RESEARCH ARTICLE

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Liver Cancer Incidence in Kazakhstan: Fifteen-Year Retrospective Study

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Abstract

Objective: The aim is to study the trends of liver cancer (LC) incidence in the regional context in Kazakhstan. **Methods:** The retrospective study was done using descriptive and analytical methods of oncoepidemiology. The extensive, crude and age-specific incidence rates are determined according to the generally accepted methodology used in sanitary statistics. The data were used to calculate the average percentage change (APC) using the Joinpoint regression analysis to determine the trend over the study period. **Results:** Between 2005 and 2019, 13,510 cases of LC were documented, comprising 59.3% males and 40.7% females. Most diagnoses were seen in age groups 55-59 years (13.3%) to 75-79 years (11.7%). LC patients' average age increased from 63.6 to 64.5 years. Incidence rates per 100,000 peaked at ages 65-69 years (35.1±1.0) and 70-74 years (43.3±1.0). LC incidence notably rose in the 70-74 years age group (APC=+0.89), contrasting with declining trends in younger age groups. Regional incidence variations revealed diverse patterns, mostly demonstrating unimodal increases, and some regions displaying bimodal growth. The age-standardized incidence rate was 5.7±0.1 per 100,000, declining from 2005 to 2012 (APC: −3.93), then rising until 2019 (APC: +1.13). Gender-specific standardized rates showed varied trends. Analyses of standardized indicators indicated declining trends in most regions but increased values in specific areas. Thematic maps classified incidence rates based on standardized indicators: low (up to 5.22), average (5.22 to 7.11), high (above 7.11 per 100,000 for the entire population). **Conclusion:** The study on liver cancer in Kazakhstan reveals marked gender and age differences. The standardized incidence rate among men was twofold greater than that among women. A distinct rise in cases was noted among individuals aged 70-74 years. Regional variations in incidence were evident. These findings emphasize the necessity for focused research to comprehend the causes behind these differences, enabling customized interventions for Kazakhstan's population.

Keywords: Liver cancer - incidence - trends - geographical variation – Kazakhstan

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Introduction

Primary liver cancer stands as a substantial global health challenge, ranking as the sixth most prevalent cancer and the third leading cause of cancer-related fatalities [1]. The primary causes encompass chronic infections like hepatitis B virus (HBV) and hepatitis C virus (HCV), alcoholic liver disease, and non-alcoholic fatty liver disease (NAFLD) [2]. Nonetheless, these causal factors exhibit significant regional variations. For instance, chronic HBV infection and aflatoxin contamination in food represent critical risk factors in China and East Africa, respectively. Conversely, in countries like Egypt and Japan, chronic HCV infection predominantly drives the occurrence of liver cancer. In Western nations, the leading causes include chronic HCV infection, alcohol

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consumption, and obesity-related diabetes for liver cancer [3].

Primary prevention of LC involves mitigating the risk factors contributing to its one, such as vaccination against hepatitis B virus (HBV) and abstaining from alcohol consumption. Secondary prevention aims to diminish LC development in individuals already at risk, primarily through antiviral therapy for HBV and HCV to impede the advancement of chronic liver inflammation and fibrosis. Tertiary prevention endeavors to avert new LC occurrences within the residual liver tissue post curative treatment in individuals who have already experienced LC development [4].

The World Health Organization (WHO) advocates universal neonatal vaccination against hepatitis B virus (HBV), emphasizing immunization for all newborns irrespective of the mother's HBV status [5]. This approach stands as a fundamental preventive measure against LC in Kazakhstan. In Kazakhstan, the hepatitis B vaccination is administered following the guidelines stipulated within the "National Vaccination Calendar of the Republic of Kazakhstan" officially sanctioned by the Government's Decree No. 612 of September 24, 2020. The national vaccination program, funded through the republic's budget, specifies the administration schedule: the HBV vaccine is administered to infants within 1-4 days after birth, at 2 and 4 months, and to adults with intervals of 1 month between the first and second doses and 5 months between the second and third doses [6]. Particularly individuals with heightened susceptibility to HBV infection, such as family members of chronic hepatitis B patients, healthcare professionals, travelers visiting areas with elevated HBV prevalence, individuals engaging in injection drug use, and those with multiple sexual partners, are recommended for HBV vaccination. Ensuring adherence to these vaccination protocols remains critical to mitigating HBV transmission and subsequently reducing the risk of LC development within the population.

Chronic liver disease of diverse origins stands as the most pivotal risk factor, contributing to approximately 80% to 90% of new cases of LC within this demographic [7]. To address the global disease burden, surveillance initiatives have been formulated to enable early detection and lower mortality rates. Current recommendations advise active participation in surveillance programs, advocating for adults afflicted with cirrhosis and individuals at high risk, even without cirrhosis, utilizing ultrasound (US) either alone or in combination with alpha-fetoprotein (AFP) assessments at intervals of six months. These guidelines represent a consensus among major international societies, inclusive of the American Association for the Study of Liver Disease (AASLD), the European Association for the Study of the Liver (EASL), and the Asian Pacific Association for the Study of the Liver (APASL) [8-10]. Surveillance programs necessitate robust recall strategies for addressing abnormal findings detected via ultrasound imaging. Lesions measuring less than 1 cm may warrant follow-up with subsequent US evaluations (with or without AFP) within a span of 3-6 months. Further management of aberrant surveillance imaging, encompassing lesions larger than 1 cm, aligns with the principles outlined in the Liver Imaging Reporting and Data System (LI-RADS). For lesions classified as LI-RADS 4 (probably LC) or LI-RADS M (malignancy but not definitively LC), diagnostic liver biopsy might be necessary [10].

Conducting an epidemiological investigation in Kazakhstan to examine the liver cancer incidence holds paramount importance in comprehending the disease's prevalence, associated patterns, and risk factors prevalent in the population. The primary aim of this study is to elucidate the trends characterizing liver cancer incidence across diverse demographic segments and geographical locales. The outcomes of this research endeavor are anticipated to contribute significantly to the development of advanced early detection methodologies and diagnostic protocols, fostering timely interventions and fostering enhanced treatment outcomes for patients. Ultimately, the findings derived from this epidemiological inquiry will serve as a pivotal framework for policymakers and healthcare authorities, empowering them to devise evidence-based public health strategies and optimize resource allocation to mitigate the liver cancer burden within Kazakhstan.

