risk of hepatocellular carcinoma development by balancing tumor-

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suppressing and tumor-stimulating factors. In contrast, cholangiocarcinoma is desmoplastic [5].

Recently, randomized studies on the effects of lifestyle and primary liver cancer have increased, in particular, the effects of full sleep [6] and intestinal flora for the prevention of liver cancer have been revealed [7].

At the same time, the absence of the influence of polluted air (including PM2.5, PM2.5-10, PM10, nitrogen dioxide and nitrogen oxides) on the development of primary liver cancer was obtained [8,9].

Of course, efforts are needed for early diagnosis and effective treatment, but an important factor is primary prevention efforts aimed at reducing not only viral hepatitis, but also the prevalence of obesity, diabetes and mycotoxin control [10,11].

Proper nutrition refers to a lifestyle, but these meta-analyses did not show the dependence of liver cancer development on nuts, eggs and sweetened drinks. The protective mechanism of legume consumption was observed in doses from 8 to 40 g/day [12].

In 2022 alone, more than 900,000 people worldwide were diagnosed with liver cancer. Currently, the recommendations of the Barcelona Liver Cancer Clinic (BCLC) recognize liver transplantation, surgical

Table 1 - The incidence of liver cancer in the population of Kazakhstan, 2013-2022, per 100 thousand people.

region*	Incidence rate "rough indicator" per 100 thousand population									μ	σ	Cv
	Years											
	2014	2015	2016	2017	2018	2019	2020	2021	202.	4,6	1,0	0,2
1	3,6	4,0	3,8	4,1	5,9	4,8	5,3	5,7	6,4	3,6		0,0
2									3,6	7,0	1,1	0,2
3	7,7	7,4	5,5	6,9	6,4	7,4	5,5	7,0	8,9	5,1	0,8	0,2
4	5,7	4,8	3,5	4,8	3,9	5,9	4,6	6,3	5,4	4,2	0,8	0,2
5	4,4	3,5	4,0	4,4	5,4	4,7	3,8	2,7	5,6	6,1	0,9	0,2
6	6,6	5,0	7,4	7,0	5,2	5,1	6,1	5,3	5,3	4,1	0,6	0,2
7	4,9	4,1	4,6	4,5	4,2	4,2	3,7	3,1	3,2	5,1	0,6	0,1
8	4,8	4,5	5,6	4,5	5,7	5,6	5,7	6,0	4,9	4,5	0,7	0,2
9	4,0	4,5	3,6	5,6	7,2	4,0	3,8	4,9	4,4	6,7	1,2	0,2
10	5,7	8,5	5,9	8,0	7,3	6,0	5,5	5,9	6,8	5,1	0,3	0,1
11	5,0	5,4	4,9	5,5	5,5	5,4	4,6	4,7	5,1	6,2		0,0
12									6,2	4,1	1,0	0,2
13	3,3	5,7	4,4	4,7	7,2	3,1	4,1	2,6	4,4	4,3	0,7	0,2
14	5,1	3,9	4,4	3,6	5,4	5,1	5,5	3,7	3,9	4,5	0,8	0,2
15	4,2	4,6	3,5	5,7	4,5	4,6	3,2	4,4	4,6	5,4	1,0	0,2
16	5,7	5,7	5,5	6,5	3,9	5,4	3,3	5,2	4,5	5,0	1,2	0,2
17					5,4	6,8	4,2	4,2	4,8	4,1	0,5	0,1
18	3,6	4,4	3,0	4,2	3,1	4,8	4,1	4,4	4,2	7,0	0,7	0,1
19	6,0	7,3	6,8	7,1	6,5	7,8	5,9	6,8	7,9	8,1	2,3	0,3
20	11	6,9	9,1	7,6	7,2	12,5	6,2	6,0	6	4,6	1,0	0,2
μ	5,4	5,3	5,0	5,6	5,6	5,7	4,7	4,9	5,3			
σ	1,9	1,4	1,6	1,4	1,4	2,1	1,0	1,4	1,4		28,6%	
Cv	0,3	0,3	0,3	0,2	0,2	0,4	0,2	0,3	0,3			

Region*

Morbidity is a "rough indicator" per 100 thousand people

*1) Aktobe; 2) Zhetysu; 3) Pavlodar; 4) Atyrau; 5) Kostanay; 6) Kyzylorda; 7) Almaty; 8) Zhambyl; 9) Mangystau; 10) Karaganda; 11) Kazakhstan; 12) Abai; 13) Turkestan; 14) North Kazakhstan; 15) Almaty; 16) Akmola; 17) Shymkent; 18) Astana; 19) East Kazakhstan; 20) West Kazakhstan

