Breast Cancer Incidence in Kyrgyzstan: Report of 15 Years of Cancer Registry

Asan Chokoev^{1,2}, Stalbek Akhunbaev¹, Indira Kudaibergenova^{2,3}, Enverbek Soodonbekov^{2,4}, Kuanysh Kulayev⁵, Kadyr Ospanov⁵, Yerlan Kuandykov⁵, Zhansaya Telmanova^{5,6}, Emil Makimbetov^{1,7}, Nurbek Igissinov⁸*

Abstract

Objective: The epidemiological features of the breast cancer (BC) incidence in Kyrgyzstan were studied. Methods: The retrospective study (2003-2017). Descriptive and analytical methods of oncoepidemiology were used. Crude (CR), age-specific (ASIR), age-standardized (ASR), 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. Results: During the study period, 7,850 new cases of BC were registered. The average annual crude and age-standardized incidence rate were 18.8±0.5 and 24.0±0.5 cases per 100,000 population of female, respectively, and their trends tended to increase (T=+1.0%; R²=0.242 and T=+0.2%; R²=0.015, respectively). The analysis of ASIR showed unimodal growth with a peak at 60-64 years – 85.9±4.9 cases per 100,000 population of female. ASIR trends decreased in the age groups of 40-59 years, and the most pronounced decrease was in 50-54 years (T=-1.5%; R²=0.391), in other age groups the trend increased and were most pronounced up to 30 years (T=+4.4%; R²=0.180). Trends in ASR of BC tended to grow in almost all regions, with higher levels in Osh (T=+3.6%; R²=0.665) and Jalal-Abad (T=+3.8%; R²=0.551) regions. The cartograms of ASR per 100,000 population of female were allocated according to the following criteria: low – up to 17.2, average – from 17.2 to 26.5, high – above 26.5. The results of the spatial analysis showed the regions with a higher levels of BC incidence rate per 100,000 population of female: Chuy (31.3), Osh city (27.1) and Bishkek city (39.2). Conclusion: The study of the epidemiological spatio-temporal features of the incidence of breast cancer is of both theoretical and practical interest and plays an important role in monitoring and evaluating anticancer activities.

Keywords: Breast cancer- incidence- trends- Kyrgyzstan

Asian Pac J Cancer Prev, 23 (5), 1603-1610

Introduction

Breast cancer is a serious medical problem. The growth of breast cancer is a grave concern, since according to the IARC, about 2.26 million new cases are registered annually, and an increase of 21% - 2.74 million is expected in 2030 (Ferlay et al., 2019; Ferlay et al., 2020A; Ferlay et al., 2020B). In the structure of oncological pathology, breast cancer takes the first place (11.7%), followed by lung cancer (11.4%) and colorectal cancer (10%). The incidence rate of breast cancer in the world is 47.8 per 100,000 women. At the same time, high morbidity rates per 100,000 women are observed in such countries as

Belgium (113.2), the Netherlands (100.9), France (99.1), and low morbidity rates in Bhutan (5.0), the Republic of the Gambia (11.0), Mongolia (11.1). According to the data, the cumulative risk of breast cancer is high in regions with a high Human Development Index (HDI): in regions with high HDI (4.57) and very high HDI (8.17), and low in regions with low and medium HDI (3.88 and 3.04, respectively).

So, the incidence in developing countries is lower than in developed countries. Because there is a paucity of data in developing countries, where there is no effective cancer registry, the age standardized incidence rates (ASIR) are estimates based on data from neighboring countries

¹International Higher School of Medicine, Bishkek, Kyrgyzstan Eurasian Institute for Cancer Research, Bishkek, Kyrgyzstan. ²International Higher School of Medicine, Bishkek, Kyrgyzstan. ³Kyrgyz State Medical Academy named after I. K. Akhunbaev, Bishkek, Kyrgyzstan, Eurasian Institute for Cancer Research, Bishkek, Kyrgyzstan. ⁴National Center for Oncology and Hematology, Bishkek, Kyrgyzstan Eurasian Institute for Cancer Research, Bishkek, Kyrgyzstan. ⁵Khoja Akhmet Yassawi International Kazakh-Turkish University, Shymkent Campus, Kazakhstan. ⁶Astana Medical University, Nur-Sultan, Kazakhstan Central Asian Institute for Medical Research, Nur-Sultan, Kazakhstan Eurasian Institute for Cancer Research, Bishkek, Kyrgyzstan. ⁷Kyrgyz-Russian Slavic University, Bishkek, Kyrgyzstan, International Higher School of Medicine, Bishkek, Kyrgyzstan. ⁸Eurasian Institute for Cancer Research, Bishkek, Kyrgyzstan, Astana Medical University, Nur-Sultan, Kazakhstan, Central Asian Cancer Institute, Nur-Sultan, Kazakhstan. *For Correspondence: n.igissinov@gmail.com

Asan Chokoev et al

and from hospital registries. There is a wide variation in incidence rates around the world and there is a trend for the ASIR to increase with the wealth of a country (Yip and Taib, 2014). Although the survival rate in breast cancer has improved, it varies in different countries distinctly (Lin et al., 2019), due to factors such as lack of early-stage screening, detection, and cost-effective therapy (Ginsburg et al., 2017).