Materials and Methods

Cancer registration and patient recruitment

Incidences of novel cases of Liver Cancer (LC) were derived from the Ministry of Health of the Republic of Kazakhstan's reporting forms (form 7) spanning the years 2005 to 2019. The identification utilized the International Disease Code 10 with the code C22.

Population denominators

The populace data was sourced from the Bureau of National Statistics, incorporating considerations of age and gender attributes along with administrative-territorial demarcations. [11].

Statistical analysis

The primary approach employed in this investigation encompassed a retrospective study employing descriptive and analytical techniques within the field of oncoepidemiology. Age-standardized rates (ASR) were computed for eighteen distinct age strata (0-4, 5-9, ..., 80-84, and 85+) by adopting the world standard population established by the World Health Organization [12], in accordance with guidelines provided by the National Cancer Institute [13].

The comprehensive crude rate (CR) and age-specific incidence rates (ASIR) were computed employing the established methodology commonly utilized in sanitary statistics. The following statistical metrics were computed: annual averages (M, P), mean error (m), Student's criterion, and a 95% confidence interval (95% CI). In statistical analysis, the mean error typically pertains to the average discrepancy between estimates and actual values [14]. Student's criterion, often referred to as the t-test, serves the purpose of comparing means between two groups by utilizing the difference in means divided by an estimate of the standard error of the difference [14].

Additionally, the degree of approximation (R2) was ascertained. The level of approximation in linear regression assesses the proximity of the linear model to the original dataset. This metric gauges the extent to which the model aligns with the data and its capacity to predict dependent variable values with accuracy, predicated upon the independent variables.

In this study, we have refrained from presenting the fundamental calculation formulas, as these are extensively elucidated within methodological guidelines and textbooks dedicated to medical and biological statistics [15, 14, 16]. The assessment of the incidence trend spanned a period of 15 years. This trend's determination was carried out utilizing the least squares methodology and facilitated by the employment of the Joinpoint program (https://surveillance.cancer.gov/joinpoint/). The dataset was harnessed for the computation of the average percentage change (APC) through the application of Joinpoint regression analysis.

During the creation of thematic maps, a 15-year (2010-2019) dataset of comprehensive CRs and ASRs was employed. The mapping technique utilized is rooted in the computation of the standard deviation (σ) from the mean value (x), as outlined by Igisinov [17]. This methodology serves as a valuable tool for illustrating spatial variations within the data. It effectively identifies regions characterized by deviations from anticipated values and visually represents dissimilarities in spatial distribution on a geographical map. The thematic maps were generated utilizing the geographic information system QGIS version 3.18.

Ethics approval

The study encompassed an examination of publicly accessible administrative data and did not necessitate interactions with individual subjects. The study's conduct received approval from the Local Ethics Commission of the Central Asian Institute for Medical Research.

Results

During the investigation, spanning from 2005 to 2019, a total of 13,510 cases of liver cancer were recorded. Of these cases, 8,006 (59.3%) were male, and 5,504 (40.7%) were female. Liver cancer was most commonly diagnosed at the age groups of 55-59 years (13.3%), 60-64 years (14.9%), 65-69 years (17.2%), followed by 70-74 years (15.4%), and 75-79 years (11.7%).

Regarding gender-specific patterns, liver cancer was most frequently diagnosed in women within the age range of 60-64 years (32.5%), 65-69 years (23.4%), subsequently in the 70-74 years age bracket (23.4%), and lastly among those aged 75-79 years (17.3%). In the case of men, the majority, representing 63.4% of liver cancer cases, were diagnosed between the ages of 55-59 years (15.3%), 60-64 years (16.6%), 65-69 years (17.6%), and 70-74 years (14.0%).

The average age of liver cancer patients exhibited a marginal increase over time, rising from 63.6±0.4 years (95% CI=62.8-64.5) in 2005 to 64.5±0.4 years (95% CI=63.8-65.2) in 2019. Specifically, the average age for all patients was 64.1±0.2 years (95% CI=63.8-64.5) with an APC of +0.1. When stratified by gender, the average age for males was 63.0±0.2 years (95% CI=62.7-63.4) with an APC of +0.09, while for females, it was 65.7±0.3 years (95% CI=65.2-66.3) with an APC of +0.14 (Table 1).

The age-specific incidence rates per 100,000 were most pronounced in the following age brackets: 65-69 years (35.1±1.0), 70-74 years (43.3±1.0), 75-79 years (43.5±1.7), and 70-74 years (36.9±2.3). Gender-stratified age-related incidence rates are illustrated in Figure 1.

The incidence of liver cancer exhibited a propensity to increase solely within the 70-74 years age group (APC=+0.89). In contrast, other age groups displayed a declining trend in liver cancer incidence, with the most notable average annual reduction observed in the 30-34 years (APC=−5.62) and 35-39 years (APC=−5.67) age groups (Table 1). Specifically, a marginal inclination towards elevated incidence was observed in men aged

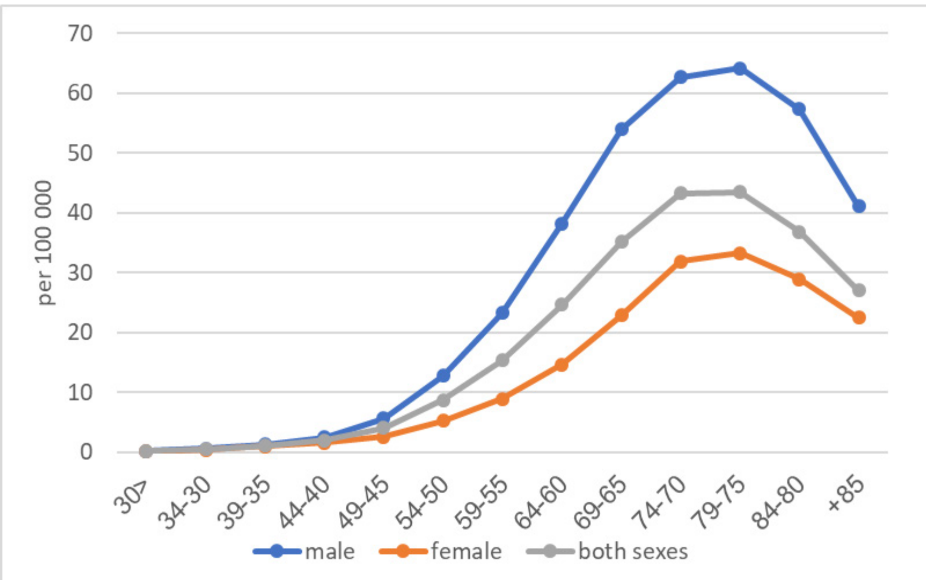


Figure 1. Age-Specific Incidence Rates of Liver Cancer in Kazakhstan, 2005-2019

between 70-74 years and those aged over 85 years. Among women, a rise in incidence was evident solely within the 70-74 years age bracket (Table 1).