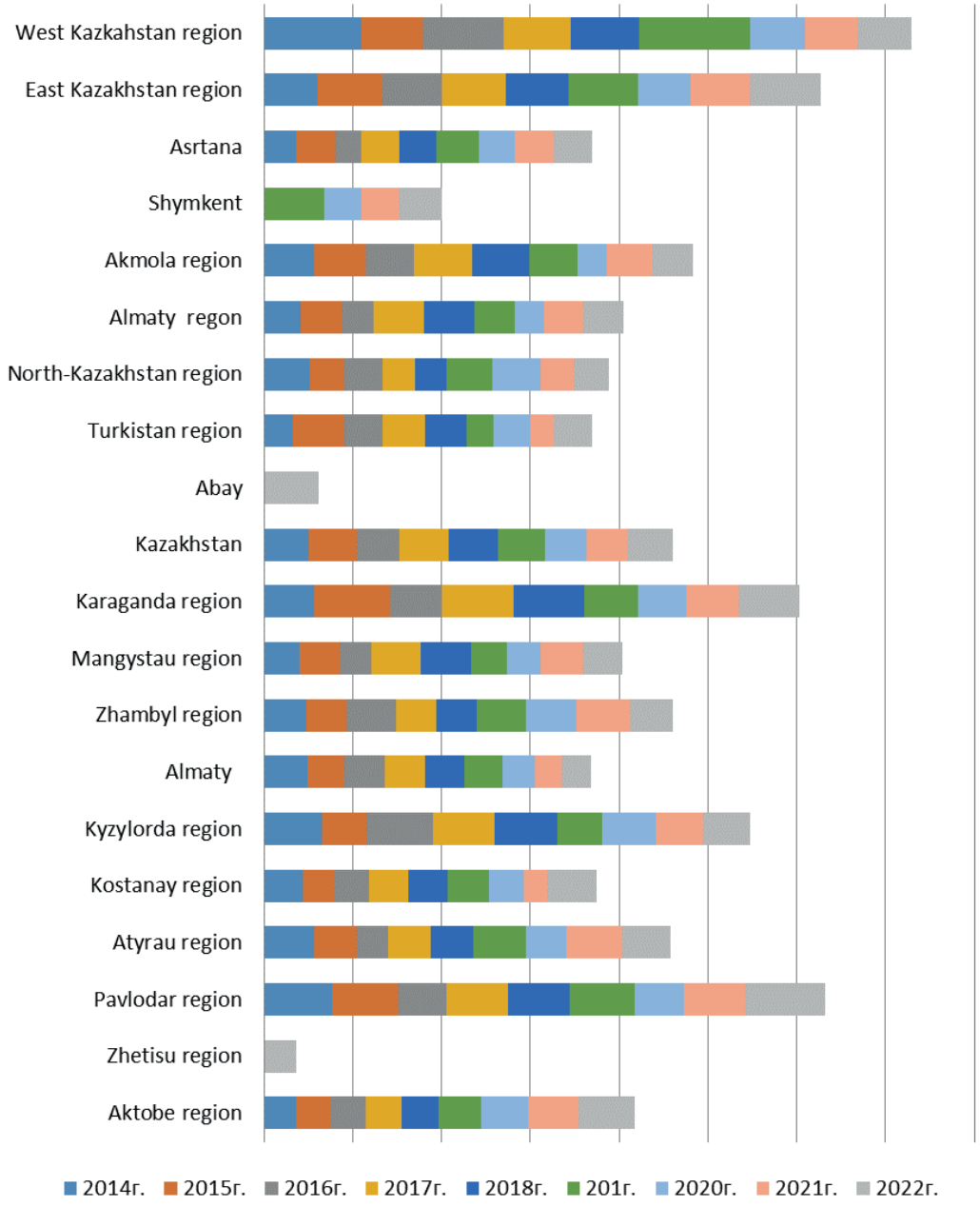


Figure 1 – Regional peculiarities of liver cancer incidence in Kazakhstan for 2013-2022, 100 thousand population

resection and thermal ablation as methods of treating HCC at very early and early stages [13].

The medical and social effectiveness of early detection of liver cancer is proven and understandable, but the cost-effectiveness of epidemiological surveillance for liver cancer (ultrasound of the liver and alpha-fetoprotein) is expensive for the state [14,15].

Thus, today one of the real methods of reducing mortality from liver cancer is primary prevention and it is necessary to improve health education taking into account marketing technologies: promotion channels.

The purpose of the study. To study the relative and absolute indicators of liver cancer (C22) in Kazakhstan over 10 years in the prism of a trend indicator (moving average), coefficient of variation (Cv), accounting reliability index (Idi).

