



## Incidence and Mortality of Cervical Cancer in the Republic of Kazakhstan: 2007-2016

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### Abstract

**Background:** Epidemiology of cervical cancer is relatively well studied in developed countries of the world, but little is known about Central Asian states. This study aimed to analyze the changing patterns of cervical cancer incidence and mortality in the Republic of Kazakhstan.

**Methods:** The statistical analysis of official data on cervical cancer mortality and morbidity was performed for the whole country. Data on cervical cancer patients were retrieved for the period 2007-2016.

**Results:** There was an increase in the incidence of cervical cancer among the population of Kazakhstan from 15.24 per 100,000 in 2007 to 18.83 per 100,000 in 2016. This might be attributed to the introduction of national health program in 2011, which improved early identification. Over the last few years, the decreasing cervical cancer mortality is observed influenced by early diagnosis. The age-standardized incidence rates show that the majority of cervical cancer cases occur in the 40-49 yr age group.

**Conclusion:** The incidence of and mortality from cervical cancer in Kazakhstan in 2007-2016 are comparable with those in the neighboring former Soviet Union countries. Significant variations in incidence and mortality rates and one-year cancer-specific survival were observed between country regions.

**Keywords:** Cervical cancer; Incidence; Mortality; Kazakhstan Republic; Survival

## Introduction

Based on the current prognosis of the International Agency for Research on Cancer (IARC), by 2020 the global number of newly diagnosed cancer cases will compose 16 million per year, while the number of cancer deaths will be as high as 10 million. Of these rates, 56% of cancer incidence

and 64% of cancer mortality will be attributed to the developing nations (1). Oncology disorders are one of the leading mortality causes in developed-world nations and the second commonest cause of death in developing countries (2). The last few decades have been characterized by the



growing number of clinical studies targeted on cancer diagnosis and treatment, while cancer epidemiology studies have become less prevalent. Meanwhile, better understanding of disease trends and patterns is essential for the development of adequate prevention programs contributing to the improved patients' satisfaction (3,4). Cervical cancer is the fourth most commonly diagnosed cancer among women with the annual rate of 528,000 new cases and the fourth commonest cause of cancer mortality with the rate of 266,000 deaths per year, according to the World Cancer Report. Like in case with other cancers, the rate of cervical cancer is consistent with the level of human development. Such, the burden of this disease is higher in low and middle-income economies and India contributes to more than one-fifth of global incidence of cervical cancer (5). On the contrary, high-income world regions, like North America, Western Europe, Australia and New Zealand have the lowest incidence rates (6). There has been a decline in cervical cancer incidence over the past 30 years, associated with the transition of many world countries to higher levels of human development.

Generally, cervical cancer is more predominant in middle-aged women (35-55 yr) and occurs in women aged 65 yr and older only in 20% of cases (7). Certain former Soviet states, like Russian Federation experience growing incidence of cervical cancer among women of reproductive age, especially in the age stratum <30 yr, explained by changes in sexual behavior since cervical cancer has a well-established human papillomavirus (HPV) etiology. Those world nations, which introduced HPV vaccination programs, experience the decrease in both cervical cancer morbidity and mortality (8). Introduction of universal screening programs also contributed to the reduction of cervical cancer mortality rates (5).

Although epidemiology of cervical cancer is relatively well studied in European countries, little is known about Central Asian states. Great variability is observed in incidence of and mortality from cervical cancer between different countries and provinces within the country, reflecting changing societal and economic factors and implementa-

tion of primary and secondary prevention programs (9). At the beginning of 2011, the Government of Kazakhstan initiated the national health program, aimed at the improvement of primary care and specialized medical care in the country (10). The impact of this program on cervical cancer prevention and early detection has not yet been fully evaluated.

This study aimed to analyze the changing patterns of cervical cancer incidence and mortality in the Republic of Kazakhstan over a period of 10 yr (from 2007 to 2016).

## **Materials and Methods**

### *Study design and procedures*

This was a retrospective cohort study based on the data obtained from the Kazakhstan Cancer Registry (KCR), which is the database of all histologically confirmed cancer cases in the country. From this database, we retrieved information on cervical cancer patients from 2007 to 2016. It is a standard practice for the Ministry of Health to obligate all medical doctors to report on newly diagnosed cancer cases to the regional oncological dispensaries using a special form and in their turn, regional oncological dispensaries manually transfer the reported data to the electronic KCR. From this, we extracted the information related to birth date, date of diagnosis, death date, and cancer stage.