Age-specific liver cancer incidence rates per 100,000 exhibited regional peculiarities in both genders. A common pattern across most regions was a unimodal increase, with the peak typically occurring in the 70-74 or 75-79 age groups. However, Almaty City stood out with the peak occurring in the 80-84 age group. In the Aktobe region and Astana City, a bimodal growth pattern was observed, with peaks in the 70-74 and 80-84 age groups (Figures 2A and 2B). These indicators of incidence by gender almost repeat the trends established in both sexes.

Crude liver cancer incidence rates per 100,000 population displayed a decreasing tendency, declining from 6.4±0.2 (95% CI=6.0-6.8) in 2005 to 4.8±0.2 (95% CI=4.5-5.2) in 2012 (APC=−3.66). Subsequently, from 2012 to 2019, there was an increase, reaching 5.5±0.2 (95% CI=5.1-5.8). The average annual incidence rate for the entire period amounted to 5.4±0.1 per 100,000 (95% CI=5.1-5.6) (APC=+2.19). In the male population, the standardized incidence rate for the study period was 8.5±0.2 per 100,000, following a similar pattern with an APC of −3.53 from 2005 to 2012 and an APC of +0.78 from 2012 to 2019 (Figure 3A). Conversely, in the female population, this rate was half that of males, at 3.9±0.1 per 100,000, showing a decreasing trend with an APC of −2.93 from 2005 to 2013 and an APC of +0.62 from 2013 to 2019 (Figure 3B). The age-standardized incidence rate for both sexes was 5.7±0.1 per 100,000 population, demonstrating a decreasing trend with an APC of −3.93 from 2005 to 2012 and an APC of +1.13 from 2012 to 2019 (Figure 3C).

Thematic maps were generated following the computation of average annual ASR LC indicators. These maps revealed variations in incidence rates between male and female populations across different regions. A cartographic representation constructed to encompass both male and female populations unveiled a pronounced concentration of elevated incidence rates in the geographical expanse situated towards the west, while demonstrating notably diminished occurrences in the northern regions (Figure 4). The ASR of LC were assessed for both genders per 100,000 individuals using the specified criteria: low rates were considered up to 5.22, average rates ranged between 5.22 and 7.11, and high rates were identified as exceeding 7.11. Consequently, distinct classifications of regions were identified based on these criteria, as illustrated in Figure 4C:

1. Regions with the lowest indicators (up to 5.22 per 100,000): North Kazakhstan (3.00), Kostanay (3.68), Almaty (4.49), Akmola (5.03), Pavlodar (5.19).

2. Regions with average indicators (from 5.22 to 7.11 per 100,000): Karaganda (5.49), Almaty city (5.51), East Kazakhstan (5.74), Zhambyl (6.15), Aktobe (6.29), Astana city (6.32), South Kazakhstan (6.90).

3. Regions with high indicators (7.11 and above per 100,000): Atyrau (7.45), Mangystau (8.24), West Kazakhstan (8.94), Kyzylorda (10.26).

Upon scrutinizing the average percentage change in

Table 1. Liver Cancer in Kazakhstan, 2005-2019

Age	All					Male					Female				
	Number	%	Incidence Rate per 100,000	APC, %	R^2	Number	%	Incidence Rate per 100,000	APC, %	R^2	Number	%	Incidence Rate per 100,000	APC, %	R^2
<30	140	1.6	0.2±0.01	−2.93	0.1475	77	1.5	0.2±0.02	−3.18	0.1244	63	1.7	0.1±0.02	−1.91	0.0374
30-34	99	0.7	0.5±0.1	−5.62	0.2297	56	0.7	0.6±0.1	−7.41	0.3655	43	0.8	0.4±0.1	−3.65	0.0325
35-39	193	1.4	1.1±0.1	−5.67	0.4205	105	1.3	1.2±0.2	−7.13	0.4584	88	1.6	1.0±0.2	−5.01	0.1032
40-44	333	2.5	2.0±0.1	−1.84	0.0796	194	2.4	2.4±0.2	−0.18	5.00E-05	139	2.5	1.6±0.2	−4.21	0.2665
45-49	645	4.8	4.0±0.2	−1.84	0.1415	425	5.3	5.6±0.4	−2.02	0.1436	220	4	2.6±0.2	−1.64	0.0773
50-54	1254	9.3	8.8±0.3	−2.25	0.5269	849	10.6	12.8±0.5	−1.63	0.2699	405	7.4	5.3±0.3	−3.55	0.6145
55-59	1794	13.3	15.3±0.7	−2.86	0.6673	1221	15.3	23.3±1.2	−2.37	0.4259	573	10.4	8.9±0.5	−4.28	0.6673
60-64	2014	14.9	24.6±0.9	−1.61	0.405	1326	16.6	38.3±1.5	−1.56	0.3297	688	12.5	14.7±0.7	−2.00	0.3994
65-69	2323	17.2	35.1±1.0	−0.95	0.1478	1408	17.6	53.9±1.5	−0.71	0.1033	915	16.6	22.8±1.0	−1.39	0.101
70-74	2077	15.4	43.3±1.0	0.89	0.221	1120	14	62.7±1.9	0.4	0.0344	957	17.4	31.9±1.2	1.54	0.2792
75-79	1578	11.7	43.5±1.7	−0.57	0.0154	771	9.6	64.1±3.2	−1.16	0.0462	807	14.7	33.2±1.5	−0.08	1.00E-06
80-84	721	5.3	36.9±2.3	−3.10	0.3734	316	3.9	57.4±4.7	−4.65	0.5405	405	7.4	28.9±2.0	−2.29	0.1535
85+	277	2.1	27.1±2.3	−1.44	0.0279	105	1.3	41.1±4.3	0.08	0.0072	172	3.1	22.5±2.2	−3.29	0.1236
Total	13510	100	5.4±0.1	−0.75	0.204	8006	100	6.6±0.2	−0.55	0.1061	5504	100	4.2±0.1	−1.05	0.2931

APC, average percentage change; R^2, the value of the approximation confidence.

