Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 Apr 04; 10(E):1227-1234.
https://doi.org/10.3889/oamjms.2022.9231
eISSN: 1857-9655
Category: *E - Public Health*
Section: *Public Health Epidemiology*

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Evaluation of the Dynamics of Breast Cancer Incidence in Kyrgyzstan: Component Analysis

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Edited by: https://publons.com/researcher/391987/mirko-spiroski/
Citation: Chokoev A, Akhunbaev S, Kudaibergenova I, Soodonbekov E, Nurtazinova G, Telmanova Z, Makimbetov E, Igissinov N. Evaluation of the dynamics of breast cancer incidence in Kyrgyzstan: Component analysis. Open Access Maced J Med Sci. 2022 Apr 04; 10(E):1227-1234.https://doi.org/10.3889/oamjms.2022.9231
Keywords: Breast cancer; Incidence; Component analysis; Kyrgyzstan
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Received: 06-Mar-2022
Revised: 23-Mar-2022
Accepted: 25-Mar-2022

Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists

Abstract

BACKGROUND: In 2020, 19.2 million cases of all types of cancer were registered worldwide, of which 11.7%, that is, 2.3 million, related to breast cancer (BC). The global burden of cancer is increasing worldwide, with the majority of new cancer cases and related deaths occurring in low- and middle-income countries.

OBJECTIVE: The study is to conduct a component analysis of the dynamics of the incidence of BC in Kyrgyzstan.

METHODS: Primary data were for registered patients with BC (International Classification of Diseases – C50) in the whole country during the period of 2003–2017. Evaluation of changes in BC incidence in the population of Kyrgyzstan was performed using component analysis according to the methodological recommendations.

RESULTS: The study period, 7850 new cases of BC were recorded. The incidence rate increased from $17.70°/_{0000}$ (2003) to $19.03°/_{0000}$ in 2017 and the overall growth was $1.34°/_{0000}$, including due to the age structure – $\sum\Delta_A=2.08°/_{0000}$, due to the risk of acquiring illness – $\sum\Delta_R=-0.55°/_{0000}$ and their combined effect – $\sum\Delta_{RA}=-0.19°/_{0000}$. The component analysis revealed that the increase in the number of patients with BC was mainly due to the growth of the population (Δ_P=+71.8%), changes in its age structure (Δ_A=+35.5%), and changes associated with the risk of acquiring illness (Δ_R=+8.4%). The increase and, in some cases, the decrease in the number of patients in the regions of the republic is due to the influence of demographic factors and risk factors for getting sick.

CONCLUSION: The component analysis assessed the role of the influence of demographic factors and the risk of acquiring the disease on the formation of the number of patients and the incidence of BC, while geographical variability was established. The implementation of the results of this study is recommended in the management of anticancer measures for BC.

Introduction

In 2020, 19.2 million cases of all types of cancer were registered worldwide, of which 11.7%, that is, 2.3 million, related to breast cancer (BC). BC is the most commonly diagnosed cancer in women and ranks second among the causes of cancer deaths in women. Analysis of geographical data from the IARC shows variability in the incidence of BC. Of the 2.3 million reported cases in 2020, 45.4% were in Asia and 23.5% in Europe, while 12.5% were reported in North America, 9.3% in Latin America, and 8.3% in Africa [1]. The global burden of cancer is increasing worldwide, with the majority of new cancer cases and related deaths occurring in low- and middle-income countries [1]. The socioeconomic conditions of the population and the supply/access to medical services in the countries determine the incidence of BC [2]. The number of BC cases in 2020 in countries with very high HDI (1 017 459) and high HDI (825,438) was higher than in countries with medium HDI (307,658) and low HDI (109,572). The incidence of BC is very high in developed countries, but it is also increasing in countries with low and medium HDI. The increase in the incidence of BC in these countries is due to many factors: First, an increase in life expectancy, improved cancer registration, and increased awareness of BC, and secondly, the likely reasons for the increase in the incidence of BC in the developing countries are changes in historical lifestyle characterized by changes in reproductive patterns, such as an earlier age of menarche, later first childbirth, lower parity, shorter duration of breastfeeding, as well as obesity and overweight [3].