To enable comparative analysis of incidence and mortality rates, we classified all regions of Kazakhstan in five geographic zones: East (East Kazakhstan and Pavlodar regions), Central (Akmola and Karaganda regions), North (Kostanay and North Kazakhstan regions), West (Aktobe, Atyrau, Mangystau, and West Kazakhstan regions) and South (Almaty, Zhambyl, Kyzylorda and South Kazakhstan regions). Moreover, this is the current practice for Kazakhstan to consider separately two cities of republican significance – Almaty and Astana (11).

We obtained approval from the Ethical Committee of Semey State Medical University, Semey, Kazakhstan (protocol 2 from 16 November

2011). Since only anonymized data from the Kazakhstan Cancer Registry were used, no informed consent from individual patients was needed.

### Statistical analysis

Incidence and mortality rates were calculated per 100,000 ( $^0/_{0000}$ ) of female population. Data on the overall number of female population and the number of females by age were obtained from the Demographic Yearbooks of Kazakhstan, issued by the Agency of Statistics of the Republic of Kazakhstan from 2007 to 2016. The 95 % confidence intervals (95 % CI) were computed for the incidence and mortality rates.

One-year survival was calculated by the life-tables method. To calculate the age at diagnosis we used the birth date and the date of diagnosis and classified it as 0–19, 20–29, 30–39, 40–49, 50–59, 60–69 and 70+ yr. Cancer stage was diagnosed with the help of the ICD-10 staging classifications and coded as I-II, III and IV.

The crude mortality rate from cervical cancer was calculated by the following formula:

Number of deaths from cervical cancer within one year in all age groups/midyear female population  $\times$  100,000.

The following formula was used to calculate the crude incidence rate of cervical cancer:

Number of new cases of cervical cancer within one year in all age groups/midyear female population  $\times$  100,000.

The standardized incidence of and mortality rates from cervical cancer were computed using the

world standard population with the following formulas:

Standardized incidence rate = crude incidence rate for a specific age group  $\times$  standard population for a specific age group.

Standardized mortality rate = crude mortality rate for a specific age group  $\times$  standard population for a specific age group (12).

All statistical tests were performed using SPSS software, ver. 20.0 for Windows (Chicago, IL, USA).

### Results

Altogether, 15,157 new cases of cervical cancer were diagnosed and there were 1,045 registered deaths from cervical cancer in the Republic of Kazakhstan during 2007-2016. Table 1 shows sex-specific incidence rates for selected female cancers. During 2007-2016, breast cancer was the most common female cancer with the incidence rate ranging from 38.03 (95% CI: 36.70-39.40) to 50.64 (95% CI: 49.19-52.11) per 100,000 of female population. Cervical cancer was the commonest reproductive cancer, followed by endometrial and ovarian cancers. Overall, the incidence rates for all selected cancer sites were increasing and 2016 was the year when peak incidence was observed for all selected female cancers, excluding breast cancer. The incidence of breast cancer was growing faster than the incidence of reproductive cancers.

**Table 1:** Incidence rates for selected female cancers (per 100,000 of female population)

Cancer site	Year									
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Breast cancer	38.03	40.12	39.61	41.39	41.11	45.46	43.83	46.33	48.50	50.64
Cervical cancer	15.24	15.50	16.38	16.19	16.93	18.70	18.51	19.95	20.14	18.83
Endometrial cancer	10.55	9.97	10.77	10.84	10.59	11.51	12.42	12.19	13.24	12.84
Ovarian cancer	10.17	10.12	10.43	10.29	10.87	11.60	10.97	11.62	12.41	11.11

Table 2 shows sex-specific mortality rates for selected female cancers. During 2007-2016, breast cancer had the highest mortality rate, which decreased from 16.9 (95% CI: 16.0-17.8) in 2007 to 14.0 (95% CI: 13.2-14.7) in 2016. The mortality rates of cervical cancer and endometrial cancer

also showed a reduction over the same period, which was less marked as compared to breast cancer. Ovarian cancer was the only reproductive cancer with the stable mortality rate for the period 2007-2016.

