RESEARCH ARTICLE

Editorial Process: Submission:04/25/2022 Acceptance:03/18/2023

Corpus Uteri Cancer in Kazakhstan: Recent Incidence Trends

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Abstract

Background: Endometrial cancer is the fifteenth most common malignant disease in the world. It is estimated that 417,367 new cases of this malignant neoplasm are diagnosed annually and 97,370 women die from it. **Objective:** The epidemiological features of the corpus uteri cancer (CUC) incidence and its spatial and temporal assessment in Kazakhstan were studied. **Methods:** The retrospective study was done for the period 2009-2018. Descriptive and analytical methods of epidemiology were used. Crude, age-specific, age-standardized, equalized incidence rates and approximation were calculated. The method of drawing up a cartogram based on the determination of the standard deviation (σ) from the mean (x) was applied. **Result:** During the study period, 10,522 new cases of CUC were registered. The average annual age-standardized incidence rate was 11.1±0.2 cases per 100,000 population of female, (T=+0.6%; R2=0.083). The analysis of ASIR showed unimodal growth with a peak at 65-69 years – 58.8±3.6 cases per 100,000 population of female. The most pronounced downward trend was revealed in the age group < 30 years (T=−2.6%), and the most pronounced annual average upward rates was in 80-84 years (T=+6.4%). The results of the spatial analysis showed regions with a higher levels of CUC incidence rate per 100,000 population of female: Pavlodar, Kostanay, Karaganda, Almaty city, North Kazakhstan and Astana city. **Conclusion:** In recent years, CUC incidence in Kazakhstan has been increasing. High incidence rates were found in the northern regions of the country, and the trend of incidence growth was more pronounced in the western and eastern regions.

Keywords: Corpus uteri cancer- incidence- trends- cartogram- Kazakhstan

Asian Pac J Cancer Prev, **24 (3)**, 849-857

Introduction

Corpus uteri cancer arises from the epithelial lining of the uterine cavity; therefore, it is most often called endometrial cancer. Cancers that occur in the stromal and muscular tissues of the myometrium are called uterine sarcomas (Amant et al., 2018). More than 90% of corpus uteri cancer are epithelial tumors (Banas et al., 2016). Endometrial cancer is the fifteenth most common malignant disease in the world. It is estimated that 417,367 new cases of this malignant neoplasm are diagnosed annually, and 97,370 women die from it. 40.1% of the cases are residents of Asian countries and 31.2% of the cases are residents of Europe (Ferlay et al., 2020). In recent years, the incidence of uterine body cancer has been increasing, which is most likely due to an aging population and an increase in obesity (Wartko et al., 2013).

More than 90% of new cases are registered in countries with high and very high Human Development Index (HDI) (Ferlay et al., 2020). The highest average incidence (14.5 per 100,000) is in areas with a very high level of human development, and the lowest incidence (3.4 per 100,000) is in areas with a low level of human development (Khazaei et al., 2020). Accurate cancer registration systems, more precise screening tests, the familiarity of women in society with the signs of cancer and the detection of cancer cases in the early stages may have contributed to an increase in incidence rates. The high incidence of uterine body cancer in developed countries is mainly associated with lifestyle factors and socio-economic factors that cause changes in the reproductive history (Lortet-Tieulent et al., 2018). Obesity (Lauby-Secretan et al., 2016), diabetes (Saed et al., 2019) and polycystic ovary syndrome (Barry et al., 2014), which are associated with metabolic syndrome, are

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risk factors for endometrial cancer. In addition, an excess of estrogen, including tumors that secrete estrogens, and estrogen therapy without progesterone, predispose women to endometrial cancer (Brinton et al., 2014). Parity and the use of oral contraceptives reduce the risk of this type of cancer. The incidence of endometrial cancer is reduced by 40% among parous compared to nulliparous women (Raglan et al., 2019). The use of oral contraceptives reduces the risk of endometrial cancer by 30-40%; longer use is associated with increased protection, which can persist even decades after discontinuation (Collaborative Group on Epidemiological Studies on Endometrial Cancer, 2015).

Symptoms of CUC are postmenopausal vaginal bleeding, enlargement of the uterus, abdominal pain and pelvic cramps, which form the basis of the clinical diagnosis (El Behery et al., 2010). To date, there is no established method for screening CUC. The diagnosis of CUC is still mainly based on the appearance of postmenopausal vaginal bleeding as a clinical symptom, and then leads to an invasive diagnosis using hysteroscopy and curettage for histological confirmation. Early diagnosis of endometrial cancer remains an unsolved problem that could improve the outcomes of the disease.