Individual, hormonal, and environmental factors, alongside a family history, affect a woman's risk of developing BC. Together, these factors can be used to assess the short- and long-term risks of BC, predict the likelihood of having a genetic predisposition to BC, or both [4], [5]. Many lifestyle factors are associated with an increased risk of incidence and mortality from BC. Higher rates of diagnostic lifestyle factors reflecting healthier behavior are associated with lower incidence and mortality among BC survivors [6]. Reducing alcohol consumption can significantly affect the burden of diseases associated with BC [7].

Annual mammographic screening, starting at the age of 40, provides the greatest reduction in BC mortality, diagnosis at an earlier stage, better surgical options, and more effective chemotherapy. Delaying the age to start screening will lead to unnecessary deaths from BC [8], [9]. The usefulness of breast screening is to identify a potential disease as early as possible without any symptoms or signs.

The country's strategy for national cancer control planning requires knowledge of the burden of disease in the country, information that is obtained when it is possible to make an accurate diagnosis of cancer and document all relevant prognostic factors for the tumor.

In Kazakhstan, recent studies in this direction show that the incidence rate increased due to the age structure – $\sum\Delta_A$=2.99, due to the risk of acquiring the disease – $\sum\Delta_R$=6.82 and their combined effect – $\sum\Delta_{RA}$=0.31. Component analysis showed that the increase in the number of patients with BC was mainly due to population growth (Δ_P=+31.1%), changes in its age structure (Δ_A=+18.0%), and changes associated with the risk of acquiring the disease (Δ_R=+41.0%) [10].

At present, organized screening for breast cancer is not carried out in Kyrgyzstan, and this study is the first in recent years to evaluate the incidence of BC in Kyrgyzstan and its trends using a component analysis.

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 [11], 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 BC 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 15 years (from 2003 to 2017) using the International Disease Code 10, code C50.

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 population of the republic, taking into account the studied regions, are used, all data are presented on the official website [12].

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 nine different age groups (0–30, 30–34,…, 60–64, and 65+) and 15 calendar periods from 2003 to 2017 (1-year intervals). ASRs standardized to the world population proposed by the World Health Organization [13] with recommendations from the National Cancer Institute (2013) were estimated for each studied year.

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 [14] [15], [16].

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.

The dynamics of the incidence of BC was studied using a component analysis according to the methodological recommendations [17]. The method of component analysis was used in this study to break down the growth of number of cases belonging to the same population, but in different time periods.

There are seven components of the increase in the number of cases. The first three components are related to changes in the population number, its age structure, and the combined influence of these factors. The true increase in the number of patients with oncological pathology is due only to a change in the risk indicator of morbidity and is represented by the 4th component. The following three components are associated with the risk of developing a malignant neoplasm, with the growth of the population, changes in its age structure, and the influence of all three factors. Thus, the last four components are associated with an increase in the risk of developing the disease. The "risk of acquiring illness" refers to the whole range of reasons that can lead to an increase, decrease, or stabilization of morbidity rates.

The method of components was applied to study the dynamics of the number of BC patients and has been performed on cases that occurred from 2003 to 2017 among the entire population of the country. Assessments of the component analysis of the dynamics of morbidity of BC in the population of Kazakhstan are presented in the relevant tables.

Viewing and processing of the received materials were carried out using the Microsoft 365 software package (Excel, Word, and PowerPoint), in addition, online statistical calculators were used [18], where Student criterion was calculated when comparing the average values.

The following symbols and abbreviations were used in this article: AN – absolute number; ASIR – age-specific incidence rate; ASP (Δ_A) − the age structure of the population; ASR – age-standardized rate; END − the expected number of diseases; NCRC − the number of BC cases; PN (Δ_P) − population number; RAI (Δ_R) − risk of acquiring illness; R^2 – the value of the approximation confidence; SI − structural indexes; P − the incidence of BC; and $^{0}/_{0000}$ – prosantimille, designation per 100,000.

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 were not required. At the same time, the submitted data are in accordance with the Law of Kyrgyz Republic No. 82 – July 8, 2019 "On official statistics" [19], 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 [20].