**Table 2:** Mortality rates for selected female cancers (per 100,000 of female population)

<i>Cancer site</i>	<i>Year</i>									
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Breast cancer	16.9	16.4	16.5	16.8	16.1	16.2	15.6	15.1	15.3	14.0
Cervical cancer	7.8	7.7	8.4	7.3	7.7	7.8	7.0	7.7	7.2	7.0
Endometrial cancer	3.5	3.3	3.6	3.4	3.4	3.4	3.8	3.1	2.8	2.8
Ovarian cancer	5.9	5.3	6.3	5.9	5.9	6.2	5.9	5.8	5.7	5.6

Table 3 shows incidence and mortality rates as well as the ration of mortality to incidence across different regions of Kazakhstan in 2016. The national incidence and mortality rates constituted

18.8 (95% CI: 17.9-19.7) per 100,000 of female population and 7.0 (95% CI: 6.5-7.6) per 100,000 of female population, respectively.

**Table 3:** Incidence and mortality rates for cervical cancer across regions of Kazakhstan, 2016 (per 100,000 of female population)

<i>Geographic zone</i>	<i>Region (City)</i>	<i>Incidence</i>	<i>Mortality</i>	<i>M/I</i>
East	East Kazakhstan	20.3	7.3	0.36
	Pavlodar	27.3	9.8	0.36
Central	Akmola	18.9	9.2	0.49
	Karaganda	18.1	7.8	0.43
North	Kostanay	28.2	6.5	0.23
	North Kazakhstan	16.5	7.1	0.43
West	Aktobe	21.9	6.9	0.32
	Atyrau	20.3	12.1	0.60
	Mangystau	12.2	6.6	0.54
South	West Kazakhstan	17.3	6.1	0.35
	Almaty	19.1	7.5	0.39
	Zhambyl	12.7	7.8	0.61
	Kyzylorda	10.4	7.0	0.68
Cities	South Kazakhstan	13.6	5.4	0.40
	Almaty	27.6	5.9	0.21
Republic of Kazakhstan	Astana	15.5	5.7	0.36
		18.8	7.0	0.37

The highest incidence rate was observed in Kostanay region (28.2 (95% CI: 23.6-33.5) per

100,000 of female population) followed by Almaty city (27.6 (95% CI: 24.4-31.2) per 100,000

of female population) and Pavlodar region (27.3 (95% CI: 22.4-32.9) per 100,000 of female population). However, the highest cervical cancer mortality rate was established in Atyrau region (12.1 (95% CI: 8.5-16.7) per 100,000 of female population). The lowest cervical cancer incidence rate was seen in Kyzylorda region (10.4 (95% CI: 7.4-14.2) per 100,000 female population), while the lowest mortality rate was observed in South Kazakhstan region (5.4 (95% CI: 4.3-6.8) per 100,000 of female population). Generally, mortality rates were lower in Astana and Almaty cities (5.7 (95% CI: 3.7-8.2) per 100,000 of female population and 5.9 (95% CI: 4.4-7.6) per 100,000

of female population, respectively) as many tertiary care medical facilities are concentrated there. The most marked increase occurred in the 40–49-yr age group, in which the age-standardized incidence of cervical cancer in 2016 was almost 50% as high as in 2007. The proportion of new cases among the three younger age groups and the oldest age group decreased over the study period, while the opposite was observed among the age groups of 40-49 yr, 50-59 yr and 60-69 years. Detailed data of the incidence and the number of new cases across all age groups are presented in Table 4.

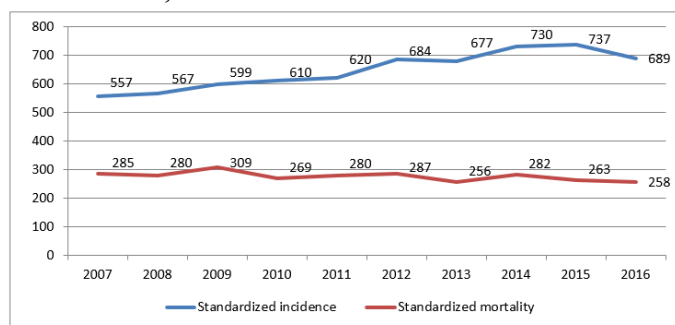
**Table 4:** Absolute number of new cases of cervical cancer (N), incidence rates (I) and proportion of all cases (%) across age groups in Kazakhstan in 2007–2016