Breast cancer is a multifactorial disease (Zendehdel et al., 2018), and various factors contribute to its occurrence, such as population structure, lifestyle, genetic factors and the environment (Hortobagyi et al., 2005; Jones et al., 2017; Gray et al., 2017; Ooi et al., 2019; Xiao et al., 2019). Changes in risk factors have led to an increase in the prevalence of breast cancer, which is growing every day (Parkin and Fernández, 2006; Budny et al., 2019; Fahad Ullah, 2019; Li et al., 2019). The incidence of breast cancer increases in proportion to the increase in life expectancy and urbanization (Bulletin of the World Health Organization, 2015).

Breast cancer is one of the three oncological diseases that the WHO recommends for screening in countries. Global breast cancer incidence patterns reflect both risk factors and the availability and use of mammography. Breast cancer is one of the most unpreventable cancers; however, it is also one of the most curable. Although screening people can reduce the burden of breast cancer, side effects, overdiagnosis and increased costs are disadvantages of this method (Niell et al., 2017; Harkness et al., 2020; Khrouf et al., 2020). This article analyzes the incidence of breast cancer in Kyrgyzstan, where there is no mammographic screening.

Materials and Methods

Cancer registration and patient recruitment

The population of Kyrgyz Republic as the 2017 census was 6.2 million, of which 3.1 million were females (National Statistical Committee of the Kyrgyz Republic, 2017), while the dynamics of the female population increased by 19.2% compared to 2003. The cancer registry of the population of Kyrgyzstan covers 7 regions and cities of national significance - Osh and Bishkek. New cases of breast cancer were extracted from the accounting and reporting forms of the Ministry of Health of Kyrgyz Republic – form 7 and form 35, which were formed from the register of oncological diseases based on the administrative-territorial division of the republic for fifteen years (from 2003 to 2017) using the International Disease Code 10, code C50.

In Kyrgyzstan, when a cancer diagnosis is established, the registration form "Notification of a patient with a cancer diagnosis for the first time in his life" (form 096/y) is filled in for all patients, in addition, a control card of dispensary observation is filled in (form 030). If a cancer case is taken into account posthumously, in addition to the notification, a protocol is filled in in case a patient has an advanced form of cancer (form 027-2y), then these accounting forms are processed and at the end of the year reporting forms 7 and 35 are issued and submitted to the regional e-health centers, then to the republican e-health

center.

Population denominators

Population denominators for calculation of incidence rates were provided by the National Statistical Committee of the Kyrgyz Republic for 2003-2017. At the same time, data on the number of female populations of the republic, taking into account the studied regions, are used, all data are presented on the official website (www.stat.kg).

Statistical analysis

The main method used in the study of incidence was a retrospective study using descriptive and analytical methods of modern oncoepidemiology. Age-standardized incidence rates (ASRs) were calculated for nine different age groups (0-30, 30-34, ..., 60-64, and 65+) and fifteen calendar periods from 2003 to 2017 (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 (2013) were estimated for each studied year. The age-standardized indicator is a weighted average of age-specific indicators, where the weights represent the proportions of individuals in the corresponding age groups of the standard population. That is, the previously calculated age-specific mortality or morbidity coefficients of each studied population group are multiplied by the corresponding relative numbers of the age distribution of the standard. The extensive, crude and age-specific (ASIR) incidence rates 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 15 years, while the trends of incidence were determined by the least squares method. To calculate the average annual growth rate and/or growth rate of the dynamic series, the geometric mean equal to the root of the power of n from the product of the annual growth rate indicators was used.