Table 2 – Liver cancer mortality in the population of Kazakhstan, 2013-2022

Region*	Mortality									μ	σ	Cv
	Years											
	2014	2015	2016	2017	2018	2019	2020	2021	2022			
1	2,6	2,7	2,9	2,4	2,9	2,3	2,2	2,2	1,3	2,4	0,5	0,2
2									1,4	1,4		0,0
3	5,0	4,9	5,1	4,1	4,1	4,3	4,4	4,7	3,6	4,5	0,5	0,1
4	4,5	3,6	3,3	3,0	2,7	2,9	2,1	2,1	2,3	2,9	0,8	0,3
5	2,8	2,6	2,0	1,4	2,2	2,9	2,9	1,6	2,4	2,3	0,6	0,2
6	6,4	5,7	3,9	3,4	2,1	2,4	3,3	1,7	2,4	3,5	1,6	0,5
7	4,0	2,7	2,7	2,9	2,1	2,5	2,3	1,9	1,5	2,5	0,7	0,3
8	4,7	4,2	4,3	4,5	3,6	3,5	2,9	3,7	2,6	3,8	0,7	0,2
9	2,5	2,8	2,4	2,5	3,7	3,0	2,9	3,0	2,4	2,8	0,4	0,1
10	3,6	5,3	4,4	3,3	4,8	3,1	3,7	3,9	3,8	4,0	0,7	0,2
11	3,9	3,8	3,6	3,3	3,2	3,4	3,1	2,8	2,9	3,3	0,4	0,1
12									3,8	3,8		0,0
13	2,9	3,5	2,9	2,6	3,6	3,1	3,5	2,2	2,7	3,0	0,5	0,2
14	4,4	2,6	2,3	2,8	3,1	3,1	2,9	2,4	2,4	2,9	0,6	0,2
15	3,2	2,9	3,4	4,1	2,2	3,3	1,8	2,1	3,1	2,9	0,7	0,3
16	3,4	4,2	3,4	5,0	2,7	2,9	3,3	3,0	3,1	3,4	0,7	0,2
17					2,3	3,5	3,5	2,3	3,4	3,0	0,6	0,2
18	3,8	2,8	3,7	2,1	3,7	3,0	2,2	2,8	3	3,0	0,6	0,2
19	4,9	5,8	5,4	5,2	4,9	6,9	4,8	5,4	5,9	5,5	0,7	0,1
20	7,0	4,9	5,5	4,7	4,1	6,9	4,8	4,2	4,7	5,2	1,1	0,2
μ	4,1	3,8	3,6	3,4	3,2	3,5	3,1	2,9	2,9			
σ	1,3	1,1	1,1	1,1	0,9	1,3	0,9	1,1	1,1		33,5%	
Cv	0,3	0,3	0,3	0,3	0,3	0,4	0,3	0,4	0,4			

Materials and methods. The data of the official statistical accounting "Indicators of the oncological service of the Republic of Kazakhstan for 2014-2022 [16-24] were retrospectively studied.

The purpose of the Moving Average is a trend indicator. It is an easy-to-use and interpretable tool that can be graphically visualized to assess the direction of a trend.

We calculated the unified risk using the Variation coefficient coefficient of variation (Cv): the ratio of the standard deviation (σ) to the arithmetic mean (μ). The interpretation is empirical – less than 30% is an indicator of the homogeneity of the population.

The Accounting Reliability Index (Idi) is an indirect indicator that is calculated by dividing the mortality rate of the population from liver cancer by the incidence. Interpretation is a favorable indicator in oncology of 0.7-0.8. In Europe, it is 0.5.

Results and discussions

The incidence of liver cancer in Kazakhstan for the period 2013-2022 increased by 177.8%, in 2014 – 3.6 per 100 thousand population, in 2022 – 5.1. At the same time, the unified risk was 28.6% for the period 2013-2022 (Table 1).

Relative uniformity of liver cancer incidence rates across the country (Cv 28.6%). The assessment of regional characteristics was carried out by the method of aggregation of morbidity indicators over 10 years and regions with a favorable trend, relatively consistently low rates of liver cancer were identified – these are the North Kazakhstan, Astana, Kostanay and Pavlodar regions.

The regions with an unfavorable trend and relatively consistently high rates of liver cancer are the West

