

# Actual issues of secondary prevention of liver cancer in Kazakhstan

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## Abstract

Liver cancer is characterized by high mortality and low survival rates in most countries of the world. According to the WHO data, more than 1.3 million people with liver cancer die annually in the world and according to the data of the 9th volume of "Cancer on five continents" - the highest standardized incidence rates are in Korea - 44.9 per 100 thousand population as well as in Thailand, Japan, China. Low rates were in Algeria, India, Belgium and the Netherlands. In Russia 61.5% of patients die of liver cancer progression in the first year after diagnosis [1,2].

Information on the global burden of cancer in 2018 showed that the specific weight of liver cancer in the structure of malignant neoplasms (MN) is 8.2%, and in 2020 - 8.3% [3].

The worldwide peculiarity of liver cancer is its late diagnosis. Several evidence-based treatment options for liver cancer are currently available: liver transplantation for hepatocellular liver cancer (HCC) (according to the Milan criteria), radiofrequency ablation as a radical treatment option (RFA), chemoembolization for intrahepatic cholangiocarcinoma (TACE), and the administration of Sorafenib as systemic therapy [4].

Current approaches for the treatment of early-stage primary liver cancer are represented by hepatic RFA, and the efficacy of this approach depends on the subjective attentiveness and visual acuity of the clinician. The latest technique used in liver RFA is the hyperspectral imaging which utilize objective assessment [2].

Ultrasound is usually used to detect liver lesions, but the detection rate is low for many reasons, such as clinician skills and technical capabilities. Modern approaches of diagnostic capabilities, such as contrast-enhanced ultrasound integrated imaging (CEUS) and comprehensive ultrasound imaging - contrast-enhanced CT (CECT) or contrast-enhanced MRI (CEMRI) for visualization of focal liver lesions (FLL) - increase the confidence of the interventional physician so it should be recommended for use as a routine procedure [5-6].

The ratio of morbidity and mortality in many countries reaches 91.6%, which represents the third most important cause of cancer deaths [7-9].

**Keywords:** liver cancer, prevalence, incidence, regions of Kazakhstan

## Introduction

Late diagnosis is the peculiarity of liver cancer worldwide. Information on the global burden of cancer in 2018 showed that the specific weight of liver cancer in the structure of malignant neoplasms (MN) - 8.2%, and in 2020 - 8.3%. In Kazakhstan in 2021 - 2.8%.

The incidence of liver cancer in the world reaches up to 44.6 per 100 thousand population and in Kazakhstan - 4.7 in 2021.

**Objective:** To study the prevalence of liver cancer in Kazakhstan.

## Material and methods

A search in the databases of PubMed, Google Scholar, Rinz, statistical and analytical indicators materials of oncological service of Kazakhstan for 2019-2021 was conducted. The method of research is desk-based, retrospective.

Results and discussion

In 2021, the incidence of malignant neoplasms (MN) increased by 7.6% and amounted to 170.3, compared to 2020 - 157.3. The growth rate increased over two years +8.3%. In the structure of malignant neoplasms, liver cancer ranked 15th with a positive growth rate of +3.1% (Table 1).

Localization	Indicators					Growth rate, %	
	abs. number		to 100 000.			2020	2021
	2020	2021	2019	2020	2021		
	2020	2021	2019	2020	2021	2020	2021
All MNs, including	29701	32572	174,8	157,3	170,3	-10,3	8,3
Mouth	76	119	0,7	0,4	0,6	-42,9	54,6
Oral cavity	481	520	2,8	2,5	2,7	-4,8	6,7
Salivary gland	112	143	0,6	0,6	0,7	-	26,1
Nasopharynx	70	76	0,4	0,4	0,4	-	7,2
Throat	164	169	0,8	0,9	0,9	-20,0	1,7
Esophagus	1082	1130	6,3	5,7	5,9	-7,3	3,1
Stomach	2497	2576	14,4	13,2	13,5	-8,5	1,9
Colon	1645	1686	9,2	8,7	8,8	-4,9	1,2
Rectum	1471	1604	8,7	7,8	8,4	-11,5	7,7
Liver	861	899	5,4	4,6	4,7	-16,3	3,1
Pancreas	1143	1128	6,0	6,1	5,9	1,9	-2,6
Larynx	339	365	2,3	1,8	1,9	-20,0	6,3
Lungs	3375	3615	20,1	17,9	18,9	-11,6	5,8
Bones	141	143	0,8	0,7	0,7	-12,5	0,1
Soft tissues	381	439	2,2	2,0	2,3	-5,0	13,8
Skin melanoma	283	360	1,9	1,5	1,9	-23,5	25,6
Mammary gland	4307	5021	26,6	22,8	26,3	-14,9	15,1
Uterine cervix	1672	1804	9,6	8,9	9,4	-8,1	6,5
Uterine corpus	1074	1240	6,4	5,7	6,5	-11,9	14,0
Ovary	1010	1249	6,2	5,3	6,5	-12,0	22,1
Prostate	970	1169	6,6	5,1	6,1	-23,6	19,0
Kidneys	1029	1292	6,7	5,5	6,8	-18,3	24,0
Bladder	667	737	4,1	3,5	3,9	-13,5	9,1
Nervous system	785	765	3,8	4,2	4,0	11,4	-3,8
Thyroid	612	712	4,3	3,2	3,7	-25,6	14,9
Blood	1702	1713	8,3	9,0	9,0	9,1	-0,6
Lymphoma	837	886	4,4	4,4	4,6	9,1	4,5
Leukemia	865	827	3,8	4,6	4,3	9,1	-0,6