Kazakhstan belongs to the countries with a high incidence and mortality rates of corpus uteri cancer. According to the age - standardized incidence rate, it is in the top 10 cancers. And in the structure of morbidity among the female population, corpus uteri cancer occupies the 5th place (6.3%) (Ferlay et al., 2020). Previous studies examining the temporal trends in the incidence of endometrial cancer in Kazakhstan were limited to selected cities or regions and were based on data for a short period (Kozgambayeva et al., 2007; Shakirova, 2014; Bokayeva et al., 2016). In this study, we study trends in the incidence of endometrial cancer at the regional level in Kazakhstan as a whole, using up-to-date data on the incidence. In addition, we have conducted studies on other cancers in the female population. According to these studies, there is an increase in the incidence of ovarian cancer (Kuanyshkaliyeva et al., 2016), cervical cancer (Igissinov et al., 2021) and breast cancer (Toguzbayeva et al., 2021). Therefore, the study of global patterns and trends in the incidence of corpus uteri cancer is necessary due to the growing epidemic of obesity, which is the main risk factor for this disease.

Materials and Methods

Cancer registration and patient recruitment

The population of republic of Kazakhstan as the 2018 census was 18.2 million, of which 9.36 million were females (The Bureau of National Statistics of the Agency for Strategic Planning and Reforms of the Republic of Kazakhstan), while the dynamics of the female population increased by 13.1% compared to 2009. The cancer registry of the population of Kazakhstan covers 14 regions and cities of national significance-Almaty and Astana. New cases of corpus uteri cancer were extracted from the accounting and reporting forms of the Ministry of Health of the Republic of Kazakhstan – form 7 and form 35, which were formed from the register of oncological diseases based on the administrative-territorial division of the republic from 2009 to 2018 using the International Disease Code 10, code C54.

Population denominators

Population denominators for calculation of incidence rates were provided by the Bureau of National Statistics for 2009-2018. At the same time, data on the number of female population of the republic, taking into account the studied regions, are used, all data are presented on the official website (https://stat.gov.kz/).

Statistical analysis

The main method used in the study of incidence was a retrospective study using descriptive and analytical methods of modern epidemiology. Age-standardized incidence rates (ASRs) were calculated for eighteen different age groups (0-4, 5-9, …, 80-84, and 85+) and ten calendar periods from 2009 to 2018 (1-year intervals). ASRs standardized to the world population proposed by World Health Organization (Ahmad et al., 2001) with recommendations from the National Cancer Institute (1976) were estimated for each studied year (WHO 2000-2025).

The extensive, crude and age-specific incidence rates (ASIR) are determined according to the generally accepted methodology used in modern sanitary statistics. The annual averages (M, P), mean error (m), Student criterion, 95% confidence interval (95% CI), and average annual upward/downward rates (T%) were calculated. We did not justify the main calculation formulas in this paper, since they are detailed in the methodological recommendations and textbooks on medical and biological statistics (Merkov and Polyakov, 1974; Glanc, 1999; dos Santos Silva, 1999). The dynamics of incidence rates was studied for 10 years, while the trends of incidence were determined by the least squares method. When compiling cartograms, crude rates and ASRs were used for 10 years (2009-2018). The method of compiling a cartogram proposed in 1974 by S.I. Igisinov (Igissinov, 1974) was used, based on the determination of the standard deviation (σ) from the average (x).

Viewing and processing of the received materials was carried out using the Microsoft 365 software package (Excel, Word, PowerPoint), in addition, online statistical calculators were used (https://medstatistic.ru/calculators/averagestudent.html), where Student criterion was calculated when comparing the average values.

Ethics approval

Because this study involved the analysis of publicly available administrative data and did not involve contacting individuals, consideration and approval by an ethics review board was not required. At the same time, the submitted data is in accordance with the Law of the Republic of Kazakhstan No. 257-IV of March 19, 2010 "About State statistics" (http://adilet.zan.kz/rus/docs/Z100000257), the information in the summary report is confidential and can only be used for statistical purposes in accordance with the Principles of the World Medical

Association (WMA, 2013).

Results

In 2009-2018, 10,522 new CUC cases were registered in the Republic of Kazakhstan. The average age of patients in Kazakhstan 60.4±0.2 year. Regions with a lower average age of patients are Kyzylorda (57.0±1.1) and high average age is in East Kazakhstan (62.0±0.3). The average age of patients in all regions practically did not change during the study period. The most downward trend was found in the Kyzylorda region (T_{down}=−0.9%), and the largest increase was in the North Kazakhstan region (T_{up}=+0.6%) (Table 1).

The crude rate of CUC incidence in the republic was 11.9±0.3 per 100,000 population of female, and it grew from 10.7±0.4 in 2009 to 11.6±0.4 in 2018 (Figure 1) in dynamics, the difference was statistically significant (p=0.112). Crude rates of mortality declined from 3.6±0.2 in 2009 to 2.5±0.2 in 2018 (p=0.000, Figure 1) and averaged equaled to 3.2±0.2 per 100,000 population of female. In the dynamics, the aligned crude rate repeated the revealed trend towards an increase in T_{up}=+1.7% (incidence) and decrease − T_{down}=−4.0% (mortality).