When compiling cartograms, crude rates and ASRs were used for 15 years (2003-2017). The method of compiling a cartogram proposed in 1974 by S.I. Igissinov was used, based on the determination of the standard deviation (σ) from the average (x). The scale of steps was calculated as follows: taking σ as an interval, the maximum and minimum levels of incidence were determined according to the formula: $x\pm 1.5 \sigma$, with the minimum indicator equal to x–1.5 σ and the maximum equal to x+1.5 σ . After that, we determined the scale of the cartogram steps: 1) $(x-1,5\sigma)+\sigma$; 2) $(x-1,5\sigma)+2\sigma$; 3) $(x-1.5\sigma)+2\sigma$; 4) $(x-1.5\sigma)+2\sigma$; 4) (x-1.5\sigma); 4) $(x-1.5\sigma)+2\sigma$; 4) (x-1.5\sigma)+2\sigma; 4) $(x-1.5\sigma)+2\sigma$; 4) (x-1.5\sigma)+2\sigma; 4) (x-1.5\sigma); 4) (x-1.5\sigma)+2\sigma; 4) σ)+3 σ , etc., and the indicators were grouped according to the formula $x\pm 0.5 \sigma$, corresponding to the average level (x-0.5 σ and x+0.5 σ), and the values that are separated from the average level of incidence by σ show reduced $((x-0.5 \sigma)-\sigma)$ and increased $((x-0.5 \sigma)-\sigma)$ incidence rate.

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 Kyrgyz Republic No. 82 of July 8, 2019 "About official statistics" (http://www.stat.kg/ru/zakon-kyrgyzskojrespubliki-o-gosudarstvennoj-statistike/), 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 2003-2017, 7,850 new BC cases were registered in the Kyrgyz Republic. The average age of patients in Kyrgyzstan 53.8 \pm 0.2 year. Regions with a lower average age of patients are Osh (50.1 \pm 0.4) and high average age is in Chuy (54.4 \pm 0.4) and in the city of Bishkek (56.9 \pm 0.3). The average age trends show that they are growing in almost all regions: from T=+0.1% (Chuy) to T=+0.7% (Osh) (Table 1).

The crude rate of BC incidence in the republic was 18.8 ± 0.5 per 100,000 population of female, and it grew from 17.7 ± 0.4 in 2003 to 19.0 ± 0.5 in 2017 (Figure 1) in dynamics, the difference was statistically significant (p=0.000).

The ASR in Kyrgyzstan was equal to 24.0 ± 0.5 cases per 100,000 population of female. Over time, the leveled ASR were growing (p=0.654; R²=0.015), with the average

Table 1. Number of Breast Cancer and Average Age of Patients by Regions of Kyrgyzstan, 2003-2017

Regions	Number (%)*	Average	age, years	T, %	\mathbb{R}^2
		P±m	95% CI		
Batken	291 (3.7)	50.6±1.1	48.4-52.8	-0.6	0.0979
Jalal-Abad	855 (10.9)	50.3±0.5	49.2-51.3	+0.2	0.0583
Isıq-Kol	714 (9.1)	53.0±0.6	51.8-54.1	+0.4	0.1548
Narın	286 (3.6)	51.4±0.6	50.2-52.6	+0.1	0.0162
Osh	774 (9.9)	50.1±0.4	49.3-51.0	+0.4	0.3339
Talas	211 (2.7)	51.3±0.9	49.6-53.1	+0.7	0.2635
Chuy	1907 (24.3)	54.4±0.4	53.7-55.1	+0.2	0.1574
City of Osh	391 (5.0)	53.2±0.6	52.0-54.4	+0.1	0.0209
City of Bishkek	2421 (30.8)	56.9±0.3	56.4-57.5	+0.1	0.0456
Kyrgyzstan	7850 (100)	53.8±0.2	53.4-54.3	+0.1	0.0492

annual upward rate of T=+0.2% (Figure 2).

BC occurrence and incidence were directly related to the age composition of the population since the age was one of the most important risk factors. Thus, the analysis of ASIR has shown a high in the age groups of 40+ years

Table 2. The Average Age-Specific Incidence Rates of Breast Cancer in Kyrgyzstan for the Years 2003-2017

Age groups,	ASIR, per 100 of f	,000 population emale	Tup/down, %	R ²
years	M±m 95% CI			
<30	0.5±0.1	0.4-0.7	+4.4	0.1795
30-34	6.6±0.6	5.4-7.7	+3.7	0.2315
35-39	17.9±0.9	16.1-19.7	+0.8	0.0338
40-44	33.9±1.5	30.9-36.9	-0.1	0.0015
45-49	50.6±1.8	47.1-54.0	-1.1	0.1544
50-54	64.8±1.9	61.1-68.5	-1.5	0.3906
55-59	78.3±3.5	71.5-85.1	-1.2	0.0973
60-64	85.9±4.9	76.3-95.6	+1.2	0.0667
≥65	77.7±3.7	70.4-85.0	+1.7	0.1805



Figure 1. Dynamics of Crude Incidence Rate of Breast Cancer in Kyrgyzstan, 2003-2017