For economically developed countries the standardized indicator of the population morbidity with MN is within 250-350, for developing countries - 100-120. According to these benchmarks, Kazakhstan is striving to reach the levels of indicators of economically developed countries in recent years.

Graphical analysis of the growth rate of liver cancer in the structure of MN in Kazakhstan showed that liver cancer is characterized by low intensity of detection compared to the previous year, despite the positive growth rate (Figure 1).

Analysis of regional peculiarities of 2021 in the structure of MN in Kazakhstan allowed to single out regions with high morbidity rates - the highest rate of MN is breast cancer in Pavlodar region - 48.0, East Kazakhstan (EKR) - 40.0 and lung cancer in North Kazakhstan - 39.0 (SKR) (Table 2).

Regions with high liver cancer incidence rates are Pavlodar region - 7.0, East-Kazakhstan - 6.8 and Atyrau region - 6.3; with low rates - Turkistan region - 2.6, Kostanay region - 2.7, North Kazakhstan - 3.7 (Figure 2).

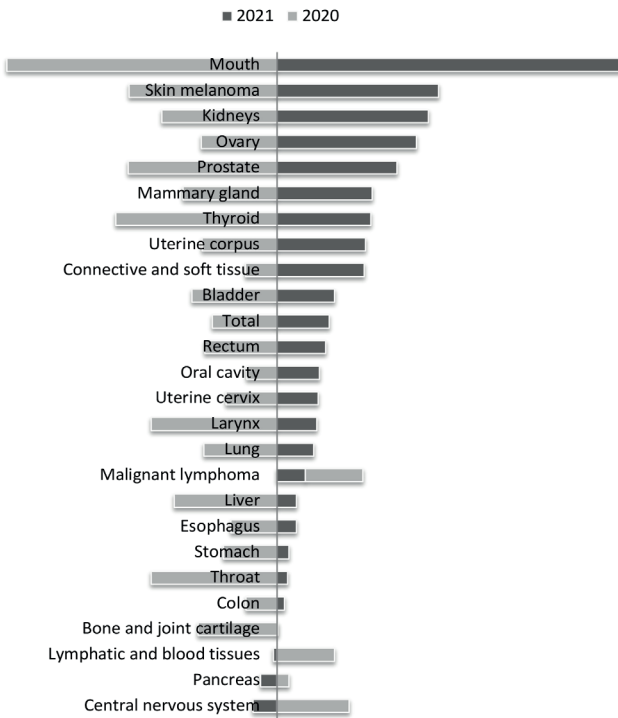


Figure 1 - Growth rate of liver cancer incidence in the structure of the population in Kazakhstan, Gr.

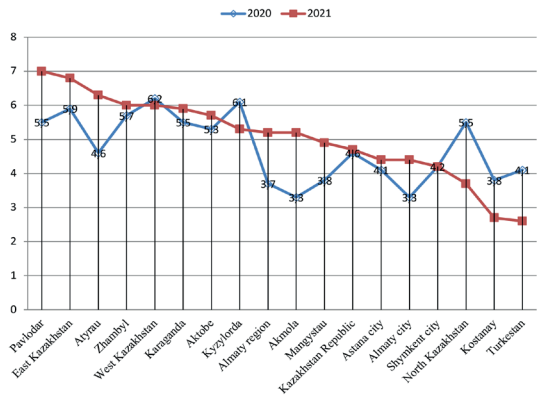


Figure 2 - Liver cancer incidence in the regions of Kazakhstan

The analysis of regional peculiarities in 2021 of MN structure in Kazakhstan showed that the highest specific weight of liver cancer in Zhambyl and Mangystau regions - 4.9% and 4.5%, Atyrau region 4.1% and Kyzylorda region - 3.9%, and less specific weight in Kostanay region - 1.1%, North Kazakhstan - 1.3% (Figure 3).