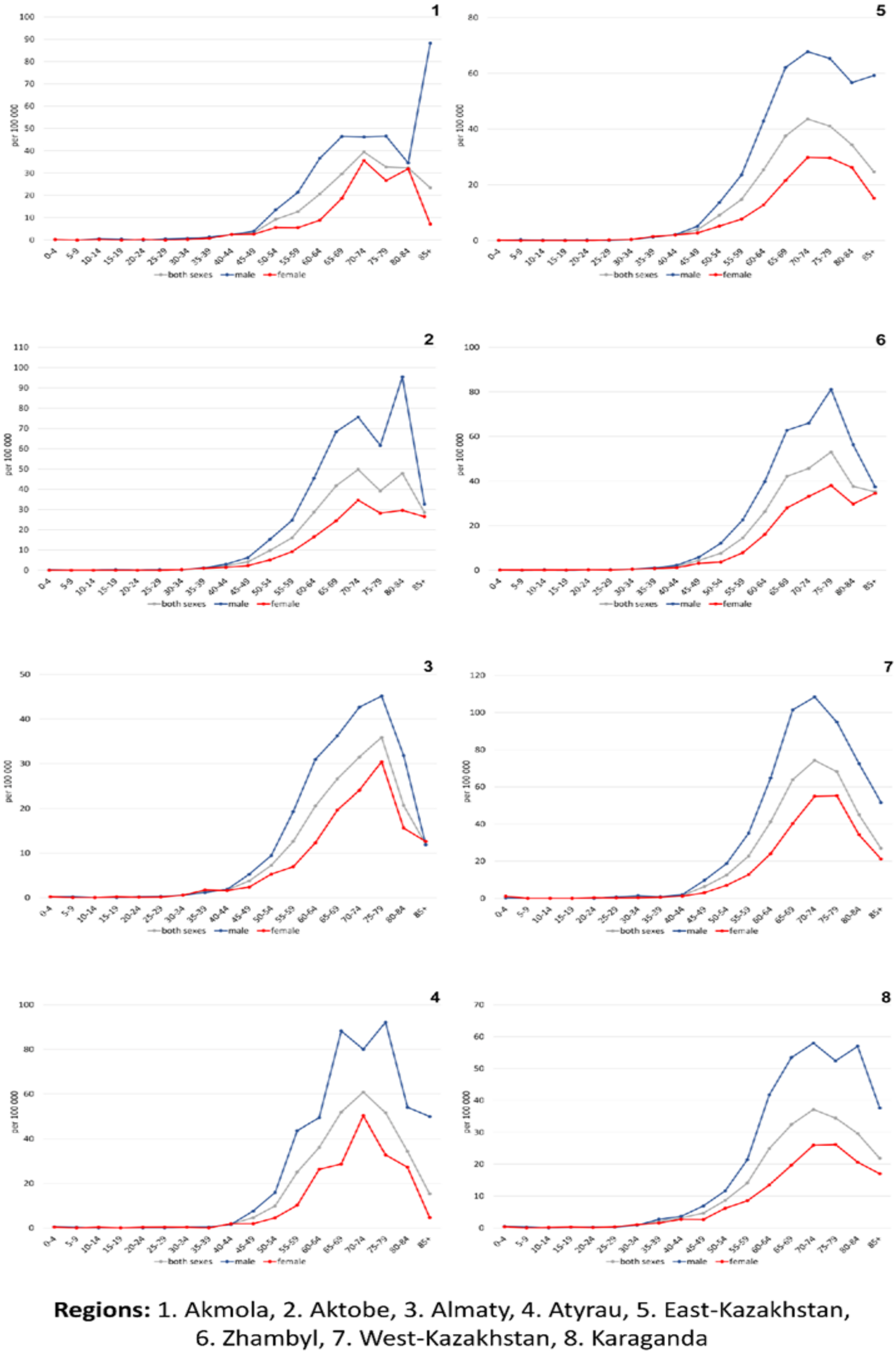


Figure 2A. Age-Specific Incidence Rate of liver cancer in Kazakhstan, 2005-2019

standardized indicators depicted in Figures 5A and 5B, it was observed that a declining trend prevailed across most regions. The Karaganda (APC=−0.42) and West Kazakhstan (APC=−0.43) regions exhibited the lowest indicators, whereas the Kyzylorda region displayed the highest (APC=−4.48). Conversely, other regions experienced an upsurge in the indicator values: Zhambyl (APC=+0.46), South Kazakhstan (APC=+0.94), Almaty