Year	Age group (yr)																				
	0-19			20-29			30-39			40-49			50-59			60-69			70+		
	N	I	%	N	I	%	N	I	%	N	I	%	N	I	%	N	I	%	N	I	%
2007	15	0.6	0.4	73	5.2	3.6	246	21.3	14.8	351	31.2	21.8	286	32.6	22.7	150	30.4	21.1	112	22.3	15.5
2008	0	0	0	53	3.8	2.5	251	21.7	14.5	363	32.3	21.5	312	35.6	23.7	162	32.8	21.9	120	23.9	15.9
2009	1	0.4	0.3	49	3.4	2.2	253	21.6	13.9	401	35.8	23.0	349	38.0	24.4	161	32.7	21.0	125	23.7	13.5
2010	0	0.0	0.0	59.0	3.9	0.0	265	21.8	13.9	410	36.4	23.2	354	38.9	24.8	167	34.2	21.8	112	21.7	13.8
2011	1	0.0	0.0	40.0	2.6	1.6	280	21.7	13.2	437	38.9	23.7	384	40.7	24.8	175	34.9	21.3	135	25.4	15.5
2012	0	0.0	0.0	64.0	4.1	2.2	302	24.1	13.3	450	40.1	22.0	452	46.4	25.5	204	39.0	21.4	153	28.5	15.6
2013	0	0.0	0.0	57.0	3.6	2.0	323	25.4	14.3	496	44.2	24.9	405	40.3	22.7	209	37.5	21.1	141	26.5	14.9
2014	2	0.1	0.0	59.0	3.8	2.0	324	25.1	13.2	519	44.4	23.5	491	47.6	25.2	239	39.6	20.9	149	28.6	15.1
2015	3	0.1	0.1	59.0	3.8	2.0	319	24.2	12.8	475	42.1	22.4	485	46.1	24.5	280	42.9	22.8	148	29.0	15.4
2016	1	0.0	0.0	58.0	3.8	2.1	294	21.7	12.1	513	45.1	25.1	451	42.3	23.6	277	40.1	22.3	136	26.5	14.7

Standardized incidence of cervical cancer increased from 557 to 689 in 2016, while standardized mortality decreased from 285 to 258 during the study period (Fig. 1).

The highest proportion of cases in 2007–2016 occurred in stage I-II cervical cancer, while the

lowest proportion of cases was registered in stage IV. The proportion of stages I and II steadily increased, from 73.6% to 86.4%, while the corresponding proportion of stage IV declined from 4.3% to 3.2% during the study period (Fig. 2).



**Fig. 1:** Standardized incidence and mortality rates of cervical cancer in the Republic of Kazakhstan in 2007–2016

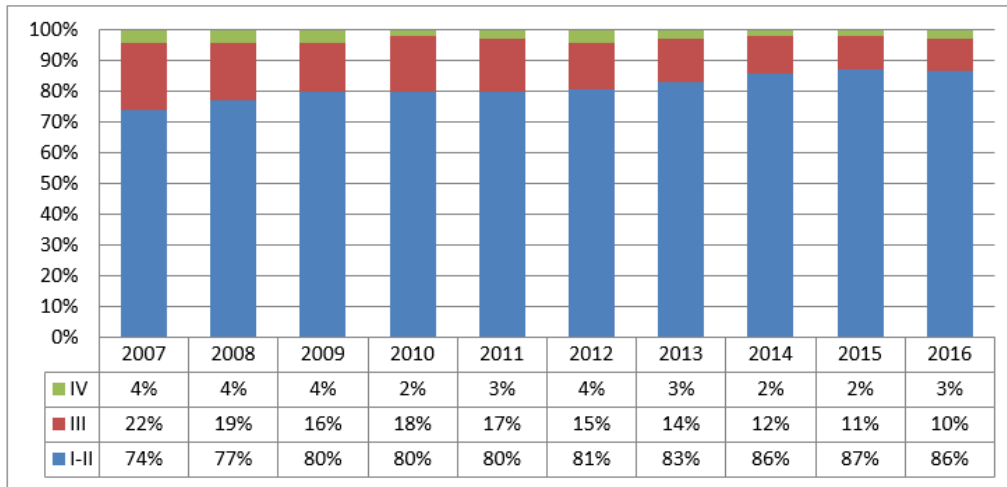


Fig. 2: Stage distribution of cervical cancer in the Kazakhstan Republic from 2007 to 2016