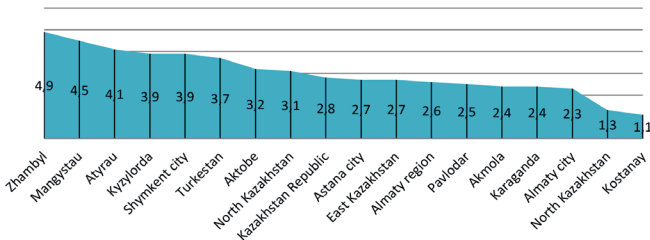
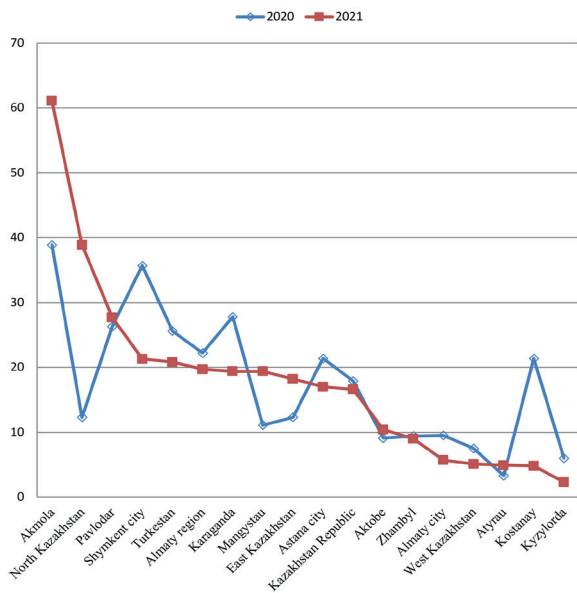


Figure 3 - Specific weight of liver cancer in the structure of MN by regions of Kazakhstan, 2021, %

Analysis of regions with a high proportion of stage 4 liver cancer in 2020-2021 showed that the most disadvantaged region is Akmola region - 38.9/61.1%, SKO - 38.9%, and Pavlodar region - 27.7% (Figure 4).

**Table 2** Incidence of liver cancer in the structure of MN in the population of the Republic of Kazakhstan in 2021, per 100 thousand population.

MN localization	Name of regions																	
	Kazakhstan Republic	Akmola	Aktobe	Almaty region	Atyrau	East Kazakhstan	Zhambyl	West Kazakhstan	Karaganda	Kyzylorda	Kostanay	Mangystau	Pavlodar	North Kazakhstan	Turkistan	Nur-Sultan city	Almaty city	Shymkent city
Total	170	216	177	119	152	255	123	192	244	137	245	110	281	287	71	166	193	109
Oral cavity	2.7	4.1	3.4	1.6	3.4	4.7	2.3	3.0	3.1	1.8	4.4	1.1	5.2	6.9	0.9	2.3	2.6	1.3
Esophagus	5.9	6.5	10	4.1	8.1	5.3	5.9	11	6.6	12	6.3	8.1	5.0	6.3	4.5	4.1	3.6	4.2
Stomach	13	17	19	11	14	18	10	19	18	12	16	9.7	17	25	6.7	13	12	7.4
Colon	8.8	10	9.0	4.7	8.7	13	5.8	10	15	4.6	16	4.9	15	13	2.7	9.0	12	4.0
Rectum	8.4	13	8.1	5.6	6.3	14	5.1	9.8	12	5.3	16	2.8	18	15	2.7	9.0	7.8	5.0
Liver	4.7	5.2	5.7	3.1	6.3	6.8	6.0	6.0	5.9	5.3	2.7	4.9	7.0	3.7	2.6	4.4	4.4	4.2
Pancreas	5.9	9.1	6.3	3.8	5.8	8.7	5.4	6.9	9.0	5.1	8.4	3.2	9.8	7.1	2.3	5.6	6.4	3.6
Lungs	19	32	20	10	21	31	14	25	29	15	25	9	35	39	7	17	17	10
Bones	0.7	1.1	1.3	0.5	1.0	0.2	0.6	0.8	0.6	2.2	0.7	0.4	0.8	2.0	0.3	0.8	0.8	0.4
Connective tissues	2.3	1.5	2.4	1.9	1.5	2.3	3.0	3.5	2.8	2.8	4.7	1.2	4.1	3.9	0.9	1.5	2.4	1.7
Melanoma	1.9	2.0	1.1	1.1	0.7	3.8	0.9	0.9	3.1	1.0	3.7	1.5	3.9	5.4	0.4	1.1	2.9	0.6
Mammary gland	26	30	24	17	16	40	15	28	40	14	36	17	48	38	12	28	35	22
Uterine cervix	9.4	12	12	9.5	12	11	5.7	11	12	8.2	11	10	17	10	5	7	8	7
Uterine corpus	6.5	9.3	6.1	4.7	4.2	10	4.6	5.7	9.6	4.8	9.4	3.1	10	15	1.3	6.5	8.5	4.3
Ovary	6.5	6.9	6.4	5.4	6.7	7.2	4.3	7.2	7.5	8.3	9.6	3.2	9.4	6.3	3.5	7.7	9.3	4.1
Prostate	6.1	7.1	3.6	4.3	1.6	14	4.4	5.6	10	1.0	12	2.7	11	16	1.0	4.3	7.6	3.1
Kidneys	6.8	0.4	6.6	4.0	6.9	9.4	4.1	4.5	9.5	3.9	10	4.9	12	14	2.5	9.4	8.4	3.1
Bladder	3.9	5.7	3.2	2.8	2.1	7.0	2.8	3.6	6.4	2.7	5.7	2.0	6.4	7.6	1.1	2.6	4.8	2.3
CNS	4.0	4.8	5.2	4.1	3.3	4.1	4.2	4.1	3.1	4.5	3.6	3.1	6.3	5.2	2.3	4.3	5.7	1.7
Thyroid	3.7	3.8	3.4	3.0	0.6	5.8	2.1	3.8	4.8	4.1	2.9	1.9	5.2	8.0	0.5	6.3	5.9	2.6
Blood	9.0	6.9	6.7	6.3	7.2	13	5.0	8.1	16	6.8	11	6.9	14	19	5.0	9.3	12	4.8