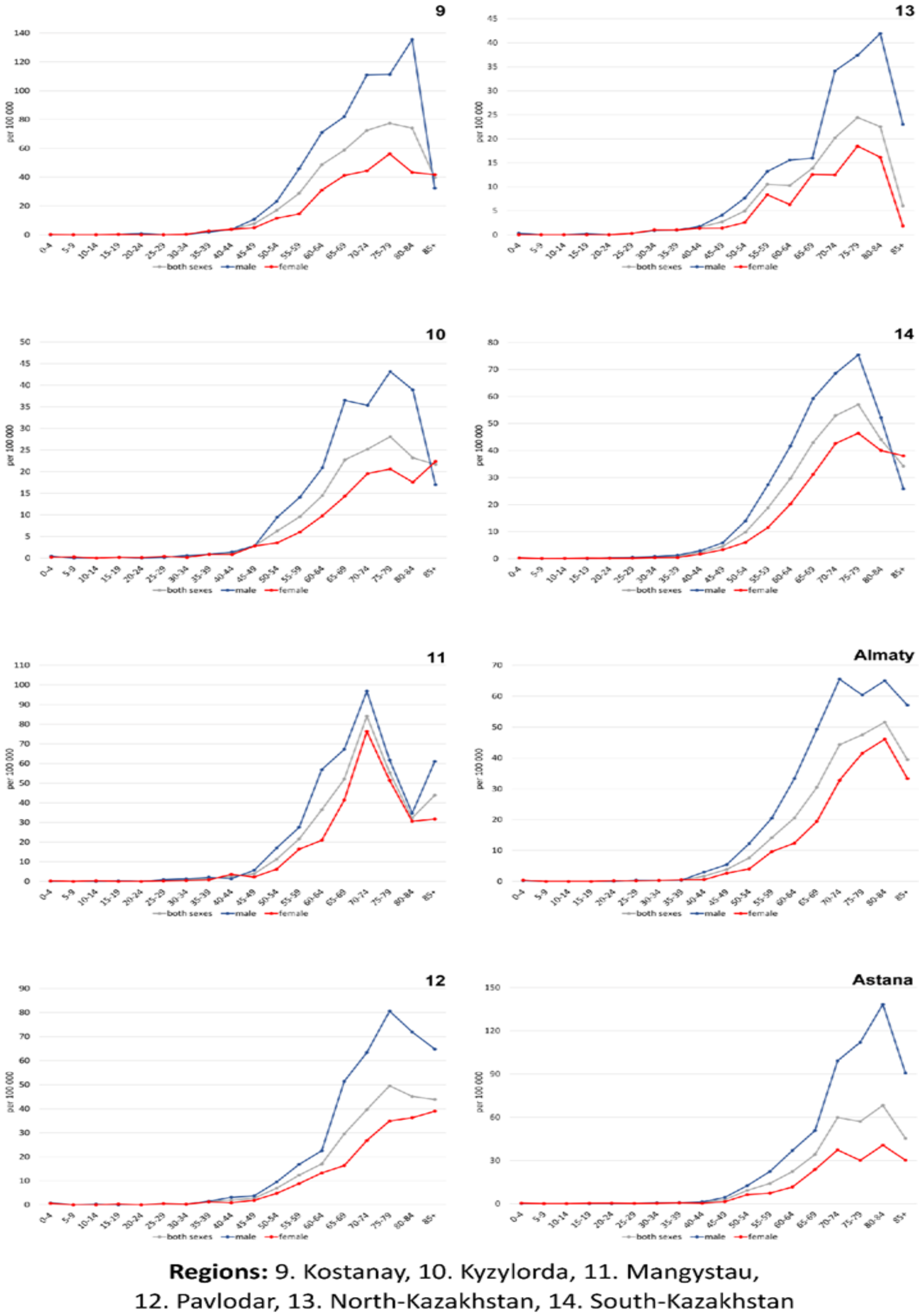


Figure 2B. Age-Specific Incidence Rate of liver cancer in Kazakhstan, 2005-2019

(APC=+1.46), Pavlodar (APC=+2.12), and North Kazakhstan (APC=+3.52) (Figure 5A and 5B).

Discussion

The decline in liver cancer incidence across most regions of Kazakhstan may be linked to the nationwide rollout of the universal hepatitis B vaccination program initiated in 1998. Additionally, since 2011, the Republic of Kazakhstan has been among the first CIS countries to offer antiviral therapy as part of the guaranteed free medical care. Broadening the reach of HBV vaccination and ensuring widespread access to antiviral therapy are recognized as significant contributors to alleviating the

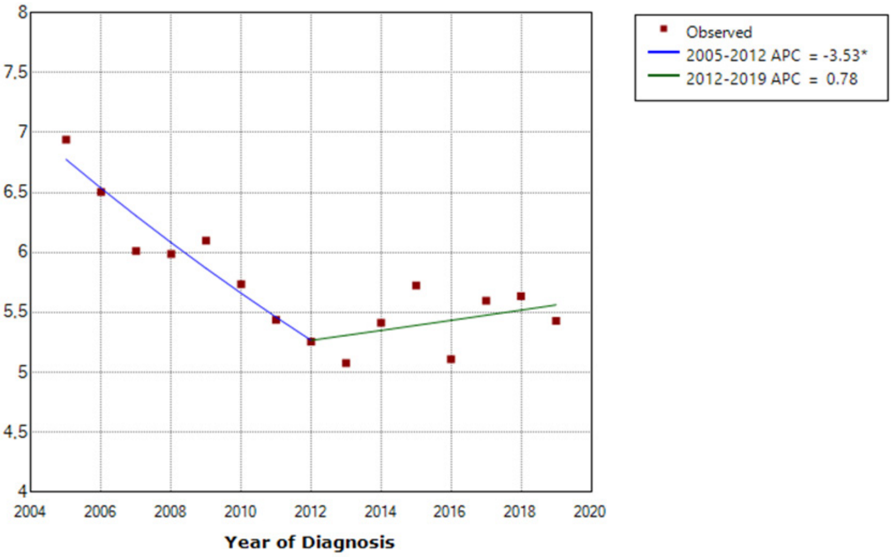


Figure 3A. Trend of Liver Cancer Incidence in the Male Population in Kazakhstan, 2005-2019

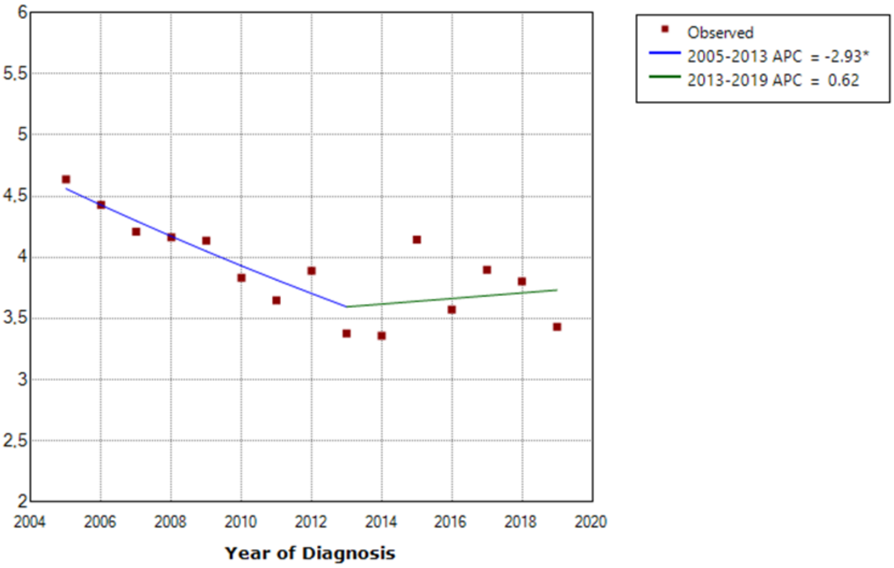


Figure 3B. Trend of Liver Cancer Incidence in the Female Population in Kazakhstan, 2005-2019