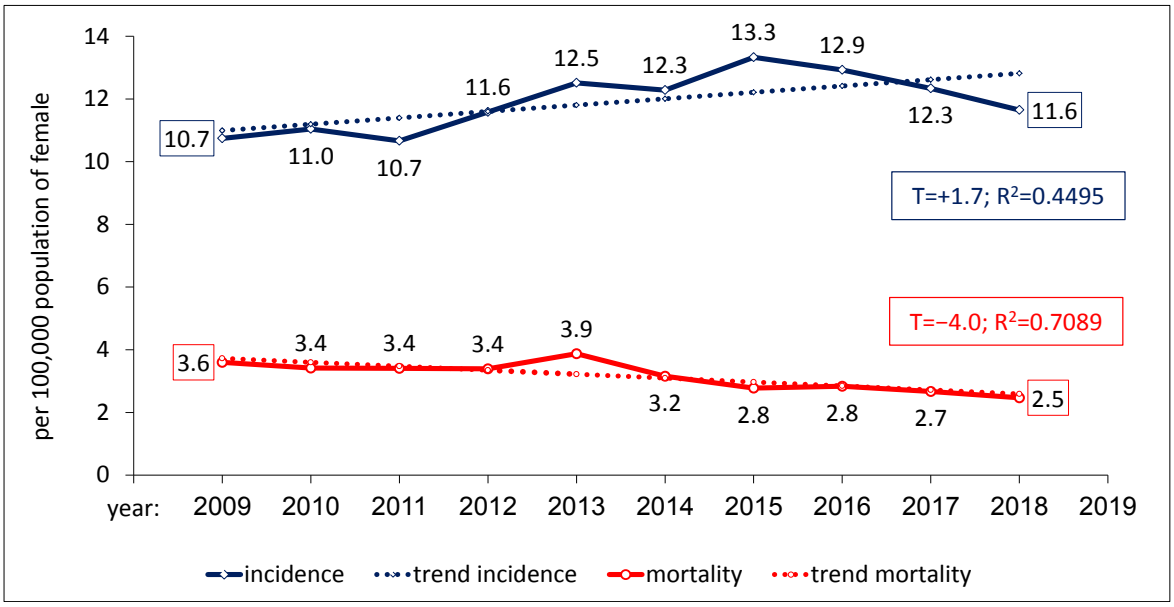


Figure 1. Dynamics of Crude Incidence and Mortality Rates of Corpus Uteri Cancer in Kazakhstan, 2009-2018

Table 1. Number of Corpus Uteri Cancer and Average Age of Patients by Regions of Kazakhstan, 2009-2018

Regions	Number (%)*	Average age, years		T, %	R^2
		P±m	95% CI		
Mangistau	127 (1.2)	59.5±0.8	57.8-61.1	+0.32	0.0511
Atyrau	147 (1.4)	57.9±1.1	55.7-60.0	+0.14	0.0052
Kyzylorda	164 (1.6)	57.0±1.1	54.9-59.1	−0.93	0.2519
Zhambyl	373 (3.5)	59.7±0.5	58.7-60.8	+0.41	0.2030
West Kazakhstan	399 (3.8)	60.4±0.7	59.1-61.7	−0.06	0.0037
Akmola	499 (4.7)	61.2±0.6	60.0-62.3	+0.35	0.1320
Astana city	505 (4.8)	59.3±0.7	58.0-60.7	−0.37	0.1060
Aktobe	527 (5.0)	58.2±0.5	57.2-59.2	−0.02	0.0003
North Kazakhstan	652 (6.2)	61.6±0.5	60.7-62.6	+0.64	0.5207
South Kazakhstan	676 (6.4)	58.9±0.5	58.0-59.9	−0.13	0.0245
Pavlodar	744 (7.1)	61.1±0.4	60.3-61.8	+0.55	0.7794
Almaty	859 (8.2)	58.1±0.5	57.1-59.2	+0.18	0.0380
Kostanay	905 (8.6)	61.7±0.4	60.8-62.6	+0.25	0.1243
East Kazakhstan	1238 (11.8)	62.0±0.3	61.4-62.7	+0.06	0.0116
Karaganda	1341 (12.7)	61.0±0.4	60.1-61.9	+0.44	0.3625
Almaty city	1366 (13.0)	60.6±0.4	59.9-61.4	−0.01	9.00E-05
Kazakhstan	10522 (100.0)	60.4±0.2	60.1-60.7	+0.15	0.3534