**Figure 4** - Specific weight of stage 4 liver cancer in Kazakhstan, %

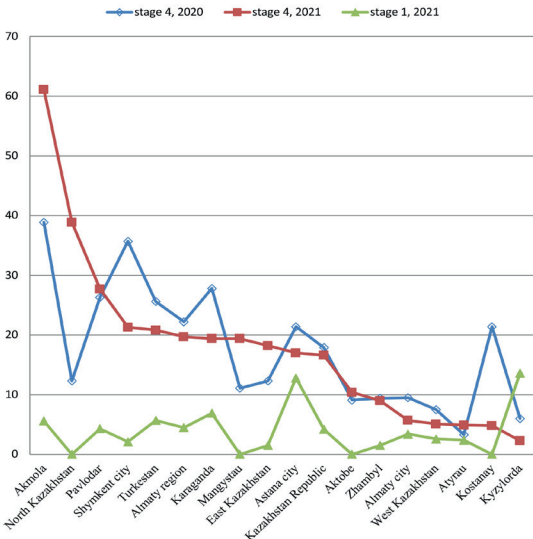
Analysis of regions with low specific weight of stage 1 liver cancer in 2020-2021 showed that the most unfavorable region is Akmola - 38.9/61.1%, North Kazakhstan - 38.9%, and Pavlodar region - 27.7% (Figure 5).

Regions with high mortality rate from liver cancer in 2020: East Kazakhstan and West Kazakhstan - 4.8; Pavlodar region - 4.4. In 2021: East Kazakhstan - 5.4; Pavlodar region - 4.7; West

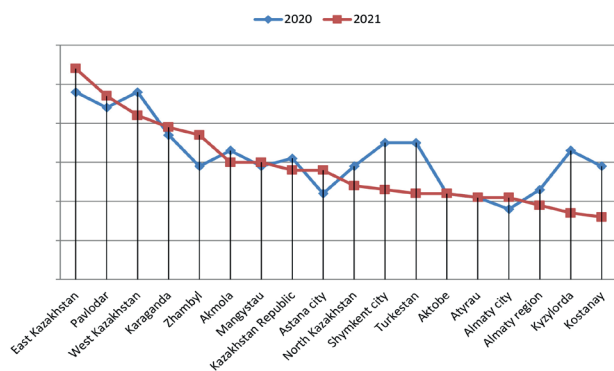
Kazakhstan - 4.2 per 100 thousand population (rough indicators).

Regions with low mortality rate from liver cancer in 2020: Almaty city - 1.8; Atyrau region - 2.1; Aktobe region - 2.2. In 2021: Kostanay region - 1.6; Kyzylorda region - 1.7; Almaty region - 1.9 per 100 thousand population (rough indicators) (Figure 5).