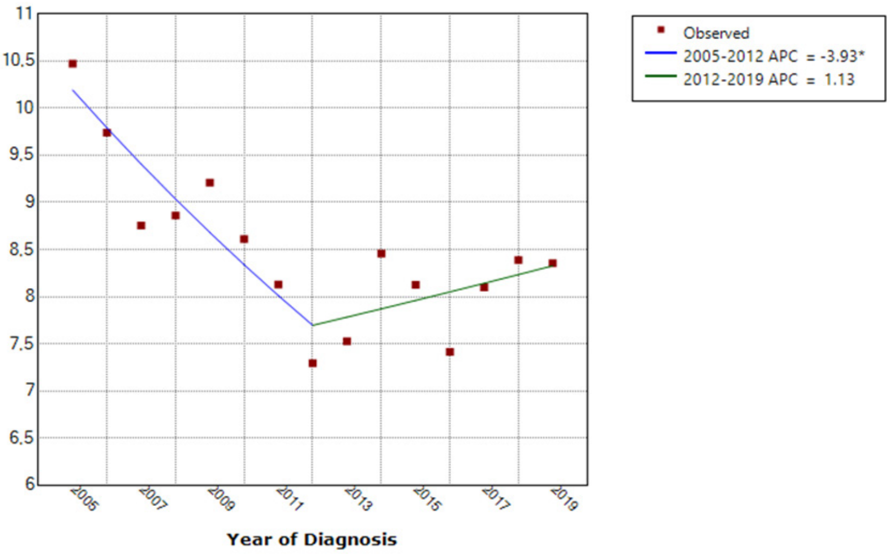
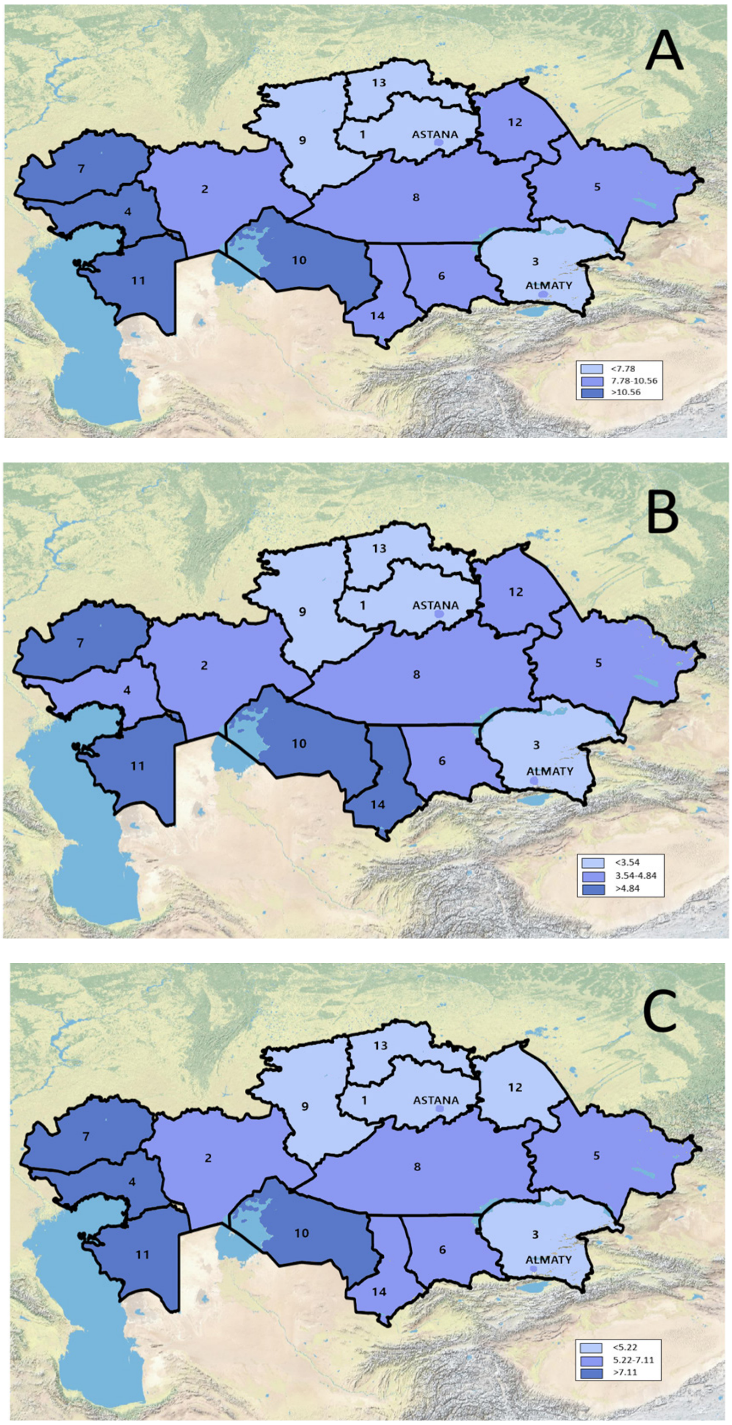


Figure 3C. Trend of Liver Cancer Incidence in Both Sex in Kazakhstan, 2005-2019 global burden of HBV-associated liver cancer [18-20].

The ambiguous trends observed in the incidence of liver cancer in Kazakhstan, characterized by a decrease from 2005 to 2012 followed by an increase from 2012 to 2019, could be attributed to multifaceted challenges affecting the real-world effectiveness of interventions. HCV therapy, renowned for its high efficacy in achieving sustained viral response rates, may encounter reduced effectiveness due to barriers like limited access to care, accuracy issues in HCV diagnostic tests, suboptimal treatment recommendations, and patient adherence [21]. Additionally, despite ultrasound's 63% sensitivity in LC surveillance, its practical effectiveness might be significantly hampered by issues such as under-recognition of cirrhosis, low utilization among diagnosed cirrhosis patients, and dependence on operator skills [22]. The increase in the incidence rate from 2012 to 2019 was most likely due to the pilot screening program for LC. In



Regions: 1. Akmola, 2. Aktobe, 3. Almaty, 4. Atyrau, 5. East-Kazakhstan, 6. Zhambyl, 7. West-Kazakhstan, 8. Karaganda, 9. Kostanay, 10. Kyzylorda, 11. Mangystau, 12. Pavlodar, 13. North-Kazakhstan, 14. South-Kazakhstan

Figure 4. Thematic map of liver cancer incidence (ASR) in Kazakhstan, 2005-2019. A, The geographical distribution of cancer incidence for male; B, The geographical distribution of cancer incidence for female; C, The geographical distribution of cancer incidence for both sex.