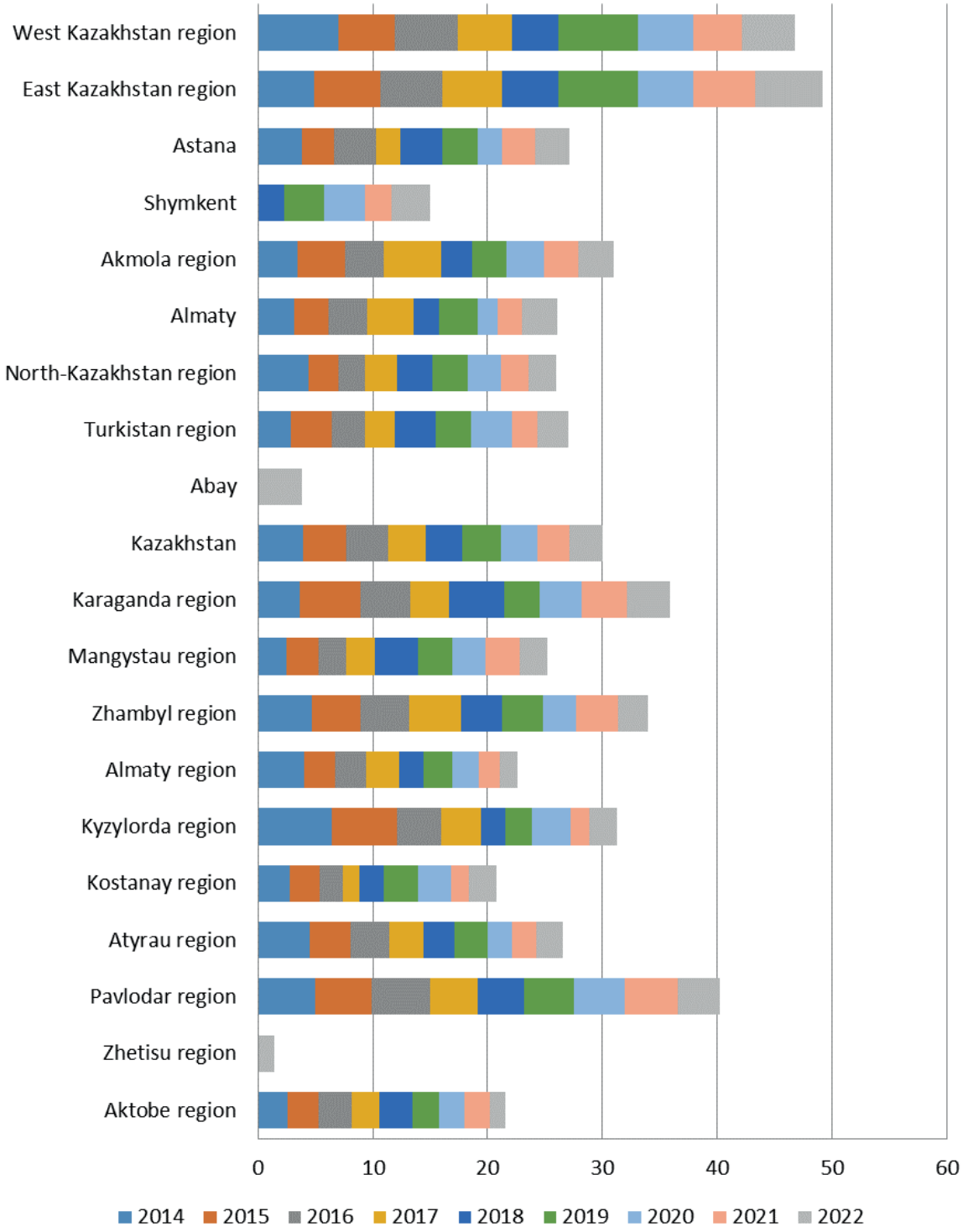


Figure 2 – Regional characteristics of liver cancer mortality in Kazakhstan for 2013-2022, 100 thousand population

Kazakhstan, East Kazakhstan, Karaganda and Almaty regions (Figure 1).

The mortality rates of liver cancer in Kazakhstan for the period 2013-2022 decreased by 56.5%, in 2014 – 2.6 per 100 thousand population, in 2022 – 1.3. At the same time, the unified risk was 33.5% for the period 2013-2022 (Table 2).

Relative uniformity of liver cancer mortality rates across the country (Cv 33.5%). The assessment of regional characteristics was carried out by the method of aggregation of morbidity indicators over 10 years and regions with a favorable trend, relatively consistently low rates of liver cancer were identified – these are Almaty, Kostanay, Aktobe regions.

The regions with an unfavorable trend and relatively consistently high rates of liver cancer are the West Kazakhstan, East Kazakhstan, and Pavlodar regions (Figure 2).

To assess the anticancer activity in Kazakhstan, we calculated the reliability of accounting using the ratio of mortality and incidence of liver cancer in the population of Kazakhstan over 10 years (Table 3).

Table 3 – Dynamics of the index of reliability of accounting for liver cancer in the population of Kazakhstan, 2014-2022