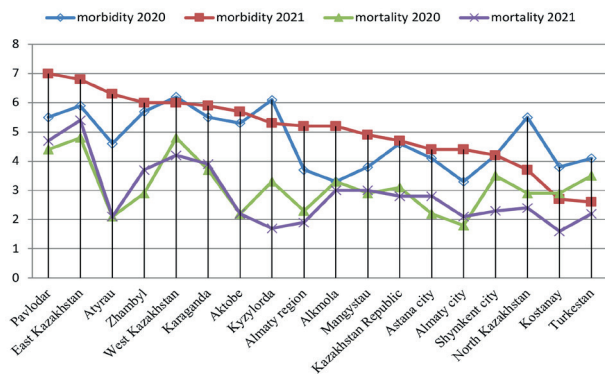
For the indicator by regions: morbidity, mortality, post-mortem (Figure 6).



**Figure 5** - Specific weight of stage 1 and 4 liver cancer in Kazakhstan, %



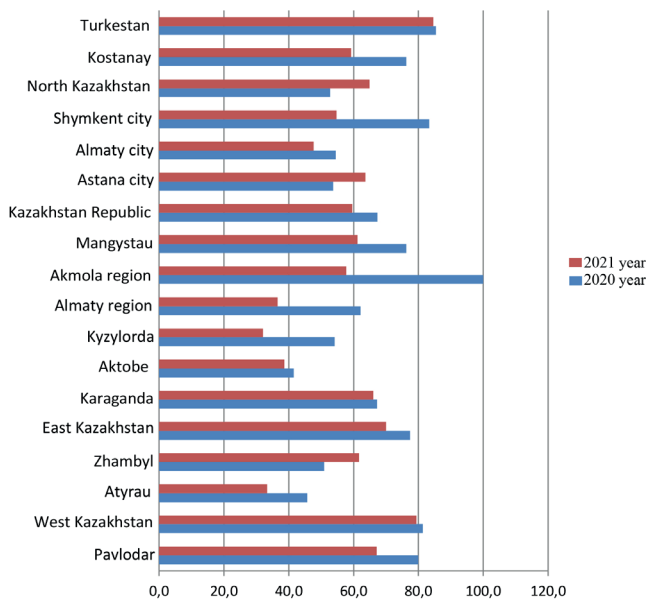
**Figure 5** - Mortality of Kazakhstan population from liver cancer by regions, per 100 thousand population.



**Figure 6** - Morbidity and mortality of liver cancer in Kazakhstan by region.

Analyzing the data of morbidity and mortality rates by regions, attention is drawn to the indicators of high morbidity and low mortality in the regions: Atyrau, Zhambyl, Aktope and Kyzylorda and North Kazakhstan.

The ratio of incidence and mortality from liver cancer in Kazakhstan in 2020-2021 is 67.4/59.57. By region, this indicator varies from 33.3 to 100: regions with high ratio - Akmola in 2020 100, in 2021 - 57.7; Turkestan 85.4/84.6, East Kazakhstan 81.4/79.4, Pavlodar region 80.0/67.4. With low ratio - Atyrau 45.7/33.3; Aktope 41.5/38.6; Kyzylorda 54.1/32.1 (Figure 8).

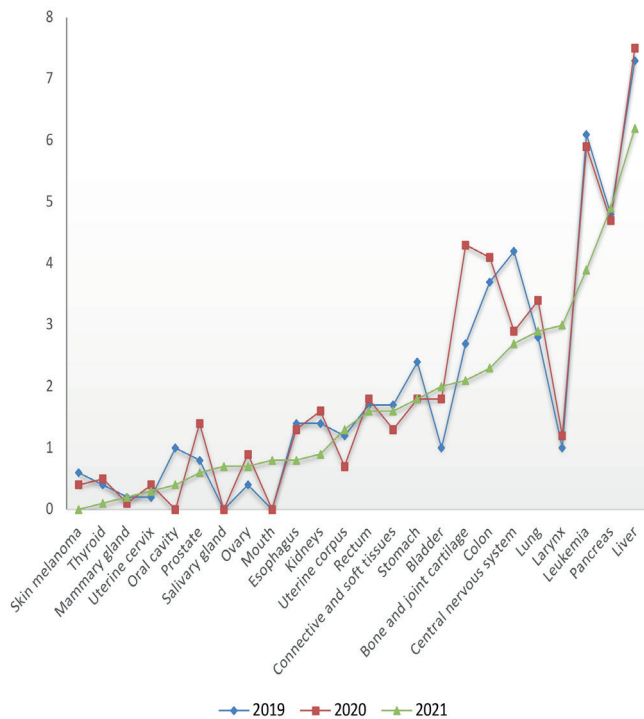


**Figure 8** - Ratio of liver cancer incidence and mortality in Kazakhstan by region

In 2020, a high ratio was observed in Akmola region, Turkestan region and Shymkent city, and in 2021 - Turkestan region, East Kazakhstan and Pavlodar region.

It is important to estimate the proportion of postmortem detected patients for the quality indicator of lifetime diagnostics of liver cancer.