Results

During the study period, 7850 new cases of BC were registered in the republic. The greatest proportion of patients falls on the age of 45–59 years (45–49 years – 14.9%, 50–54 years – 15.9%, and 55–59 years – 14.1%) (Table 1).

Table 1: Breast cancer in Kyrgyzstan, 2003–2017

Age	n (%)	Incidence				
		P ± m ($^{0}/_{0000}$)	95% CI ($^{0}/_{0000}$)	T (%)	p	R^2
< 30	133 (1.7)	0.5 ± 0.1	0.4–0.7	+ 4.4	1.000	0.1795
30–34	200 (2.5)	6.6 ± 0.6	5.4–7.7	+ 3.7	0.056	0.2315
35–39	478 (6.1)	17.9 ± 0.9	16.1–19.7	+ 0.8	0.333	0.0338
40–44	850 (10.8)	33.9 ± 1.5	30.9–36.9	− 0.1	0.750	0.0015
45–49	1166 (14.9)	50.6 ± 1.8	47.1–54.0	− 1.1	0.083	0.1544
50–54	1245 (15.9)	64.8 ± 1.9	61.1–68.5	− 1.5	0.023	0.3906
55–59	1108 (14.1)	78.3 ± 3.5	71.5–85.1	− 1.2	0.830	0.0978
60–64	812 (10.3)	85.9 ± 4.9	76.3–95.6	+ 1.2	0.020	0.0667
65 +	1858 (23.7)	77.7 ± 3.7	70.4–85.0	+ 1.7	0.455	0.1805
Total	7850 (100.0)	18.8 ± 0.5	17.9–19.7	+ 1.0	0.251	0.2424

CI: Confidence interval, P: the annual average, m: mean error, T: average annual upward/downward rates

Age-related indicators of BC incidence had a peak in 60–64 years (85.9 ± 4.9$^{0}/_{0000}$). Age-related indicators of BC incidence had a different trend. Young people (up to 30 years – T=+4.4%, 30–34 years – T=+3.7%, and 35–39 years – T=+0.8%) and older (60–64 years – T=+1.2% and 65+ years – T=+1.7%) have an increase in morbidity rates, while middle-aged people (40–44 years – T=−0.1%, 45–49 years – T=−1.1%, 50–54 years – T=−1.5%, and 55–59 years – T = −1.2%) have a downward trend. The highest growth rate was found in the age group up to 30 years, and the largest decrease was at the age of 50–54 years. It should be noted that the value of the accuracy of the approximation is not significant (Table 1).

Trends in age-related indicators affected the overall incidence rates, so the crude incidence rates of BC increased from 17.70 (2003) to 19.03 per 100,000 female population in 2017 (p = 0.251), the total increase was 1.34$^{0}/_{0000}$ (Table 2) and depended on changes in the age structure of the population ($\sum\Delta_A$=+2.08$^{0}/_{0000}$), the risk of acquiring illness ($\sum\Delta_R$=−0.55$^{0}/_{0000}$), and the combined influence of the age structure and the risk of acquiring illness ($\sum\Delta_{AR}$=−0.19$^{0}/_{0000}$). At the same time, the average annual growth rate of the aligned indicator was T=+1.0%, and the approximation confidence value was R^2=0.2424 (Table 2).

Then, we will consider the component analysis results of the dynamics of the number of patients with BC in the republic as a whole (Tables 3 and 4). The results of the study show that the growth in the number of patients with BC in the republic was associated with the influence of the following factors:

1. Growth of population number Δ_P=+71.8%.
2. Changes in the age structure of the population Δ_A=+35.5%.
3. Combined effect of changes in population number and its age structure Δ_{PA}=+8.4%.
4. Risk of acquiring illness Δ_R=−9.4%.
5. Combined effect of changes in the risk of acquiring illness and population number Δ_{PR}=−2.2%.
6. Combined effect of changes in the risk of acquiring illness and age structure of the population Δ_{RA}=−3.3%.
7. Combined effect of the changes in the risk of acquiring illness of the population and its age structure Δ_{RAP}=−0.8%.