Region	Accounting reliability index								
	Years								
	2014	2015	2016	2017	2018	2019	2020	2021	2022
Aktobe	0,7	0,7	0,8	0,6	0,7	0,5	0,4	0,4	0,2
Zhetisu									0,4
Pavlodar	0,6	0,7	0,9	0,6	0,6	0,6	0,8	0,7	0,4
Atyrau	0,8	0,8	0,9	0,6	0,6	0,5	0,5	0,3	0,4
Kostanay	0,6	0,7	0,5	0,3	0,5	0,6	0,8	0,6	0,4
Kyzylorda	1,0	1,1	0,5	0,5	0,3	0,5	0,5	0,3	0,5
Almaty	0,8	0,7	0,6	0,6	0,5	0,6	0,6	0,6	0,5
Zhambyl	1,0	0,9	0,8	1,0	0,8	0,6	0,5	0,6	0,5
Mangistau	0,6	0,6	0,7	0,4	0,7	0,8	0,8	0,6	0,5
Karaganda	0,6	0,6	0,7	0,4	0,6	0,5	0,7	0,7	0,6
Kazakhstan	0,8	0,7	0,7	0,6	0,6	0,6	0,7	0,6	0,6
Abay									0,6
Turkistan	0,9	0,6	0,7	0,6	0,8	1,0	0,9	0,8	0,6
North-Kazakhstan	0,9	0,7	0,5	0,8	0,9	0,6	0,5	0,6	0,6
Almaty	0,8	0,6	1,0	0,7	0,4	0,7	0,6	0,5	0,7
Akmola	0,6	0,7	0,6	0,8	0,4	0,5	1,0	0,6	0,7
Shymkent						0,5	0,8	0,5	0,7
Astana	1,1	0,6	1,2	0,5	0,9	0,6	0,5	0,6	0,7
East-Kazakhstan region	0,8	0,8	0,8	0,7	0,7	0,9	0,8	0,8	0,7
West Kazakhstan region	0,6	0,7	0,6	0,6	0,5	0,6	0,8	0,7	0,8

Visually, the dynamics of liver cancer in the regions of Kazakhstan has been calculated over 9 years and by the method of aggregation, regions with high and low trends can be distinguished.

The regions with a high level of the index of reliability of accounting are East Kazakhstan, Astana, Turkestan, Zhambyl, North Kazakhstan.

The regions with a low level of the index of reliability of accounting are Aktobe, Kostanay, Karaganda, Kyzylorda regions (Figure 3).

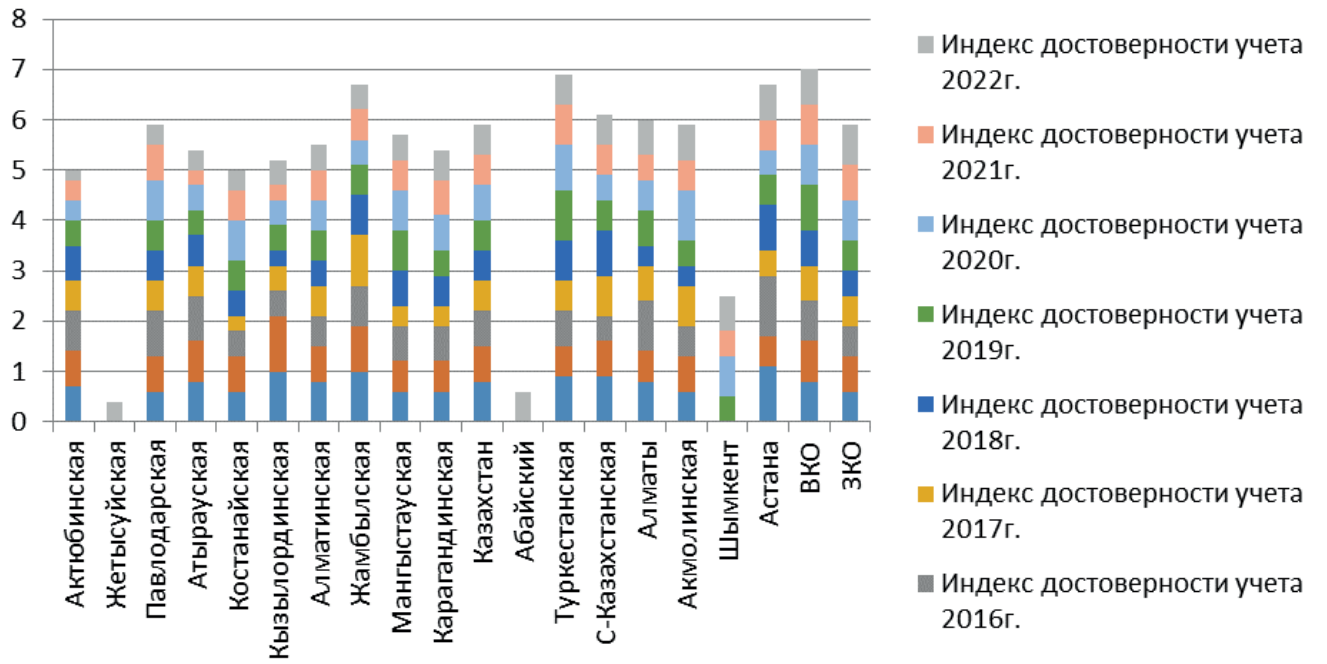


Figure 3 – The index of reliability of accounting for liver cancer in Kazakhstan for 2014-2022, 100 thousand people