* the table is built taking into account the sorting from A to Z of the number of patients

Table 2. The Average Age-Specific Incidence Rates of Corpus Uteri Cancer in Kazakhstan for the Years 2009-2018

Age groups. years	ASIR. per 100.000 population of female		$T_{up/down}$. %	R^2
	M±m	95% CI		
<30	0.1±0.0	0.1-0.2	−2.6	0.0618
30-34	1.2±0.1	0.9-1.5	−0.2	0.0003
35-39	3.5±0.3	2.8-4.2	+0.9	0.0077
40-44	7.5±0.6	6.4-8.6	+1.2	0.0248
45-49	16.3±0.4	15.6-17.1	+0.4	0.0244
50-54	28.1±0.8	26.5-29.8	−1.1	0.1453
55-59	42.4±1.8	39.0-45.9	+1.4	0.1200
60-64	55.6±1.5	52.6-58.5	−1.7	0.3950
65-69	58.8±3.6	51.8-65.9	+3.7	0.3449
70-74	49.4±2.1	45.2-53.6	+1.7	0.1622
75-79	44.8±1.2	42.3-47.2	−1.7	0.3830
80-84	27.1±2.0	23.1-31.1	+6.4	0.6714
≥85	13.7±0.9	12.0-15.5	−0.9	0.0216

The standardized incidence rate does not have a pronounced increase. The aligned curve indicates a slight growth rate. The incidence rate for this period of time actually remains unchanged, amounting to 11.1±0.2 per 100,000 female population (p=0.55; R^2=0.083; T_{up}=+0.6% (Figure 2).

Age-specific incidence rates had a unimodal increase with a peak in 65-69 years. The ASIR analysis showed a high rate in the age groups of 55-79 years per 100,000 female population: 42.4 in 55-59 years, 55.6 in 60-64 years, 58.8 in 65-69 years, 49.4 in 70-74 years and 44.8 in 75-79 years (Table 2). The incidence of CUC tended to decrease in half of the studied age groups. The most pronounced downward trend was revealed in the age group < 30 years (T_{down}=−2.6%), and the most pronounced annual average upward rates was in 80-84 years (T_{up}=+6.4%) (Table 2).

The analysis of ASIR in the context of regions showed (Table 3) that they had a unimodal peak of incidence. Almost all regions had a peak incidence in the age group of 60-69 years, except for the Kyzylorda region, which had a peak incidence in the age group of 50-59 years (21.5±3.4 per 100,000 female population) and the city of Astana, which had a peak incidence in 70 years and older (74.2±9.0 per 100,000 female population).

The trends of ASIR according to regions had a different tendency. Thus, in the age group up to 30 years, the most pronounced values of the average annual growth rates were established in the city of Astana (T_{up}=+85.8; R^2=0.132), and the pronounced rate of decline in the Pavlodar region (T_{down}=−26.5; R^2=0.271) region. High ASIR decline in the age group 30-39 were revealed in Zhambyl region (T_{down}=−13.4; R^2=0.180) and growth in Mangistau region (T_{up}=+16.8; R^2=0.063). In 40-49 years, significant decrease was noted in the Pavlodar region (T_{down}=−7.6; R^2=0.394) and in Mangistau region was a tendency of pronounced growth (T_{up}=+42.4; R^2=0.442) (Table 3). The increase of ASIR at age group 50-59 was