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

Regions	Indicators	Age groups, years								
		<30	30-34	35-39	40-44	45-49	50-54	55-59	60-64	≥65
Batken	P±m	0.5±0.2	6.1±2.0	10.7±3.1	22.6±2.2	29.5±4.5	42.4±6.6	31.6±5.0	33.9±9.6	30.0±4.9
	T, %	+5.0	+19.0	-6.0	-0.7	+0.5	-3.9	+3.2	-3.6	-5.4
	\mathbb{R}^2	0.0243	0.189	0.0572	0.0075	0.0017	0.0888	0.0563	0.0232	0.1478
Jalal-Abad	P±m	0.6±0.1	4.8±1.2	15.5±1.9	24.0±2.7	34.5±2.2	52.5±4.5	55.7±4.7	48.7±7.7	30.5±5.0
	T, %	+14.2	+3.2	+2.4	+3.1	+2.0	+4.0	+2.6	+0.6	+10.4
	\mathbb{R}^2	0.3161	0.0228	0.0559	0.1026	0.1418	0.2874	0.1291	0.0018	0.3865
Isıq-Kol	P±m	1.1±0.3	10.3±2.4	20.2±3.6	37.3±5.4	56.3±6.3	63.9±8.3	69.3±6.6	99.9±13.5	68.9±8.8
	Т, %	+2.4	+10.8	+0.6	+1.8	-1.1	-4.4	-1.2	+2.0	+6.6
	\mathbb{R}^2	0.0145	0.2009	0.0014	0.0204	0.0144	0.1593	0.0232	0.0302	0.3147
Narın	P±m	0.2±0.1	8.1±3.1	15.8±3.0	43.8±6.5	61.8±9.4	46.8±8.2	49.0±8.1	53.2±12.1	38.4±5.8
	Т, %	-19.7	+0.5	+5.7	-0.2	+2.0	+7.2	+1.4	-1.1	+1.7
	\mathbb{R}^2	0.0486	0.0002	0.1115	0.0001	0.0231	0.1934	0.0098	0.0033	0.0169
Osh	P±m	0.3±0.1	5.4±0.9	14.2±1.9	28.8±2.8	30.4±2.7	36.8±3.0	37.5±3.3	42.5±6.5	27.8±2.0
	Т, %	+9.5	-1.6	+5.0	+0.8	+2.6	+2.4	+3.6	+8.5	+5.3
	\mathbb{R}^2	0.1747	0.0122	0.1704	0.0108	0.1149	0.1224	0.2263	0.3313	0.6909
Talas	P±m	0.2±0.1	3.6±1.6	16.7±3.9	36.9±7.2	33.7±7.5	54.7±6.4	61.0±16.8	51.3±12.8	26.8±6.7
	Т, %	-11.5	+4.1	+1.6	+2.1	-0.3	-1.3	-1.2	+9.9	+10.5
	\mathbb{R}^2	0.028	0.0103	0.0068	0.0154	0.0003	0.0172	0.0026	0.1576	0.1716
Chuy	P±m	0.8±0.2	10.8±1.5	24.9±2.1	46.7±2.6	71.0±4.0	81.9±4.1	99.9±10.3	109.9±8.4	94.5±5.3
	Т, %	+3.7	+3.0	-1.5	-1.5	-2.2	-0.6	-0.7	+0.7	+2.7
	\mathbb{R}^2	0.0306	0.0669	0.0449	0.1003	0.2237	0.0243	0.0059	0.0121	0.3225
City of Osh	P±m	0.2±0.2	3.8±1.5	15.9±3.7	37.6±6.2	64.5±8.4	72.8±6.1	95.6±12.8	106.4±19.1	83.3±15.0
	Т, %	+1.5	+17.2	+2.5	+2.8	-2.1	-0.7	-0.2	+3.1	+1.4
	\mathbb{R}^2	0.0005	0.2254	0.0164	0.0379	0.0368	0.0104	0.0005	0.0414	0.0088
City of Bishkek	P±m	0.7±0.2	6.2±1.4	21.1±2.5	36.0±3.4	68.7±6.3	96.8±6.5	132.5±10.0	139.6±11.1	168.0±11.9
	Т, %	-0.8	+1.7	-0.2	-2.9	-3.0	-4.9	-2.3	+1.2	-0.9
	\mathbb{R}^2	0.0015	0.0072	0.0003	0.134	0.1555	0.7526	0.1355	0.0297	0.0255
Kyrgyzstan	P±m	0.5±0.1	6.6±0.6	17.9±0.9	33.9±1.5	50.6±1.8	64.8±1.9	78.3±3.5	85.9±4.9	77.7±3.7
	Т, %	+4.4	+3.7	+0.8	-0.1	-1.1	-1.5	-1.2	+1.2	+1.7
	\mathbb{R}^2	0.1795	0.2315	0.0338	0.0015	0.1544	0.3906	0.0978	0.0667	0.1805