The highest share of postmortem-detected cancer patients in Kazakhstan was recorded for 2019-2021 for liver cancer and amounted to - 7.3-7.5-6.2%. The minimum share is within 0-0.9% for 12 localizations, average - from 1 to 3% for localizations and above average from 3-7.5% for 6 localizations (Figure 9).



**Figure 9** - Share of liver cancer deaths not registered with oncology organizations, %

Full 100% confirmation of the postmortem diagnosis by autopsy in 2020 was provided by oncological organizations of Zhambyl, Karaganda, Kostanay regions and Almaty city. Autopsies were not performed in 2020 and 2021 in Aktope and Turkestan regions. In Kazakhstan, the overall rate of posthumously detected patients was -1.8% in 2019, 2.0% in 2020, and 1.6% in 2021. If we compare it with the indicators in Russia, the average indicator is 5.3% [The state of oncological care in Russia in 2019].

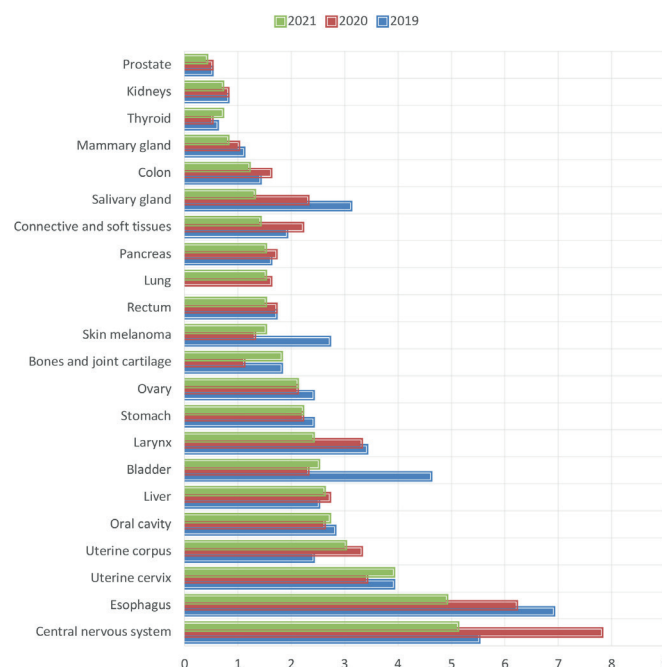
The ratio of one-year mortality and neglect (stage 4) in the republic in 2019-2021 was 1,9 – 1,8 - 1,7 , the recommended indicator is 1.0. In the first place of the worst indicator was taken by the central nervous system, but, liver cancer was in 6th place (Figure 10).

For the period 2019-2021, liver cancer in the ratio between one-year mortality and stage 4 negatively is ranked sixth place.

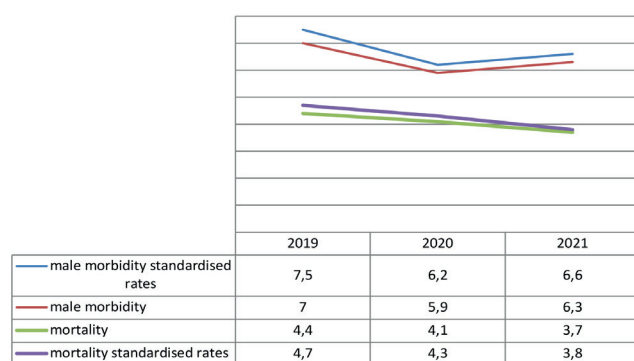
Analyzing liver cancer rates by gender for the study period, there is a positive indicator in the decreasing the incidence in men - Increase rate of -14.3% in 2020 and a significant increase in incidence rate of +7.3% in 2021. At the same time, mortality is steadily decreasing by -9.7% (Table 3).

The growth rate of morbidity and mortality shows how fast the indicator is increasing or decreasing in comparison with previous year. The values used for calculation are current value and comparable value according to the formula: current value/ comparable value x 100%. 543/634 x 100% - 100%





**Figure 10** - Correlation between one-year mortality and liver cancer neglect in the structure of MN in Kazakhstan (stage 4).



**Figure 11** - Features of morbidity and mortality of liver cancer in Kazakhstan in men, per 100 thousand population.

**Table 3**

Indicators of first-time diagnosis of liver cancer in Kazakhstan in men, rough indicators

Men								
Indicators	abs. number			to 100 000.			growth rate	
	years							
	2019	2020	2021	2019	2020	2021	2020	2021
Morbidity	634	543	583	7,0	5,9	6,3	-14,3	+7,3
Mortality	397	373	341	4,4	4,1	3,7	-6,8	-9,7

The incidence of MN population in the males was 151.3 or 14048 cases (2020 142.3 - 13036 cases) per 100,000 and in females was 171.5 and 188.3 in 2021.