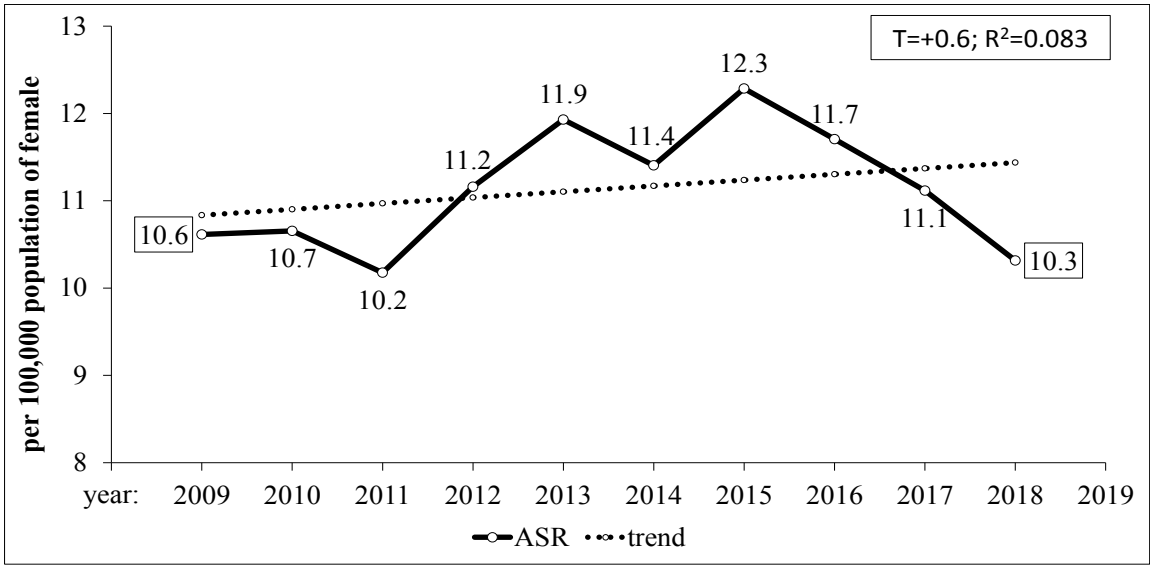


Figure 2. Dynamics of Age-Standardized Incidence Rate of Corpus Uteri Cancer in Kazakhstan, 2009-2018

Table 3. Average ASIR of Corpus Uteri Cancer in the Regional Context. 2009-2018

Regions	Indicators	Age groups. years					
		<30	30-39	40-49	50-59	60-69	≥70
Akmola	P±m	0.1±0.1	3.0±0.9	10.1±1.1	31.3±2.5	50.7±3.7	37.7±4.1
	T. %	+12.0	+13.4	−3.4	+3.3	+0.5	+7.9
	R^2	0.165	0.165	0.097	0.167	0.005	0.468
Aktobe	P±m	0.2±0.1	1.3±0.2	19.8±3.0	42.4±4.5	51.7±4.6	39.0±3.6
	T. %	−3.4	−2.2	+6.2	+5.5	+1.3	+1.6
	R^2	0.004	0.016	0.153	0.250	0.021	0.029
Almaty	P±m	0.2±0.1	2.5±0.4	11.1±2.2	29.1±3.0	41.5±3.3	24.7±2.8
	T. %	+4.2	+4.3	+2.1	−0.7	+0.1	+0.8
	R^2	0.013	0.062	0.011	0.004	0.000	0.005
Atyrau	P±m	0.1±0.1	1.4±0.5	8.1±1.5	17.2±3.7	30.1±4.1	15.5±4.0
	T. %	−18.7	+7.1	+11.8	+1.0	−2.4	+16.5
	R^2	0.165	0.033	0.321	0.002	0.032	0.268
East Kazakhstan	P±m	0.3±0.1	2.1±0.5	11.9±1.1	38.2±1.9	64.2±3.2	45.5±2.3
	T. %	−18.8	+9.9	−1.0	+3.8	+2.3	−0.4
	R^2	0.201	0.148	0.012	0.544	0.214	0.007
Zhambyl	P±m	0.1±0.0	1.5±0.4	7.0±1.3	22.9±1.0	38.2±3.0	23.6±4.1
	T. %	−18.0	−13.4	−5.9	+0.4	+2.8	−4.8
	R^2	0.121	0.180	0.111	0.007	0.124	0.082
West Kazakhstan	P±m	0.1±0.1	1.8±0.6	11.1±2.3	34.6±2.5	56.1±4.9	32.7±4.4
	T. %	−18.7	−1.4	+9.4	+4.4	+0.7	+4.1
	R^2	0.165	0.002	0.168	0.349	0.007	0.086
Karaganda	P±m	0.2±0.1	4.6±0.7	15.1±1.5	42.8±2.1	73.4±5.2	52.4±4.0
	T. %	+5.1	−6.2	−4.0	+1.8	+2.0	−0.4
	R^2	0.016	0.194	0.176	0.132	0.079	0.002
Kyzylorda	P±m	0.1±0.1	0.8±0.4	6.2±1.1	21.5±3.4	17.9±3.1	16.6±5.1
	T. %	+26.6	−4.5	+6.8	+0.1	−0.3	−22.6
	R2	0.119	0.006	0.143	5.00E-05	0.000	0.352
Kostanay	P±m	0.1±0.1	2.6±0.5	15.8±1.8	45.4±3.2	74.8±6.1	49.1±3.6
	T. %	+22.7	+5.5	+1.7	−4.2	+0.0	−0.7
	R^2	0.084	0.081	0.024	0.359	4.00E-06	0.009
Mangistau	P±m	0.1±0.1	0.7±0.4	4.2±1.3	17.9±2.1	30.4±3.4	24.6±7.4
	T. %	−21.7	+16.8	+42.4	+1.6	+1.6	+21.6
	R^2	0.084	0.063	0.442	0.019	0.021	0.274
Pavlodar	P±m	0.1±0.1	3.4±0.5	15.7±1.9	43.1±3.0	75.4±3.4	47.8±3.0
	T. %	−26.5	−7.2	−7.6	−2.4	+1.2	−2.1
	R^2	0.271	0.288	0.394	0.121	0.071	0.117
North Kazakhstan	P±m	0.3±0.1	4.8±1.2	14.5±2.1	43.5±5.0	76.6±5.0	50.6±4.7
	T. %	+2.3	−7.0	+0.0	−0.2	+2.7	+4.3
	R^2	0.003	0.080	1.00E-06	0.000	0.171	0.208
South Kazakhstan	P±m	0.0±0.0	1.1±0.3	7.0±0.8	20.7±1.6	34.6±2.2	20.8±2.3
	T. %	−1.1	+5.0	−4.3	+5.1	−4.6	−2.1
	R^2	0.000	0.026	0.159	0.420	0.545	0.036
Almaty city	P±m	0.2±0.1	2.5±0.4	16.1±1.2	47.2±2.9	73.8±3.6	49.8±2.7
	T. %	−7.9	+4.9	+3.1	−1.7	+1.9	−0.1
	R^2	0.042	0.073	0.164	0.075	0.145	0.000
Astana city	P±m	0.2±0.1	2.6±0.8	14.5±1.6	44.1±3.3	72.7±4.8	74.2±9.0
	T. %	+85.8	−0.6	+0.0	−1.9	−3.0	−5.8
	R^2	0.132	0.000	1.00E-05	0.062	0.218	0.236
Kazakhstan	P±m	0.1±0.0	2.3±0.1	11.9±0.4	34.7±1.0	56.8±1.6	39.9±0.7
	T. %	−2.6	+0.3	+0.3	+0.5	+0.7	+0.2
	R^2	0.062	0.002	0.008	0.036	0.067	0.0100