Table 3. Average ASIR of BC in the Regional Context, 2003-2017

Regions	ASR, per 100,000 population of female		ion of female	Significance		T, %*	R ²
	2003	2017	Mean	t	р		
Batken	15.2±3.6	10.0±2.3	12.2±0.7	1.22	0.23	-1.6	0.111
Jalal-Abad	11.6±2.1	20.5±2.2	15.1±0.9	2.93	0.00	+3.8	0.551
Isıq-Kol	26.6±4.1	21.3±3.1	24.7±1.2	1.03	0.31	+1.3	0.103
Narın	15.5±4.3	18.8±4.0	18.4±1.4	0.56	0.58	+1.9	0.088
Osh	9.5±1.8	15.5±1.8	12.9±0.7	2.36	0.02	+3.6	0.665
Talas	13.0±4.0	22.8±4.8	15.9±1.5	1.57	0.13	+2.2	0.074
Chuy	31.7±2.9	31.0±2.6	31.3±0.5	0.18	0.86	+0.2	0.012
City of Osh	23.1±5.7	20.0±4.1	27.1±2.5	0.44	0.66	+0.9	0.013
City of Bishkek	40.7±3.4	30.9±2.5	39.2±2.1	2.32	0.02	-1.7	0.138
Kyrgyzstan	23.7±1.2	23.0±1.0	24.0±0.5	0.45	0.65	+0.2	0.015

 Table 4. Changes in the Age-Standardized Incidence Rate of Breast Cancer in 2003-2017

per 100,000 population of female: 33.9 in 40-44 years, 50.6 in 45-49 years, 64.8 in 50-54 years, 78.3 in 55-59 years, 85.9 in 60-64 years, and 77.7 in 65+ years (Table 2).

BC incidence had a downward trend in four studied age groups: 40-44 years (T=-0.1%), 45-49 years (T=-1.1%), 50-54 years (T=-1.5%) and in the age of 55-59 years (T=-1.2%). In other age groups, the leveled BC incidence was growing, with the most pronounced annual average upward rates in the age groups of under 30 years (T=+4.4%), 30-34 (T=+3.7%), and over 65 years (T=+1.7%) (Table 2).

The analysis of ASIR in the context of regions showed (Table 3) that mainly they had a unimodal peak of morbidity. So, the peak incidence per 100,000 population of female at age 50-54 was established in Batken region (42.4). The peak incidence per 100,000 population of female at age 55-59 was in Jalal-Abad (55.7) regions. The peak incidence per 100,000 population of female at age 60-64 was in Isiq-Kol (99.9), Osh (42.5), Chuy (109.9) regions, and in city of Osh (106.4). The peak incidence at 65 years and older was detected only in city of Bishkek

(168.0 per 100,000 population of female). In Narin region bimodal growth was established with peaks at 45-49 years (61.8 per 100,000 population of female) and 60-64 years (53.2 per 100,000 population of female). Also in Talas region bimodal growth was established with peaks at 40-44 years (36.9 per 100,000 population of female) and 55-59 years (61.0 per 100,000 population of female).

The trends of ASIR according to regions had a different tendency. Thus, in the age group under 30, the most pronounced values of the average annual decline rate was established in Narin (T=-19.7; R²=0.0486) region. High ASIR decline in the age group 30-34 were revealed in Osh region (T=-1.6; R²=0.0122) and growth in Batken region (T=+19.0; R²=0.189). In 35-39 years, a significant decrease was noted only in the Batken (T=-6.0; R²=0.0572) and Chuy regions (T=-1.5; R²=0.0449), a very insignificant decrease was in city of Bishkek (T=-0.2; R²=0.0003), in other regions there was a tendency of growth and most pronounced in Narin (T=+5.7; R²=0.1115) and Osh (T=+5.0; R²=0.1704) regions (Table 3). In the age group 40-44, the most



Regions: 1. Batken, 2. Jalal-Abad, 3. Isiq Kol, 4. Narin, 5. Osh, 6. Talas, 7. Chuy

Figure 3. Cartogram of Breast Cancer Incidence in Kyrgyzstan, 2003-2017 (A - CR; B - ASR)

Asian Pacific Journal of Cancer Prevention, Vol 23 1607

pronounced values of the average annual growth rate was established in Jalal-Abad (T=+3.1; R²=0.1026) region. High ASIR decline in 40-44, 45-49, 50-54, 55-59 ages group was revealed in city of Bishkek (T=-2.9; R²=0.134; T=-3.0; R²=0.1555; T=-4.9; R²=0.7526; T=-2.3; R²=0.1355). In the age group 45-49, 55-59 high ASIR growth were established in the Osh region (T=+2.6; R²=0.1149; T=+3.6; R²=0.2263). The increase of ASIR at age group 50-54 was found in Narin region (T=+7.2; R²=0.1934). The incidence rates at 60-64 and over 65 years had a pronounced upward trends revealed in Talas region (T=+9.9; R²=0.1576; T=+10.5; R²=0.1716), and downward trends in Batken region (T=-3.6; R²=0.0232; T=-5.4; R²=0.1478) (Table 3).