Liver cancer in males were 7.0 - 5.9 - 6.3 per 100,000 population and in females were 4.4 - 4.1 - 3.7 respectively (Figure 11) in 2019-2021.

For women, growth rate of morbidity decreased -15.9 in 2019, and -0.6% in 2021, and mortality were 19.2% and -4.7%, respectively (Table 4).

The morbidity of the male population of MN is 151.3 or 14048 cases (2020 142.3 - 13036 cases) per 100,000 population and in females 171.5 and 188.3 in 2021.

What are the dangers of fast and slow rates? Fast positive rates can lead to unrealistic expectations and negative fast rates

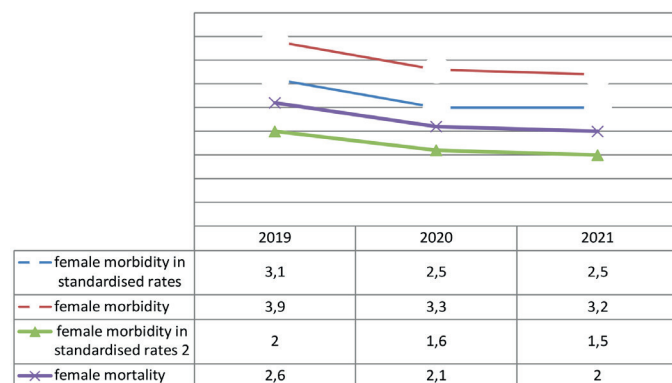
**Table 4**

Indicators of diagnosis liver cancer in Kazakhstan among women for the first time their life, rough indicators

Women								
Indicators	abs. number			to 100 000.			growth rate	
	years							
	2019	2020	2021	2019	2020	2021	2020	2021
Morbidity	378	318	316	3,9	3,3	3,2	-15,9	-0,6
Mortality	245	207	197	2.6	2.1	2.0	-19.2	-4.7

can lead to unreasonable funding. To analyze a negative growth rate, other indicators need to be analyzed: the status of liver cancer detection in population screenings and post-mortem liver cancer detection rates.

Liver cancer rates for men were 7.0 - 5.9 - 6.3 per 100,000 population, for women, respectively, 3.9 - 3.3 - 3.2 in 2019-2021 (Figure 12).

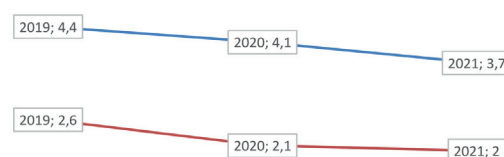


**Figure 12** - Features of liver cancer morbidity and mortality in women in Kazakhstan, per 100 thousand population.

By analyzing the data of liver cancer by sex, no significant difference was found in results ( $p \leq 0.05$ ).

The mortality rate from MN decreased in both sexes by 4.5%, from 74.9 to 71.5 per 100,000 population, and the standardized mortality rate decreased by 5.1% in 2021.

The ratio of the standardized mortality rate from MN of men to that of women is stable at 1.6:1.0. The ratio of standardized liver cancer mortality rate is 2.5:1.0 in 2021, while there is a decrease in mortality in women over the three years to 4.4 in 2019, 4.1 in 2020 and 3.7 in 2021. Males also show a decrease in mortality rate of 4.4-4.1-3.7, respectively (Figure 13).



**Figure 13** - Liver cancer mortality by sex, per 100,000 population.

In 2021, the number of patients with MN decreased from 647 to 562 deaths, or by 13%, and was 1.6%, in 2020 - 2.0%. Comparatively, in Russia this indicator in 2020 was 6.9%.

By regions of Kazakhstan mortality rates from MN show dependence on the sex and age composition of the population. The specific weight of liver cancer in the structure of MN in Kazakhstan for 2019-2021 ranked 5/8 in men and 12/12 in women.

The most consistently low five-year survival rate of patients with MN in Kazakhstan with liver and pancreatic cancer, and high - MN of bones and articular cartilage and larynopharynx (Figure 14).