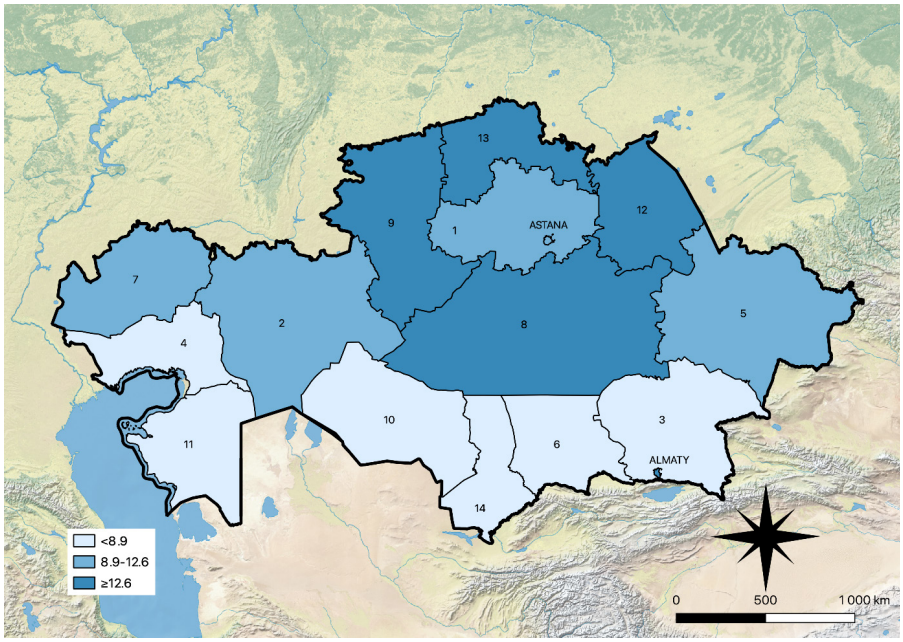
Table 4. Changes in the Age-Standardized Incidence rate of corpus uteri cancer in 2009-2018