The total increase in the absolute number of patients overall equals the sum of components:

$n_2 - n_1$=106+53+12-14−3−5−1=148 or +33.1% in comparison with the primary number of patients (148÷447×100=33.1%).

At the same time, the components of the increasing in the percentage at the primary level are equal for the women population:

$$\underbrace{23.8\% + 11.8\% + 2.8\%}_{38.3\%}\ \underbrace{-3.1\%}_{-3.1\%}\ \underbrace{-0.7\% - 1.1\% - 0.3\%}_{-2.1\%} = 33.1\%$$

Table 2: Component analysis of the breast cancer incidence growth in Kyrgyzstan, 2003–2017

Age group (i)	ASP		Growth (S_{i2}–S_{i1}) (3)–(2)	Incidence			Incidence growth		
							General (P_{i2}–P_{i1}) (6)–(5)	Including due to changes of	
	2003 (S_{i1})	2017 (S_{i2})		2003 (P_{i1})	2017 (P_{i2})	Growth	Δ_A (4) × (5)	Δ_R (2) × (7)	Δ_{RA} (4) × (7)
1	2	3	4	5	6	7	8	9	10
< 30	0.6004	0.5689	− 0.0315	0.26	0.34	+ 0.07	− 0.008	+ 0.044	− 0.002
30–34	0.0728	0.0800	+ 0.0072	3.26	7.60	+ 4.33	+ 0.024	+ 0.315	+ 0.031
35–39	0.0668	0.0625	− 0.0043	19.56	15.35	− 4.21	− 0.084	− 0.281	+ 0.018
40–44	0.0659	0.0555	− 0.0104	37.88	35.75	− 2.12	− 0.393	− 0.140	+ 0.022
45–49	0.0499	0.0527	+ 0.0028	57.17	42.50	− 14.67	+ 0.161	− 0.731	− 0.041
50–54	0.0367	0.0490	+ 0.0122	78.70	53.58	− 25.12	+ 0.963	− 0.923	− 0.307
55–59	0.0183	0.0453	+ 0.0271	69.30	66.32	− 2.98	+ 1.875	− 0.054	− 0.081
60–64	0.0235	0.0315	+ 0.0080	53.90	85.17	+ 31.26	+ 0.434	+ 0.735	+ 0.252
65+	0.0658	0.0546	− 0.0112	79.45	86.76	+ 7.32	− 0.891	+ 0.481	− 0.082
Total	$\sum S_{i1}$=1.0	$\sum S_{i2}$=1.0		P_1=17.70	P_2=19.03	+ 1.34	$\sum\Delta_A$ = +2.08	$\sum\Delta_R$ = −0.55	$\sum\Delta_{RA}$ = −0.19

ASP – age structure of the population, ΔA − the age structure of the population, ΔR − risk of acquiring illness, ΔRA − risk of acquiring illness and age structure of the population.

Table 3: Component analysis of the breast cancer incidence in dynamics in Kyrgyzstan from 2003 to 2017

Age group (i)	NTC (n_{ij})		PN (N_{ij})		Crude (P_{ij})		Standardized		END in 2017
	2003 (j=1)	2017 (j=2)	2003 (j=1)	2017 (j=2)	2003 (j=1)	2017 (j=2)	2003 (j=1)	2017 (j=2)	($P_{ij}N_{i2}10^{-5}$) (6) × (5) × 10^{-5}
1	2	3	4	5	6	7	8	9	10
< 30	4	6	1,516,553	1,778,646	0.26	0.34		0.203	4.7
30–34	6	19	183,840	250,065	3.26	7.60		0.553	8.2
35–39	33	30	168,747	195,497	19.56	15.35		1.025	38.2
40–44	61	62	166,332	173,409	37.88	35.75		2.354	65.7
45–49	73	70	125,951	164,707	57.17	42.50		2.119	94.2
50–54	73	82	92,754	153,042	78.70	53.58		1.968	120.4
55–59	32	94	46,176	141,729	69.30	66.32		1.212	98.2
60–64	33	84	59,366	98,630	53.90	85.17		2.002	53.2
65+	132	148	166,147	170,576	79.45	86.76		5.707	135.5
Total	n_1=447	n_2=595	N_1=2,525,866	N_2=3,126,301	P_1=17.70	P_2=19.03	=17.70	=17.14	E (n_2) = 618
Growth	$\frac{n_1 - n_2}{n_1}100 = 33.1$		$\frac{N_1 - N_2}{N_1}100 = 23.8$		$\frac{P_1 - P_2}{P_1}100 = 7.5$		$\frac{P_1^c - P_2^c}{P_1^c}100 = -3.1$		

NCC: new cancer cases, PN: population number, END: the expected number of diseases.