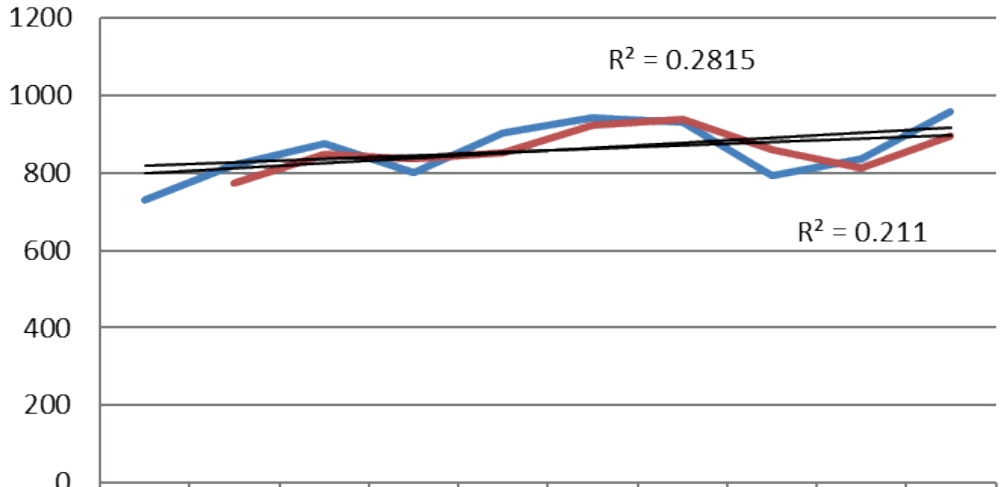
For clarity of the analysis in dynamics over 10 years, we have calculated the indicators of the dynamic range. The number of newly diagnosed with liver cancer is 31% higher, the absolute increase over 10 years is 123, the growth rate for 2022 was 15 compared to the baseline, and the growth rate was 115. Absolute chain increases are scattered in the amplitude from -140 to +123, which makes it much more difficult to make forecasts for this period (table 4).

Table 4 – Liver cancers detected for the first time in the population of Kazakhstan, abs

Indicators	Years										In total for 10 years
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
first identified,absolte	731	819	876	800	905	944	932	792	836	959	-
absolute increase (decline)	-	88	57	-76	105	39	-12	-140	44	123	228
growth (loss) rate, %	-	12	7	-8,7	13	4,3	-1,3	-15	5,5	15	31,2
growth rate (loss)%	-	112	107	91,3	113	104,3	99	85	105	115	131,2
Absolute value of the increase%		7,33	8,1	8,7	8,1	9,1	9,2	9,3	8,0	8,2	7,31
visibility indicator	100%	112	120	109	124	129	127,5	108	114	131	-

When analyzing the intensive indicator of newly diagnosed liver cancer in the population of Kazakhstan for 2013-2022, it was found: 1) over 10 years, the number of newly diagnosed liver cancers in Kazakhstan increased by 31.2%; 2) the rate of decrease in the number of newly diagnosed liver cancers varied unevenly over the years, which demonstrates a high rate and amplitude of change from 105 da -140; 3) the absolute value of 1% of the number of newly diagnosed with liver cancer increased slightly from 7.33 to 8.2.

In 10 years, the absolute rates of newly diagnosed liver cancer have increased by 31%, and in the last two years by 15%. Figure 4 shows the intensive indicators for 10 years of newly diagnosed with liver cancer in Kazakhstan (Figure 4).



	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Впервые выявленные, абс	731	819	876	800	905	944	932	792	836	959
скользящая средняя		775	847	838	852	924	938	862	814	897

Figure 4 – Dynamics of newly diagnosed liver cancers in Kazakhstan over 10 years, abs