Regions	ASR. per 100.000 population of female			Significance		$T_{up/down}$. %*	R^2
	2009	2018	Mean	t	p		
Astana city	13.8±2.5	9.7±1.5	15.33±0.96	1.41	0.16	−2.9	0.223
Pavlodar	15.8±1.8	13.2±1.6	14.2±0.64	1.08	0.28	−1.8	0.165
Kyzylorda	3.3±1.1	5.9±1.2	5.1±0.48	1.60	0.12	−1.5	0.026
Kostanay	14.7±1.6	11.7±1.4	14.3±0.61	1.41	0.16	−1.2	0.078
Zhambyl	7.0±1.2	6.4±1.0	7.2±0.28	0.38	0.70	−1.0	0.064
South Kazakhstan	6.6±0.9	5.4±0.7	6.5±0.26	1.05	0.29	−0.8	0.038
Karaganda	14.1±1.3	14.9±1.2	14.4±0.53	0.45	0.65	+0.4	0.011
Kazakhstan	10.6±0.4	10.3±0.3	11.1±0.23	0.60	0.55	+0.6	0.083
Almaty city	15.4±1.4	14.3±1.2	14.64±0.48	0.60	0.55	+0.7	0.048
Almaty	8.4±1.0	6.7±0.8	8.7±0.79	1.33	0.19	+0.7	0.007
North Kazakhstan	12.5±1.8	12.3±1.8	14.8±0.74	0.08	0.94	+1.7	0.116
East Kazakhstan	10.8±1.1	13.0±1.1	12.3±0.28	1.41	0.17	+1.8	0.584
Akmola	6.8±1.2	9.7±1.4	10.1±0.55	1.57	0.12	+3.2	0.336
West Kazakhstan	10.2±1.9	11.1±1.7	10.7±0.59	0.35	0.73	+3.3	0.342
Atyrau	5.0±1.6	6.6±1.7	5.9±0.52	0.69	0.50	+3.8	0.176
Aktobe	11.8±1.8	11.0±1.6	12.2±1.12	0.33	0.74	+4.1	0.191
Mangistau	4.0±1.6	8.7±1.8	5.8±0.56	1.95	0.06	+6.6	0.421

*the table is built taking into account the sorting from A to Z of the Tup/down value

found in South-Kazakhstan (T_{up}=+5.1; R^2=0.420) and Aktobe (T_{up}=+5.5; R^2=0.250) regions, in Kostanay region was the most pronounced downward trend (T_{down}=−4.2; R^2=0.359). The incidence rates at 60-69 years had a different tendency, a pronounced downward trend revealed in South-Kazakhstan region (T_{down}=−4.6; R^2=0.545), and upward trends were in North-Kazakhstan region (T_{up}=+2.7; R^2=0.171) and in Zhambyl region (T_{up}=+2.8; R^2=0.124). The incidence trends at age group 70 years and older were the most pronounced in Kyzylorda (T_{down}=−22.6; R^2=0.352) and in Atyrau (T_{up}=+16.5; R^2=0.268), Mangistau (T_{up}=+21.6; R^2=0.274) regions (Table 3).

In dynamics, ASR had differences by region, which generally affected the indicator for the republic. In southern regions such as Kyzylorda (T_{down}=−1.5%; R^2=0.026), Zhambyl (T_{down}=−1.0%; R^2=0.064) and South Kazakhstan regions (T_{down}=−0.8%; R^2=0.038), CUC



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 3. Cartogram of Corpus Uteri Cancer Incidence in Kazakhstan, 2009-2018

incidence is decreasing. However, the changes in the initial and final indicators were statistically insignificant, and the approximation values were low. We are concerned about the fact that a significant increase in incidence has been detected in the western regions: West Kazakhstan (T_{up}=+3.3; R^2=0.342), Atyrau (T_{up}=+3.8; R^2=0.176), Aktobe (T_{up}=+4.1; R^2=0.191), Mangistau (T_{up}=+6.6; R^2=0.421). In the eastern part of the country, the corpus uteri cancer incidence increases with a high level of approximation (East Kazakhstan – T_{up}=+1.8; R^2=0.584) (Table 4).

Based on the calculated average annual ASR CUC indicators, the cartogram was compiled. The levels of CUC ASR per 100,000 population of female based on the following criteria were determined: low – up to 8.9, average – from 8.9 to 12.6, high – above 12.6. As a result, the following groups of regions were revealed (Figure 3):

1. Regions with the lowest indicators (up to 8.9 per 100,000 population of female): Kyzylorda (5.1), Mangystau (5.8), Atyrau (5.9), South Kazakhstan (6.5), Zhambyl (7.2), Almaty (8.7).

2. Regions with average indicators (from 8.9 to 12.6 per 100,000 population of female): Akmola (10.1), West Kazakhstan (10.7), Aktobe (12.2), East Kazakhstan (12.3).

3. Regions with high indicators (12.6 and above per 100,000 population of female): Pavlodar (14.2), Kostanay (14.3), Karaganda (14.4), Almaty city (14.6), North Kazakhstan (14.8) and Astana city (15.3).

Thus, the incidence cartogram more clearly reflects the spatial distribution of CUC in the republic, while the discrepancy between the theoretical and actual distribution of CUC incidence by regions and cities is small, the Pearson criterion (χ^2) equals 5.3.