Figure 3 presents the 1-year cancer specific survival across all regions of Kazakhstan in 2010 and 2016. The reason behind such presentation is the initiation of the national health program by the authorities of Kazakhstan in 2011. This program may have increased the early detection of cancer and/or improved survival of cancer patients due to the provision of better treatment. One-year survival in 2010 varied from 77.8% for West Kazakhstan region to 98.0% for North Ka-

zakhstan region. However, in 2016 the lowest 1-year survival rate was observed in Mangystau region (80.0%) and the highest – in Almaty region and in Almaty city (96.8% and 97.2%, respectively). Generally, the 1-year survival rates increased in the majority of the country’s regions. In 2010 the national rate of 1-year cancer-specific survival constituted 93.3% as compared to 93.4% in 2016.

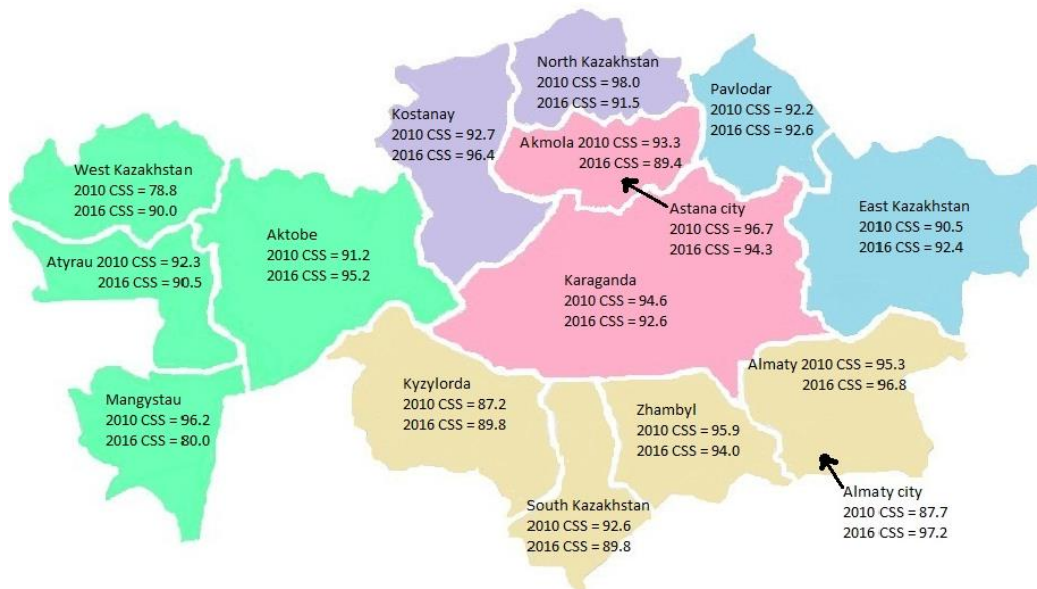


Fig. 3: One-year cancer-specific survival (CSS) across regions of Kazakhstan in 2010 and 2016

## Discussion

The results from this study indicated that incidence of cervical cancer in the Republic of Kazakhstan has increased during the study period, in contrast with what has been observed in most developed nations of the world. Still, the mortality rate has gradually declined, which is consistent with findings from the established advanced economies (2). Both incidences of and mortality from cervical cancer in the Republic of Kazakhstan are comparable to those reported on the neighboring Russian Federation in 2009 (18.82 and 8.11 per 100,000, respectively) (11).

Basically, this research is one of the first epidemiological studies presenting internationally comparable data on incidence of and mortality from cervical cancer in the Republic of Kazakhstan, complementing earlier study on epidemiology of cervical cancer in Kazakhstan in 1999–2008 (13). The results of this study also support the data from Central and Eastern European states, which face increase in cervical cancer incidence (14). Similar to Kazakhstan, most former Socialist economies achieved a reduction in cervical cancer mortality due to implementation of screening program and improved treatment. Still, certain states like Latvia, Lithuania, Romania and Bulgaria reported an increase in cervical cancer mortality to the current levels of 7.0, 6.3, 10.8, 7.5 per 100,000, respectively (2). In neighboring Central Asian states, the wide variation in reported rates of incidence and mortality is observed. Such, the incidence rates of cervical cancer range from 6.7 per 100,000 of female population in Turkmenistan to 26.5 per 100,000 of female population in Kyrgyzstan, while the mortality rates range from 3.7 per 100,000 of female population in Turkmenistan to 13.4 per 100,000 of female population in Kyrgyzstan (15).