In dynamics, ASR tended to decrease in only Batken region (T=-1.6%; R²=0.011), as well as in the city of Bishkek (T=-1.7%; R²=0.179). However, the changes were not statistically significant, as indicated by the low values of the approximation (Table 4).

In other regions, trends in ASR were growing, while a statistically significant difference between the indicators of 2003 and 2017 was found in the following areas: Jalal-Abad (p=0.00), Osh (p=0.02), Talas (p=0.13), Isiq Kol (p=0.31) (Table 4).

Based on the calculated average annual CR and ASR BC indicators, the cartograms were compiled. The levels of BC CR per 100,000 population of female based on the following criteria were determined: low – up to 13.2, average – from 13.2 to 22.8, high – above 22.8. As a result, the following groups of regions were revealed (Figure 3A):

1. Regions with the lowest indicators (up to 13.2 per 100,000 population of female): Batken (8.8), Osh (9.0), Jalal-Abad (10.8), Talas (12.2).

2. Regions with average indicators (from 13.2 to 22.8 per 100,000 population of female): Narin (14.4), Isiq-Kol (21.1) and city of Osh (19.3).

3. Regions with high indicators (22.8 and above per 100,000 population of female): Chuy (30.8) and Bishkek city (35.6).

The levels of BC ASR per 100,000 population of female based on the following criteria were determined: low – up to 17.2, average – from 17.2 to 26.5, high – above 26.5. As a result, the following groups of regions were determined (Figure 3B):

1. Regions with the lowest indicators (up to 17.2 per 100,000 population of female): Batken (12.2), Osh (12.9), Jalal-Abad (15.1), Talas (15.9).

2. Regions with average indicators (from 17.2 to 26.5 per 100,000 population of female): Narin (18.4) and Isıq-Kol (24.7).

3. Regions with high indicators (26.5 per 100,000 population of female and above): Chuy (31.3), Osh city (27.1), Bishkek city (39.2).

Thus, the incidence cartograms more clearly reflect the spatial distribution of BC in the republic, while the discrepancy between the theoretical and actual distribution of BC incidence by regions and cities is small, the Pearson criterion (χ 2) equals 9.0 and 7.8 (for a crude and age-standardized indicator, respectively).

The growth of BC incidence in Kyrgyzstan corresponds to the global trend. The incidence of breast cancer during the study period among the female population of the country was determined as 18.8 cases per 100,000. Crude incidence rates for the period 1989-1994 in the Kyrgyzstan separate mountain regions amounted to 25.2 per 100,000 female population (Igisinov et al., 2002). And in our previous study, the incidence of breast cancer among women of reproductive age (1995-2002) was 12.3 cases per 100,000 female population (Igisinov et al., 2005). The average age of patients with BC in the republic during the study period was 53.8 years. While the average age of breast cancer patients in Kyrgyzstan in 1989-1994 was 57.4 (Igisinov et al., 2002). It should be noted that the age of breast cancer patients is an important risk factor and prognostic factor. So there is a study (Chen et al., 2016), the results of which show that young patients with breast cancer had a more aggressive disease than older patients. Also, middle-aged patients showed better survival than young patients, with the exception of patients with stage III of the disease. However, the age of 60 years or more was a significant independent predictor of a poor prognosis.

Age analysis of BC incidence in Kyrgyzstan has revealed a unimodal growth with a peak of incidence at the age of 60-64 years (85.9 cases per 100,000 population of female). This trend has continued since the last study was performed (Igisinov et al., 2002), similar data were obtained in our studies on Kazakhstan (Toguzbaeva et al., 2021).

Analyzing with historically past spatial studies (cartograms), the incidence is growing in all regions, and the Osh region (including the Batken region), Talas region also belong to regions with a low frequency of breast cancer, Isyq-Kol to regions with average values, and data for the Chuy region – to high indicators. At the same time, there have been changes: the Naryn region has moved to regions with an average incidence rate (Igisinov, 2007).