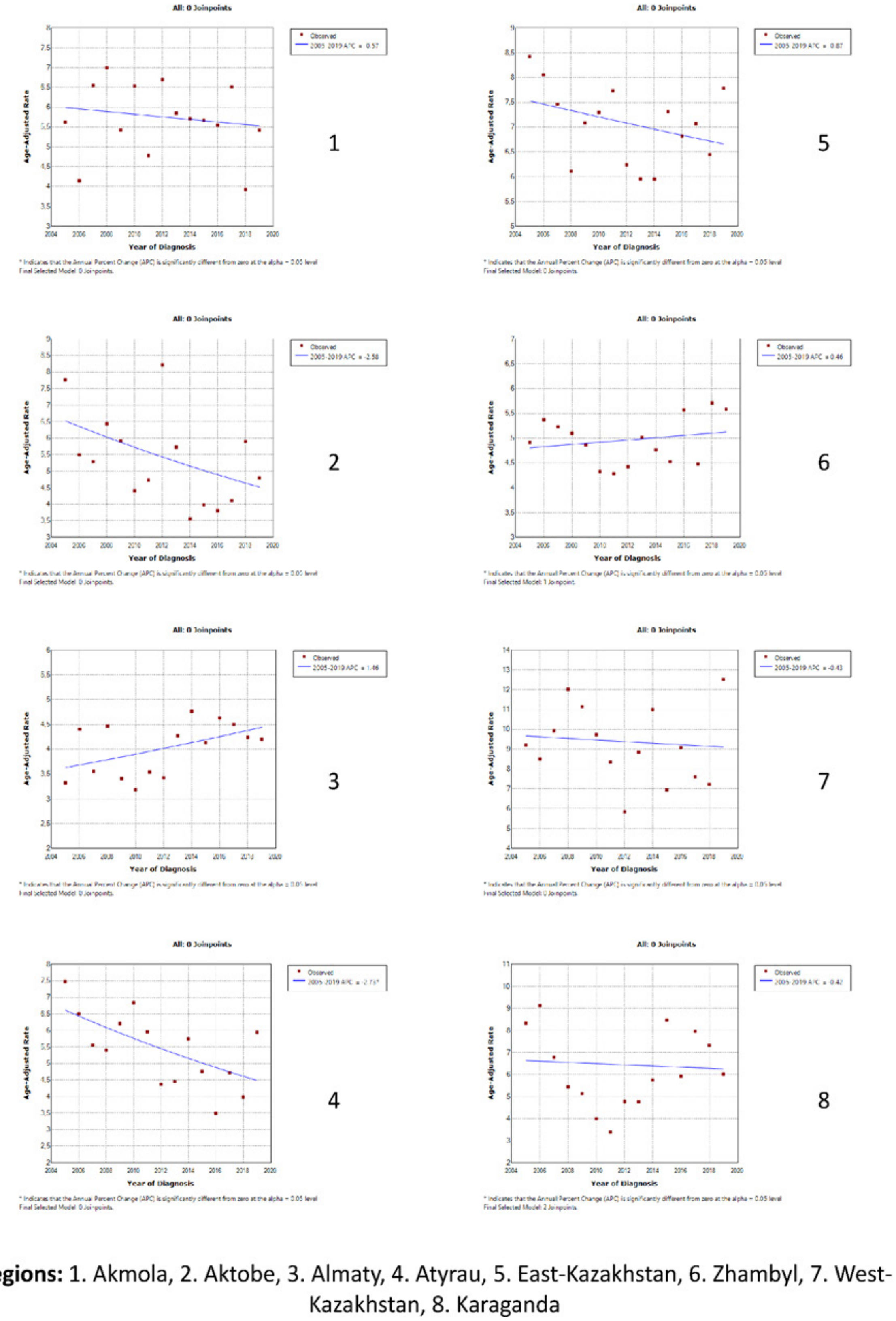


Figure 5A. Trends of Age-Standardized Incidence Rates of Liver Cancer in Kazakhstan, 2005-2019.

order to detect malignant neoplasms early and improve the provision of oncological care to the population of the Republic of Kazakhstan, according to the order of the acting The Minister of Health of the Republic of Kazakhstan dated January 8, 2013 No. 8 "On the introduction of screening for early detection of esophageal, stomach, liver and prostate cancer in pilot regions" in East Kazakhstan, West Kazakhstan, Kyzylorda, Pavlodar regions, the cities of Astana and Almaty, a screening program for early detection of liver cancer was introduced [23]. Since 2018, the pilot project of the screening program for early detection of liver cancer has been suspended