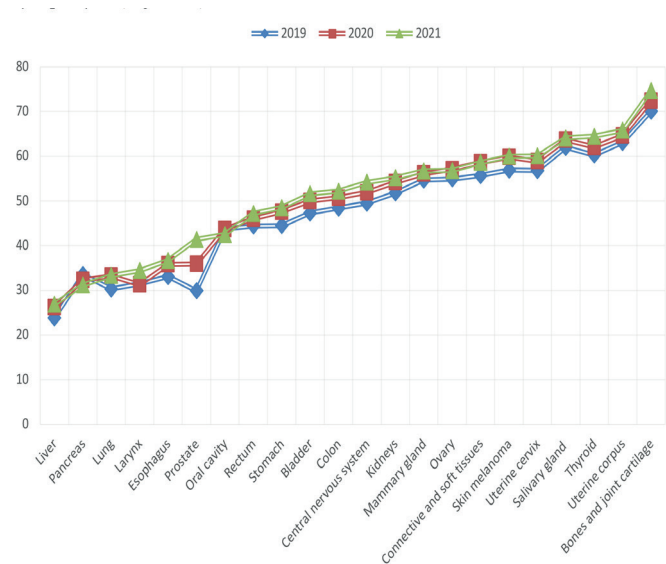


Figure 14 - Five-year survivability of patients with liver cancer in Kazakhstan, %

The five-year survivability of liver cancer is the lowest - this is another factor confirming liver cancer in the early stages. Official statistical compilations do not take into account the coverage of special treatment in oncology. The radical treatment of liver cancer is interventional method in the early stages in Kazakhstan (Figure 15).

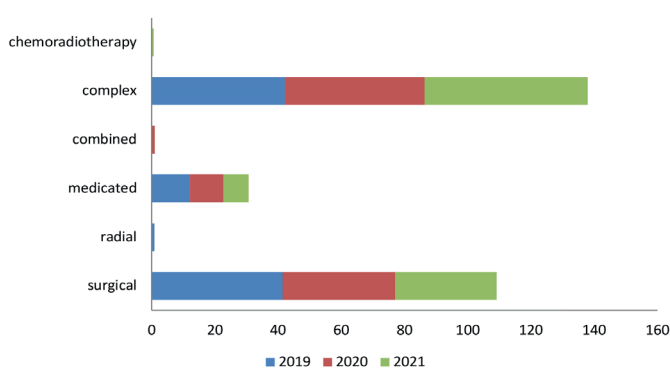


Figure 15 - Coverage of specialized treatment for liver cancer patients in the Republic of Kazakhstan

Results and discussion

For the period 2019-2020, liver cancer ranked 7th in the structure of standardized morbidity rates in men and its specific weight was 7.5% in 2019, and 6.2% and 9th in 2020, growth rate = -17.3 in the structure of malignant neoplasms (MN) morbidity in Kazakhstan. In females it is 3.1/2.5, growth rate = -19.3. Standardized incidence rates of liver cancer were 4.9 per 100,000 population in 2019 and 4.1 in 2020, growth rate = -16.3. Mortality from liver cancer was 3.4 per 100,000 population in 2019 and 3.1 in 2020: in men 4.4/4.1 and in women 2.6/2.1 respectively. Place in mortality structure was 10th place - in 2019; and 8th in 2020. In 2020, the top three regions with high mortality rates from liver cancer were East Kazakhstan - 4.8. West-Kazakhstan

- 4.8, Pavlodar - 4.4; the three lowest indicators were identified: Almaty city - 1.8; Atyrau - 2.1; Aktoobe and Astana - 2.2. The number of deaths from malignant neoplasms not registered with oncological organizations - liver cancer in the first place in 2019 and 2020, blood cancer in the second place, pancreatic cancer in the third place. The top three diseases with the highest one-year mortality rates are pancreatic cancer at 59.6%, liver cancer at 46.9% and oesophageal cancer at 43.4% in 2020. At the same time, compared to 2019, liver cancer showed a worsening of this indicator by 17.7%. The leading negative place over 2 years for the ratio between one-year mortality and neglect (stage 4) belonged to malignant neoplasms of the central nervous system - 5.5 and 7.8 The positive ratio (1.0) was breast cancer in 2019 and bone and articular cartilage cancer - 1.1 in 2020. In Kazakhstan, the lowest five-year survival rate for liver cancer patients was 23.8 % in 2019 and 26.2 %in 2020. Pancreatic cancer has a slightly better statistics like 33.5% and 32.3%, and also, blood cancer numbers at 53.7% and 54.4%.

Conclusion

In Kazakhstan, standardized indicators of liver cancer incidence are low, and in the structure of morbidity they are not among the top ten of the number of registered malignant diseases, while liver cancer is in first place among the deceased who are not registered at the dispensary during 2019 and 2020. Also, liver cancer is one of the three stable anti-leaders of malignant neoplasms with mortality within a year and low five-year survival. It is necessary to introduce new modern approaches to early diagnosis and modern treatment of liver cancer in Kazakhstan. It is necessary to include in the monitoring of liver cancer treatment methods - an interventional method that is used worldwide in routine practice for early diagnosis of liver cancer.

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