We associate the factors contributing to a decrease or increase in morbidity with the organization of accounting and registration of breast cancer, as well as with anticancer measures. Unfortunately, mass mammological breast screening is not carried out in Kyrgyzstan, which in turn does not show an accurate picture of the burden of breast cancer. A recent study of breast cancer in Africa confirms the importance of adapting breast cancer education and breast health awareness for both patients and the general population to local conditions, taking into account educational and cultural characteristics. (Olayide et al., 2021).

Early detection of breast cancer with screening mammography significantly reduces the risk of death from the disease (Smith et al., 2004; Tabar et al., 2015). The strongest evidence is provided by randomized controlled trials (RCTs), and pooled estimates show that screening mammography can reduce breast cancer mortality by at least 20% (Oeffinger et al., 2015). The USPSTF, ACS, and ACR are the 3 main organizations that have issued evidence-based guidelines for breast cancer screening in average-risk women. All 3 guidelines state that annual

mammography should remain an option for women starting at age 40 because annual screening mammography beginning at age 40 saves the most lives from breast cancer (Oeffinger et al., 2015; Mainiero et al., 2013; Siu, 2016).

Limitations of the current study include the quality of the primary data. Since there are changes in the policy of providing cancer care, and accounting and registration require additional resources, this may eventually affect the results of the study. Currently, it is not yet possible to get data from the reporting forms for ethnic groups, not in the forms of the district level (we have data for regions, which in its turn consist of districts). Such data would allow us to study more deeply the issues of epidemiology, in particular ethnoepidemiology, and to make district cartograms. Thus, at this moment we have generalized data. Nevertheless, there is no doubt about it, since the results of the analysis show that the common trends in the incidence of breast cancer in this study coincide with the same data in the world. Consequently, our findings should be correct.

Thus, the study of the epidemiological spatio-temporal features of the incidence of breast cancer is of both theoretical and practical interest and plays an important role in monitoring and evaluating anticancer activities.

Author Contribution Statement

Conceptualization: EM, NI. Data curation: ACh, ES, ZhT. Formal analysis: ACh, ZhT. Investigation: ACh, SA, IK. Methodology: ACh, ES, NI. Supervision: NI, EM, IK. Writing – original draft: ACh, ZhT. Writing – review & editing: NI, EM.

Acknowledgments

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

This study was not funded, it was performed within the framework of the Asan Chokoev's PhD dissertation, the topic of the dissertation was approved at the International Higher School of Medicine.

Conflict of interest

The authors declare that there is no conflict of interest.

References

- Ahmad OE, Boschi-Pinto C, Lopez AD, et al (2001). Age standardization of rates: a new who standard. GPE Discussion Paper Series: No.31 EIP/GPE/EBD World Health Organization.
- Budny A, Starosławska E, Budny B, et al (2019). Epidemiologia oraz diagnostyka raka piersi [Epidemiology and diagnosis of breast cancer]. *Pol Merkur Lekarski*, **46**, 195-204.

Bulletin of the World Health Organization (2015). 93, 283-360.

- Chen HL, Zhou MQ, Tian W, Meng KX, He HF (2016). Effect of Age on Breast Cancer Patient Prognoses: A Population-Based Study Using the SEER 18 Database. *PLoS One*, **11**, e0165409.
- Fahad UM (2019). Breast Cancer: Current Perspectives on the Disease Status. *Adv Exp Med Biol*, **1152**, 51-64.
- Ferlay J, Colombet M, Soerjomataram I, et al (2019).

Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer*, **144**, 1941–53.