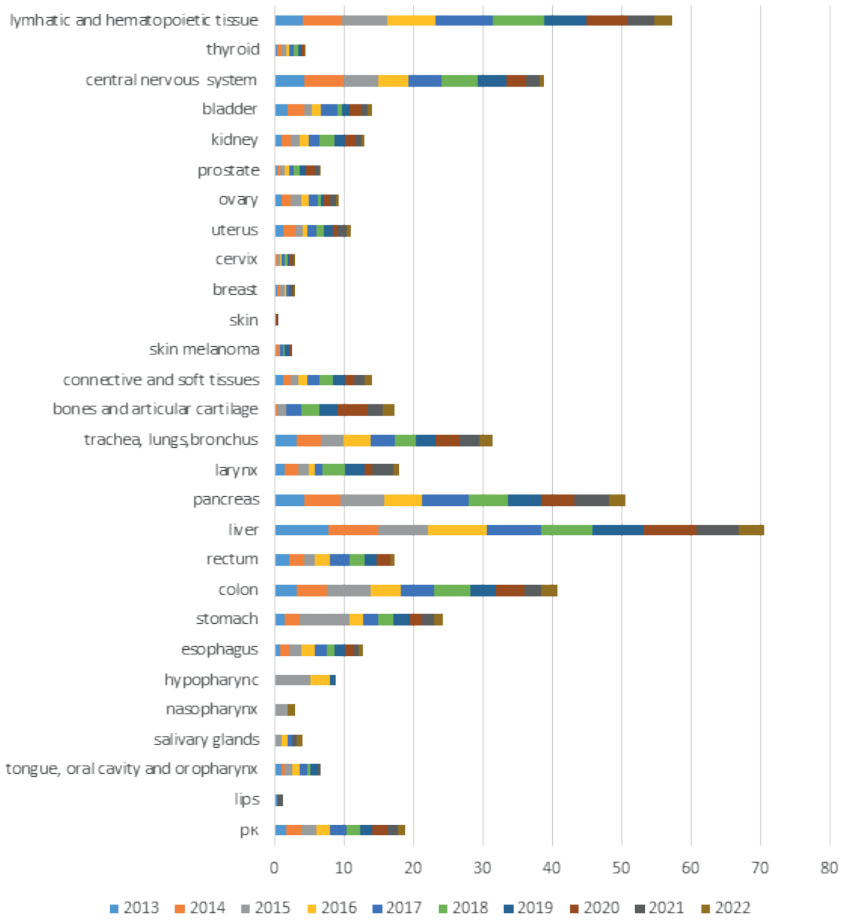


Figure 5 – The proportion of posthumously diagnosed cancer in the structure of all identified patients with cancer of various localizations, over 10 years, %

The calculation of the moving average of absolute indicators of liver cancer detected for the first time in Kazakhstan over 10 years has shown a trend of stability, and it can be interpreted as negative (R2 = 0.2), given that liver cancer in Kazakhstan has been consistently ranked 1st in the structure of all malignant diseases of the country for 10 years, which are taken into account posthumously (Table 5)

Table 5 - Posthumously registered patients with liver cancer in Kazakhstan in the structure of all oncological diseases for the period 2013-2014, %

Specific gravity counted posthumously, %	Years									
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
	7,8	7,1	7,2	8,5	7,9	7,4	7,3	7,5	6,2	3,6
Ранг в структуре всех ЗН	1	1	1	1	2	2	1	1	1	1

A visual analysis of the proportion of posthumously diagnosed liver cancer in Kazakhstan in the structure of all patients with liver cancer in comparison with other malignant diseases (Figure 5).

Further, we analyzed the intensive indicators of the considered posthumously diagnosed with liver cancer in 2013-2022 (Table 6).

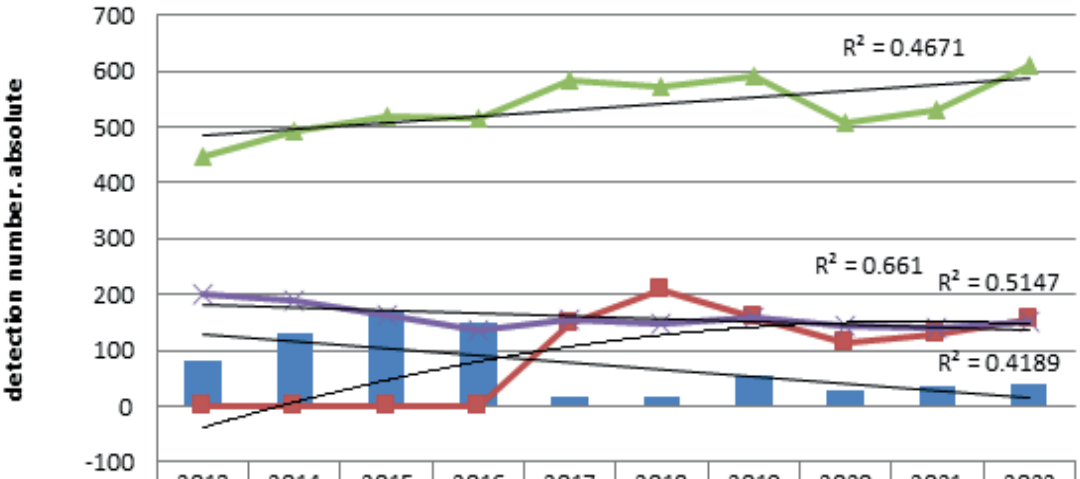
Table 6 – Number of patients diagnosed with liver cancer posthumously in Kazakhstan, abs

Counted posthumously,absolutely	Years										In total for 10 years
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	
	62	63	68	75	78	74	74	65	56	36	-
Absolute increase (decrease)		1	5	7	3	-4	0	-9	-9	-20	-26
Growth rate (decrease) %	-	1,61	7,94	10,29	4,00	-5,13	0,00	-12,16	-13,85	-35,71	-41,94
Growth (decrease)rate, %	-	101,61	107,94	110,29	104,00	94,87	100,00	87,84	86,15	64,29	58,06
Absolute value of the rate%		0,62	0,63	0,68	0,75	0,78	0	0,74	0,65	0,56	0,62
Visibility indicator	100%	101,6	109,6	120,9	125,8	119,3	119,3	104,8	90,32	58,06	-