Thus, BC is characterized by an increase in the number of cases as a result of changes in the total number and structure of the female population (38.3% of the total increase of 33.1%).

Next, we analyzed the dynamics of the incidence of breast cancer in the regional segment. Thus, in the Jalal-Abad region, the overall increase in the incidence of BC was the highest and amounted to +7.82/100,000 female population, increased from 7.4°/$_{0000}$ (2003) to 15.2°/$_{0000}$ in 2017 (p = 0.000) (Table 5), and depended primarily on the risk of acquiring illness ($\sum\Delta_R$=+5.38°/$_{0000}$), and second, on changes in the age structure of the population ($\sum\Delta_A$=+1.66°/$_{0000}$), and third on the combined influence of age structure and risk of acquiring illness ($\sum\Delta_{RA}$=+0.78°/$_{0000}$). At the same time, the average annual growth rate of the aligned indicator was T=+5.7%, and the value of the approximation confidence was R^2=0.811. Analyzing the role of various components, it was found (Table 5) that the increase of patients in this area is associated with demographic factors (Δ_{P+A+PA}=+34.2%) and the complex influence of the risk of acquiring illness (Δ_R=+45.2%) with the components of the population number, its age structure, and the influence of all three of the above

Table 4: Influencing components on the number of cases of breast cancer in Kyrgyzstan

Components of growth in the number of cases due to	AN	Percentage growth	
		To (n_2–n_1)	To n_1
1. Growth PN $\Delta_P = \frac{N_1 - N_2}{N_1} n_1$	+ 106	+ 71.8	+ 23.8
2. Changes ASP $\Delta_A = \frac{N_1}{N_2}(E(n_2) - n_2 - \Delta_H$	+ 53	+ 35.5	+ 11.8
3. Combined effect of changes in PN+ASP $\Delta_{PA} = \frac{N_2 - N_1}{N_1}\Delta_A$	+ 12	+ 8.4	+ 2.8
Components of growth in the number of cases due to	AN	$\sum_{1-3}$ = + 115.7	$\sum_{1-3}$ = + 38.3
4. Change of RAI $\Delta_R = N_1\left(P_2^c - P_1^c\right)\times 10^{-5}$	− 14	− 9.4	− 3.1
5. Combined effect of changes of RAI+PN $\Delta_{RP} = \frac{N_2 - N_1}{N_1}\Delta_R$	− 3	− 2.2	− 0.7
6. Combined effect of changes of RAI+ASP $\Delta_{RP} = \frac{N_2 - N_1}{N_1}\Delta_R$	− 5	− 3.3	− 1.1
7. Combined effect of the changes RAI+PN+ASP $\Delta_{PAR} = \frac{N_1}{N_2}\left(n_2 - n_1 - \sum_{x=1}^{5}\right)$	− 1	− 0.8	− 0.3
Components of growth in the number of cases due to	AN	$\sum_{4-7}$ = − 15.7	$\sum_{4-7}$ = − 5.2
Total$\sum_{1-7}$	+ 148	100.0	33.1

AN: Absolute Number.