- Ferlay J, Ervik M, Lam F, et al (2020A). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https:// gco.iarc.fr/today.
- Ferlay J, Laversanne M, Ervik M, et al (2020B). Global Cancer Observatory: Cancer Tomorrow. Lyon, France: International Agency for Research on Cancer. Available from: https://gco. iarc.fr/tomorrow.
- Ginsburg O, Bray F, Coleman MP, et al (2017). The global burden of women's cancers: a grand challenge in global health. *Lancet (London, England)*, **389**, 847–60.
- Glanc S (1999). Biomedical statistics. Moscow, Practice, p 459.
- Gray JM, Rasanayagam S, Engel C, Rizzo J (2017). State of the evidence 2017: an update on the connection between breast cancer and the environment. *Environ Health*, **16**, 94.
- Harkness EF, Astley SM, Evans DG (2020). Risk-based breast cancer screening strategies in women. *Best Pract Res Clin Obstet Gynaecol*, 65, 3-17.
- Hortobagyi GN, de la Garza Salazar J, Pritchard K, et al (2005).
 ABREAST Investigators The global breast cancer burden: variations in epidemiology and survival. *Clin Breast Cancer*, 6, 391–401.
- Igisinov N, Kokteubaeva N, Kudaibergenova I (2005). Epidemiology of breast cancer in females of reproductive age in Kyrgyzstan. *Asian Pac J Cancer Prev*, **6**, 37-40.
- Igisinov NS (2007). Epidemiology of cancer of the reproductive system in the female population of Kyrgyzstan. Diss Doctor of Medical Sciences. *Almaty*, P 273.
- Igisinov S, Soodonbekov E, Igisinov N, Subanbaev T (2002). Epidemiology of Esophagus, Lung and Breast Cancer in Mountainous Regions of Kyrgyz Republic. Asian Pac J Cancer Prev, 3, 73-6
- Igissinov SI (1974). Preparation and application method of cartograms in oncology. *Healthcare Kazakhstan*, 2, 69-71.
- Isabel dos Santos Silva (1999). Cancer epidemiology: principles and methods. Lyon, France, IARC, p 442.
- Jones ME, Schoemaker MJ, Wright LB, Ashworth A, Swerdlow AJ (2017). Smoking and risk of breast cancer in the Generations Study cohort. *Breast Cancer Res*, **19**, 118.
- Khrouf S, Letaief KF, Ayadi M, Belhaj ARH, Mezlini A (2020). Breast cancer screening: a dividing controversy. *Tunis Med*, **98**, 22-34.
- Li N, Deng Y, Zhou L, et al (2019). Global burden of breast cancer and attributable risk factors in 195 countries and territories, from 1990 to 2017: results from the Global Burden of Disease Study 2017. *J Hematol Oncol*, **12**, 140.
- Lin L, Yan L, Liu Y, et al (2019). Incidence and death in 29 cancer groups in 2017 and trend analysis from 1990 to 2017 from the Global Burden of Disease Study. *J Hematol Oncol*, **12**, 96.
- Mainiero MB, Lourenco A, Mahoney MC, et al (2013). ACR appropriateness criteria breast cancer screening. *J Am Coll Radiol*, **10**, 11–4.
- Merkov AM, Polyakov LE (1974). Sanitary statistics. Leningrad, Medicine, p 384.
- Niell BL, Freer PE, Weinfurtner RJ, Arleo EK, Drukteinis JS (2017). Screening for Breast Cancer. *Radiol Clin North Am*, 55, 1145-62.
- Oeffinger KC, Fontham ET, Etzioni R, et al (2015). Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA*, **314**, 1599–614.
- Olayide A, Isiaka A, Ganiyu R, et al (2021). Demographic Pattern, Tumor Size and Stage of Breast Cancer in Africa: A Meta-analysis. *Asian Pac J Cancer Care*, **6**, 477-92.
- Ooi BNS, Loh H, Ho PJ, et al (2019). The genetic interplay

Asian Pacific Journal of Cancer Prevention, Vol 23 1609

Asan Chokoev et al

between body mass index, breast size and breast cancer risk: a Mendelian randomization analysis. *Int J Epidemiol*, **48**, 781-94.

- Parkin DM, Fernández LM (2006). Use of statistics to assess the global burden of breast cancer. *Breast J*, **12**, 70–80.
- Siu AL, U.S. Preventive Services Task Force (2016). Screening for breast cancer: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med, 164, 279–96.
- Smith RA, Duffy SW, Gabe R, et al (2004). The randomized trials of breast cancer screening: what have we learned?. *Radiol Clin North Am*, **42**, 793–806.
- Tabar L, Yen AM, Wu WY, et al (2015). Insights from the breast cancer screening trials: how screening affects the natural history of breast cancer and implications for evaluating service screening programs. *Breast J*, **21**, 13–20.
- Toguzbayeva A, Telmanova Z, Khozhayev A, et al (2021). Impact of Screening on Breast Cancer Incidence in Kazakhstan: Results of Component Analysis. *Asian Pac J Cancer Prev*, **22**, 2807-17.
- WMA Declaration of Helsinki (2013) Ethical Principles for Medical Research Involving Human Subjects. https://www. wma.net/.
- Xiao Y, Xia J, Li L, et al (2019). Associations between dietary patterns and the risk of breast cancer: a systematic review and meta-analysis of observational studies. *Breast Cancer Res*, **21**, 16.
- Yip CH, Taib NA (2014). Breast health in developing countries. *Climacteric*, **17**, 54-9.
- Zendehdel M, Niakan B, Keshtkar A, Rafiei E, Salamat F (2018). Subtypes of Benign Breast Disease as a Risk Factor for Breast Cancer: A Systematic Review and Meta-Analysis Protocol. *Iran J Med Sci*, **43**, 1–8.



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.