In 2016 the national mortality to incidence ratio (M/I) was 0.37 with some regional variations (from 0.21 in Almaty city to 0.68 in Kyzylorda region). The earlier research reported a higher national M/I ratio (0.55 in 1999-2008) (11). The majority of Central Asian states have uniformity in the M/I ratios, which are around 0.5 in most

countries. However, the M/I ratios are more heterogeneous in Central and Eastern European states, being lower in Bulgaria, Czech Republic, Slovakia and Slovenia ( $\leq 0.3$ ) (15).

There is a disparity in incidence of and mortality from cervical cancer between different regions of Kazakhstan. In 2016 higher incidence rates ( $>20.0$  per 100,000 of female population) were established in East Kazakhstan, Pavlodar, Kostanay, Aktobe and Atyrau regions. These regions of Kazakhstan have colder climates, lower population density and well-developed industry (16). Some of these regions, like Atyrau also demonstrated higher mortality rates but this was not always the case. In the USA higher incidence and mortality rates were reported in the South (17), while in Pacific region the highest mortality and incidence rates were found in Melanesia and the lowest rates in Micronesia (18).

Cervical cancer incidence is highly affected by the prevalence of human papillomavirus (HPV) infection. The prevalence of high-risk HPV in former Soviet Union countries, including Central Asian states ranged from 0-48.4% in women with normal cytology, and varied from 29.2% to 100% in women with low-grade cervical lesions (19). The prevalence of high-risk HPV in general population of Western Kazakhstan was 26.0% with the highest rate observed among younger adults aged 16-29 yr (62.4%) (20). Since HPV testing as a means of cervical cancer screening appears to be the most promising approach (15), Ministry of Health plans to introduce it as a population-based screening in 2019-2020 (21).

In 2016 the one-year cancer-specific survival rate in Kazakhstan has remained stable when compared to 2010 levels. Significant variations in cancer-specific survival rates were observed between country regions. Geographical diversity in one-year cancer survival was also established in England. Although most cancers improved the one-year survival by up to 10% points, this did not happen with cervical cancer (22). Cancer stage migration due to the introduction of near-universal screening program may explain this lack of improvement in cervical cancer survival (23). Near-universal screening leads to early cancer

detection at an in situ stage and to provision of timely treatment before cancer becomes invasive. Thus, invasive cancers now identified in countries with near-universal screening programs predominantly occur in non-attendees to cervical screening or have aggressive nature with poor prognosis (24).

There are two types of screening programs for cervical cancer in Kazakhstan: national population-based screening covering women aged 30-70 yr with 4-year interval and opportunistic screening, carried in women beyond the specified age range visiting a gynecologist for any reason (25). Beginning 2008, screening is provided by a Pap smear and since 2011 cervical cytology is reported by the Bethesda system (26). In 2014 liquid-based cytology became widely used (27). All these interventions may have contributed to the improved early detection and increase in the incidence observed after 2011 (Figs. 1 and 2). Still, cervical screening coverage among the targeted female population in Kazakhstan could not be considered near-universal as only 67.7% were screened in 2014 and 45.9% in 2016 (21). There is a need for strategies to improve screening uptake by the target population.

The main strength of this study is that it is based on a national cancer registry of sufficient data quality. However, the main weakness of this study is that KCR does not include data on ethnicity, place of residence, socio-economic status, and cancer risk factors. Further research is needed to elucidate the factors contributing to incidence of and mortality from cervical cancer and survival patterns.

## Conclusion

The incidence of and mortality from cervical cancer in Kazakhstan in 2007-2016 are comparable with those in the neighboring former Soviet Union countries. Incidence rate of cervical cancer in the Republic of Kazakhstan has increased during the study period, while the mortality rate has gradually declined, attributed to the provision of national population-based screening. Significant

variations in incidence and mortality rates and one-year survival were observed between country regions. There is a need to further investigate the factors helped enable better understanding of cancer epidemiology in Kazakhstan.

## Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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