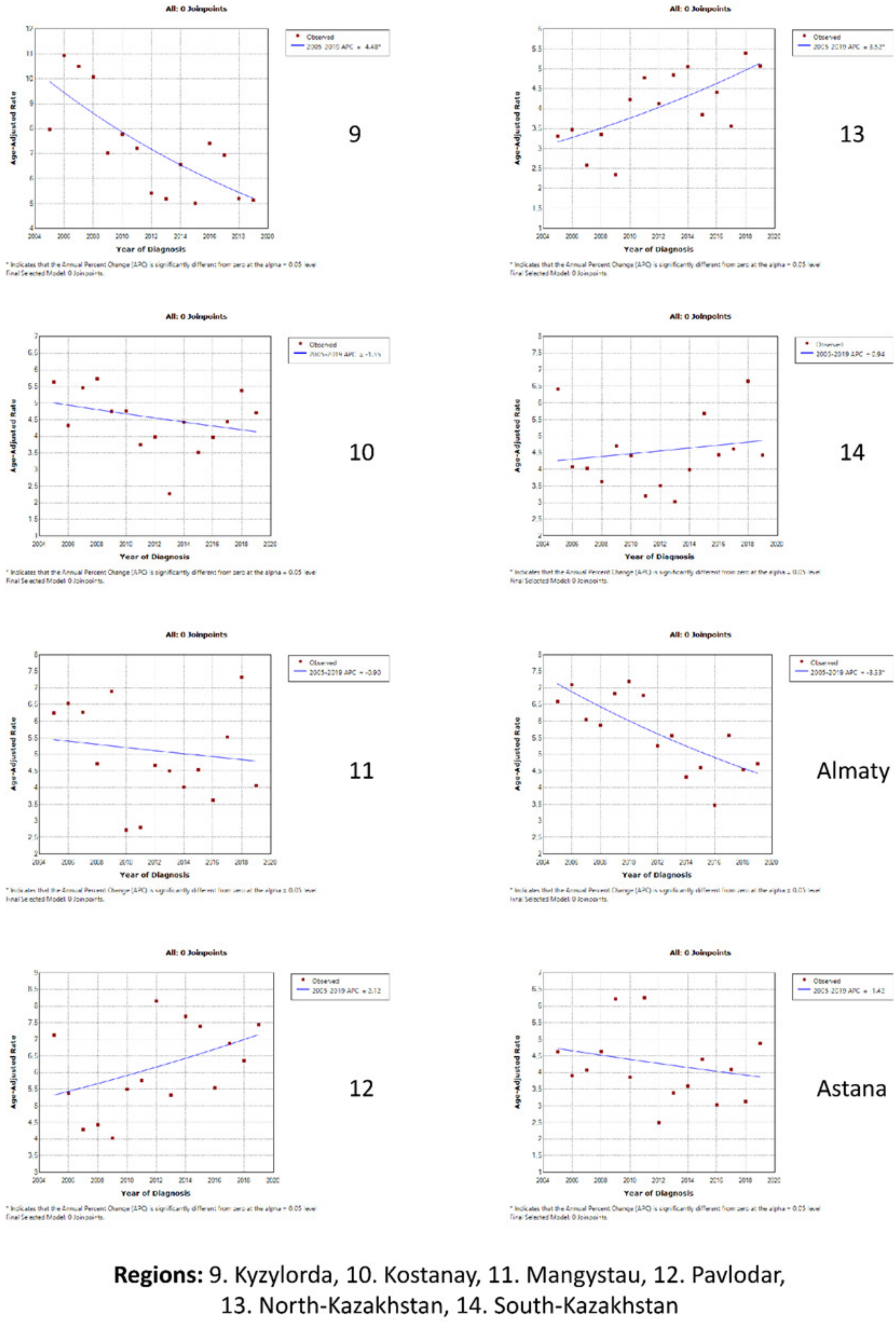


Figure 5B. Trends of Age-Standardized Incidence Rates of Liver Cancer in Kazakhstan, 2005-2019

[24]. The target group was men and women who were on dispensary registration for cirrhosis of the liver of viral and non-viral etiology, with the exception of persons on antiviral therapy and who did not receive an assessment of the effectiveness of antiviral therapy during screening for early detection of liver cancer. In clinical practice, the complexity of LC screening involves several crucial steps, including identifying at-risk populations, accurately recognizing cirrhosis, ensuring healthcare system capacity for surveillance tests, ensuring patient compliance, and proper follow-up for abnormal results [25]. However, potential shortcomings at each stage, coupled with factors like limited patient access to healthcare, gaps in provider knowledge, and system limitations, can collectively reduce the overall effectiveness of LC screening efforts [26].

Globally, older men and Asians remain the group with the highest risk of LC [27]. Liver cancer exhibits a higher prevalence in men compared to women, as indicated by a male-to-female ratio ranging from 2:1 to 4:1 [1]. In our investigation, we observed that the standardized incidence rate among men was twofold greater than that among women. This disparity can be attributed to the substantially elevated risk of LC in men, which is consistently 2-4 times higher across nearly all liver disease etiologies [22]. Gender-specific behavioral patterns and environmental factors, such as alcohol consumption, may contribute to some of these variations.

The rise in global alcohol per capita consumption, driven by increasing economic prosperity, has been suggested as a potential factor contributing to the escalated burden of alcohol-related liver cancer [28]. Liver cancer due to alcohol consumption demonstrates a rising trend in incidence and mortality rates, contrasting with HBV and HCV-related liver cancers [29]. This surge aligns with increased alcohol consumption documented by WHO data [30]. Prolonged and excessive alcohol consumption stands as an autonomous contributor to the onset of liver cirrhosis and LC. Moreover, it amplifies the susceptibility to liver cirrhosis and LC in individuals with preexisting chronic liver conditions. Although alcohol consumption in Kazakhstan among adults decreased from 7.4 to 4.5 liters per person per year between 2005 and 2019 [31], this figure remains noticeably high. Consequently, initiatives directed at reducing the incidence of LC should prioritize strategies aimed at curtailing excessive alcohol intake. In the Republic of Kazakhstan, a distinctive governmental strategy has been instituted since the 1990s aimed at curbing alcoholism and promoting abstemious behavior among citizens. Statistical evidence over the past decade underscores the efficacy of this state policy, demonstrating a consistent downward trajectory in alcohol consumption trends.

The incidence of liver cancer linked to nonalcoholic steatohepatitis/nonalcoholic fatty liver disease (NASH/NAFLD) is markedly escalating [32], primarily due to NAFLD prevalence surpassing 25% globally [33, 34]. This trend suggests a continued increase in NASH/NAFLD-related liver cancer over an extended period. Kazakhstan's 5th National Research revealed a concerning obesity rate, affecting 31.2% of adults [35]. Moreover, the Kazakh National Diabetes Register reported around 225,618 cases of type 2 diabetes mellitus (T2DM), witnessing an annual rise of 1.8% [36]. These factors are recognized as significant contributors to the development of fatty liver disease.

The recent study conducted by Jumabayeva et al. in 2022 revealed a notable increase in new cases of hepatitis B, C, and D in Kazakhstan during the period of 2015-2020 [37]. This rise in hepatitis prevalence might heighten the necessity for an extensive approach to referring patients for liver cancer (LC) screening, as proposed by Harris et al. in 2019 [38]. The multifaceted strategy for LC screening involves identifying at-risk individuals, confirming cirrhosis diagnosis, and actively counseling patients. Integrating LC surveillance reminders within routine screening for cirrhosis-related complications aligns with the potential increase in liver disease cases observed in Kazakhstan, emphasizing the importance of early identification through surveillance programs, particularly among cirrhotic patients and high-risk individuals with chronic HBV infection without cirrhosis. Additionally, recognizing the significance of surveillance adherence and exploring strategies to improve surveillance rates remain crucial objectives for healthcare providers, given the rising prevalence of hepatitis and associated liver diseases.

The observed disparity in liver cancer incidence between the high rates in western regions and low rates in northern regions of Kazakhstan may stem from multifaceted factors outlined in global literature. These could include diverse prevalence of risk factors, differing environmental exposures such as pollutants or industrial activities, disparities in healthcare access and quality, variations in dietary habits and lifestyle choices, as well as differences in population demographics. Further in-depth epidemiological studies and region-specific investigations would be essential to pinpoint the exact causes behind these distinct regional variations in liver cancer incidence.

Author Contribution Statement

DO, ZhT, AJ, ISh, KK– Collection and preparation of data, primary processing of the material and their verification. US, NS, ZB, DO, KA – Statistical processing and analysis of the material, writing the text of the article (material and methods, results). SM, FD, DT, KR, LS – Writing the text of the article (introduction, discussion). NI, GI, IK– Concept, design and control of the research, approval of the final version of the article. All authors approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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