Discussion

In recent years, the incidence of CUC in Kazakhstan has been increasing, while mortality from this pathology is decreasing with a high level of approximation. At this, the increase in morbidity was due to changes in the age structure of the population (+1.270/0000) and the increase in the number of patients was mainly due to demographic component (+117.3%) (Telmanova et al., 2021). Since CUC develops in older age groups, this explains the increase in morbidity in the country. After all, the relative number of elderly people in Kazakhstan is growing (Sidorenko et al., 2018). In addition, there is evidence of positive changes in the indicators of the oncological service: in Kazakhstan the proportion of morphological verification and early detection of CUC is increasing, at the time of diagnosis the proportion of patients with advanced cancer is decreasing (Telmanova et al., 2022). This may be due to the gradual increase in awareness of endometrial cancer both among the general public and among medical professionals, with an increase in the level of medical care and with improved access to medical care over the past decades.

Compared to all other cancers, endometrial cancer has the strongest association with obesity. The main reason for the high incidence of CUC in our republic may be the widespread overweight and obesity. Thus, the incidence of CUC according to the results of our study is high where there is an average and high incidence of obesity (Igissinov and Baltakaeva, 2011). In Kazakhstan, there is a tendency to increase overweight and obesity among the adult population. The age-standardized prevalence of overweight (BMI ≥25 kg/m^2) among adults was 54% for men and 53% for women (WHO, 2017A). In addition, 19% of men and 23% of women are obese (BMI ≥30 kg/m^2) (WHO, 2017B). Given the growing incidence of highly differentiated clinically aggressive tumors in the world among obese women (Lu and Broaddus, 2020), one of the main measures to combat uterine body cancer should be to reduce the spread of obesity among women, including in Kazakhstan.

In Poland in 1985-1990, there was the same trend of increasing morbidity as in our country, that is, an increase in the indicator from 10.60/0000 to 11.80/0000 (Banas et al., 2016). In Asian countries, the incidence rates, as in our country, are found in Saudi Arabia (10.90/0000), Turkey (11.30/0000) and in United Arab Emirates (11.70/0000) (Ferlay et al., 2020).

Over the past 10 years, the rate of increase in the incidence of CUC has been +1.7%. This trend has also been found in many countries: Uganda (+1.7% in 1991-2012), Norway (+1.7% in 1988-2010), Israel (+1.9% in 1983-2007), Spain (+1.9% in 1988-2007) (Lortet-Tieulent et al., 2018).

Age is an important factor for the development of hormone-dependent tumors, including for this form of cancer. Worldwide, the incidence among women at premenopausal age (age 25-49 years) and postmenopausal age (age 50 years and older) differ 4-20 times in favor of older age (Lortet-Tieulent et al., 2018). The age-related incidence rates of CUC increased with age and the highest rate was set at 65-69 years. The same trend was established in the Kamrup urban District in 2010-2014 (Barman et al., 2017). Also in Denmark, the age-related incidence rates reach a peak of about 70 years. Also in Denmark, the age-related incidence rates reach a peak of about 70 years (Ør Knudsen et al., 2016). But at the same time, in Denmark, the incidence is several times higher in the age group of 70 years or more, when in Kazakhstan the highest rates belong to the age group of 60-69 years.

Elderly patients generally have more aggressive histological subtypes and later stages when making a diagnosis (Bourgin et al., 2016). The high rate of increase in morbidity in the age group 80-84 is alarming, since we know that older women have a very high risk of mortality from CUC (Nolen et al., 2017).

Limitations of the current study include the quality of primary data, the lack of data on ethnic groups. For our future research, a deeper study of epidemiology issues, in particular ethnoepidemiology, and the compilation of district cartograms will be priority areas. At the moment, we have generalized data on the incidence of uterine cancer in Kazakhstan, which are of both theoretical and practical interest and play an important role in monitoring and evaluating anti-cancer measures implemented in the country.

In conclusion, the study revealed that the incidence of CUC in Kazakhstan is increasing. And, most likely, this

is due to the increased influence of risk factors such as population aging, declining fertility, obesity, and it is also caused by socio-demographic, ethnic factors and factors of reproductive anamnesis. High incidence rates were found in the northern regions of the country, and the trend of incidence growth was more pronounced in the western and eastern regions.

Author Contribution Statement

ZhT, AA, KK, YK: Collection and preparation of data, primary processing of the material and their verification; DK, GD, ZJ, YSh: Statistical processing and analysis of the material, writing the text of the article (material and methods, results); ZA, GO, KI, TK, DT, VM: Writing the text of the article (introduction, discussion); NI, GI, ZB, ZK: Concept, design and control of the research, approval of the final version of the article; All authors approved the final version of the manuscript.

Acknowledgements

The authors greatly appreciate the contribution of the Ministry of Health of the Republic of Kazakhstan to the current research by providing the data.

This study was not funded, the work was of an initiative nature, and was carried out within the framework of cooperation between these organizations. The study was approved by the Scientific Council of the NGO "Central Asian Institute for Medical Research" (Protocol 19 of Feburary 26, 2022).

Conflict of interest

The authors declare that there is no conflict of interest.

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