When analyzing the intensive indicator of newly diagnosed liver cancer in the population of Kazakhstan for 2013-2022, it was found: 1) over 10 years, the number of posthumously registered liver cancers in Kazakhstan decreased by 42%; 2) the rate of decrease in the number of newly diagnosed liver cancers varied unevenly over the years, which demonstrates a high rate and amplitude of change from 10.29 to -35.7; 3) the absolute value of 1% of the number of newly diagnosed with liver cancer decreased slightly from 0.62 to 0.56

Table 7 - Posthumously registered patients with liver cancer in the structure of all oncological diseases

Counted posthumously,absolutely, %	Years									
	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
	7,8	7,1	7,2	8,5	7,9	7,4	7,3	7,5	6,2	3,6
Range of malignant tumors	1	1	1	1	2	2	1	1	1	1



	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Stage 1	82	129	172	148	15	16	55	28	35	39
Stage 2	0	0	0	0	149	209	158	113	130	155
Stage 3	448	493	518	515	582	572	590	508	530	610
Stage 4	200	188	164	136	156	146	160	142	139	152

Figure 6 – Dynamics of newly diagnosed liver cancer by stages of the disease in Kazakhstan over 10 years, abs

To assess the structure of the newly diagnosed cancer, we analyzed the stage of the identified process. Over the period 2013-2022, patients are consistently more often detected already in the third stage, but there has been a positive trend and the number of patients newly diagnosed in the second stage has increased (Figure 6).

When analyzing the indicator of the specific gravity of the trend by stages of detected liver cancer: in 2013, the proportion with stage 1 was 11.2% (2022 – 4.4%), stage 2 – 0% (16.2%), stage 3 – 61.4% (63.8%), stage 4 – 27.4% (15.9%). The positive trend in newly diagnosed liver cancer of stage 1 is almost 2.5 times; stage 2 is 16 times and stage 4 is 1.7 times, and the third stage remains unchanged - the leading predominant and occupies more than 60% (Figure 7).

Figure 7 – The proportion of liver cancer detected by stage of the disease in Kazakhstan over 10 years, %

Analyzing the age strata by the method of enlargement over 10 years, it can be seen that the group of relatively able-bodied male population prevails - 55-69 years old, and female – 65-69 years old (Figure 8).

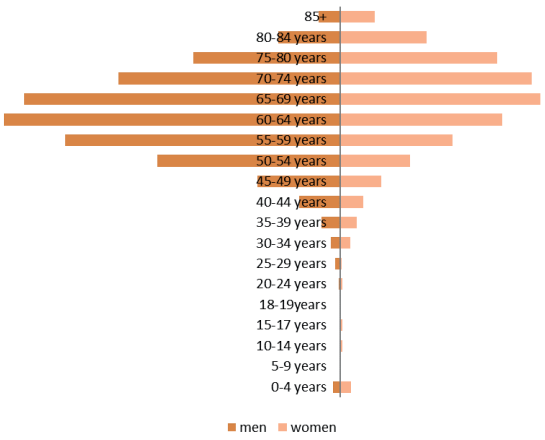


Figure 8 is the sex and age characteristics of liver cancer first detected in Kazakhstan over 10 years, abs

Thus, it is important to pay attention to the age category starting from 45 years of age for the risk of liver cancer in the population in Kazakhstan.

Table 8 - Evaluation of the effectiveness of the oncological service by ranking the Index of reliability of accounting for liver cancer (C22) in the world, 2020 [https://gco.iarc.fr/today/data-sources-methods]

Region	Standardized indicator		Iду
	Mortality	Morbidity	
East Asia	17,8	16,1	0,9
North Africa	14,5	15,2	0,9
North America	4,7	6,8	0,7
Western Europe	4,5	5,4	0,8
Central America	5,9	6,3	0,9
Northern Europe	3,9	4,9	0,8
South-central Asia	2,8	3,0	0,9
Russia	7,25	6,12	1,1
Kazakhstan	2,9	5,1	0,57
Vietnam		27,1	
Switzerland		12,7	
Georgia		10,5	
India		2,5	
World	10,7	11,6	0,9

CONCLUSIONS

1) In Kazakhstan, the standardized incidence rates of liver cancer are low and amounted to 6.6 per 100 thousand of the population, and in the structure of morbidity they are not among the top ten registered malignant diseases, while liver cancer is in the first place among those who died who were not registered at the dispensary for the period 2013-2022. Also, liver cancer is one of the three leaders of malignant neoplasms with a low five-year survival rate;

2) It is necessary to introduce new modern approaches to early diagnosis and modern treatment of liver cancer in Kazakhstan;

3) To improve the effectiveness of oncological care for liver cancer in Kazakhstan, it is necessary to strengthen continuity at the stages of providing medical care to patients.

Authors's contribution

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Ethical approval

The study was approved by the West Kazakhstan Marat Ospanov University ethics committee.

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