Table 5: Component analysis of breast cancer incidence by regions of Kyrgyzstan, 2003-2017

Regions	Incidence, $^{0}/_{0000}$		Incidence growth, $^{0}/_{0000}$				T, %	p	R^2	AN	Change/Combined, %							Total
			general*	Including							Δ_P	Δ_A	Δ_{PA}	Δ_R	Δ_{RP}	Δ_{RA}	Δ_{RAP}	
	2009	2018		Δ_A	Δ_R	Δ_{RA}												
City of Bishkek	37.3	29.2	−8.11	+1.49	−9.14	−0.47	−1.8	0.036	0.175	+4	+1169.9	+150.3	+46.9	−919.0	−286.7	−46.8	−14.6	100.0
City of Osh	14.0	17.0	−2.90	+4.47	+0.53	−2.09	+2.2	0.530	0.100	+7	+38.8	+81.8	+12.3	+9.7	+1.5	−38.3	−5.8	100.0
Batken	9.9	7.6	−2.33	+1.39	−3.58	−0.13	−0.02	0.414	0.000	−1	−480.7	−280.2	−67.3	+721.4	+173.4	+26.9	+6.5	100.0
Chuy	32.4	30.6	−1.81	−1.63	−1.72	+1.54	+0.2	0.644	0.011	+18	+146.6	−34.6	−7.4	−36.5	−7.8	+32.7	+7.0	100.0
Isıq-Kol	21.2	19.5	−1.70	+3.65	−4.17	−1.18	+2.5	0.690	0.265	+2	+305.2	+387.8	+52.6	−443.0	−60.1	−125.6	−17.0	100.0
Kyrgyzstan	17.7	19.0	+1.34	+2.08	−0.55	−0.19	+1.0	0.251	0.242	+148	+71.8	+35.5	+8.4	−9.4	−2.2	−3.3	−0.8	100.0
Narın	10.8	15.8	+5.01	+2.30	+2.44	+0.27	+2.9	0.271	0.189	+8	+13.1	+37.1	+2.8	+39.3	+2.9	+4.4	+0.3	100.0
Osh	6.2	11.5	+5.34	+1.09	+3.71	+0.54	+4.7	0.002	0.760	+43	+20.1	+12.8	+3.6	+43.4	+12.1	+6.3	+1.8	100.0
Talas	10.5	18.1	+7.55	−0.15	+5.43	+2.27	+2.9	0.136	0.124	+12	+20.0	−1.3	−0.3	+47.3	+10.3	+19.7	+4.3	100.0
Jalal-Abad	7.4	15.2	+7.82	+1.66	+5.38	+0.78	+5.7	0.000	0.811	+55	+16.6	+13.9	+3.7	+45.2	+12.2	+6.6	+1.8	100.0

factors ($\Delta_{R+PR+RA+RAP}$=+65.8%). The overall decrease in the incidence of BC was found in Bishkek city and amounted to −8.11 per 100,000 female population, decreased from 37.3°/$_{0000}$ (2003) to 29.2°/$_{0000}$ in 2017 (p = 0.036), and depended on the risk of acquiring the disease (Δ_R=−9.14°/$_{0000}$).

Furthermore, when analyzing the average annual growth rates of aligned BC incidence rates, it was found that the largest increase was in the Jalal-Abad region, followed by the Osh region (T=+4.7%; R^2=0.760), while the growth in 2017 was statistically significant compared to 2003, and the values of approximation reliability were expressed.

Analyzing the results of the influence of various components by region (Table 5), it was found that due to changes in the population, there is a pronounced decrease in the Batken region (Δ_P=−480.7%) and the largest increase in the city of Bishkek (Δ_P=+1169.9%) and in the Isıq-Kol region (Δ_P=+305.2%). The role of the influence of age structure in increasing the number of patients was positive in many regions, and the most pronounced was in the Isıq-Kol region (Δ_A=+387.8%) and in the city of Bishkek (Δ_A=+150.3%) regions. At the same time, in some regions of the country, this indicator negatively affected the increase in the number of patients and was more pronounced in the Batken region (Δ_A=−280.2%). The combined effect of changes in the population number and its age structure showed a decline only in Batken (Δ_{PA}=−67.3%), Chuy (Δ_{PA}=−7.4%), and Talas (Δ_{PA}=−0.3%) regions, while in the other regions, there was an increase – especially in Isıq-Kol region (Δ_{PA}=+52.6%), as well as in Bishkek city (Δ_{PA} =+46.9%). The reduction in the absolute number of patients with BC due to the risk of acquiring the disease was detected in the city of Bishkek (Δ_R=−919.0%), as well as in the Isıq-Kol (Δ_R=−443.0%) and Chui (Δ_R=−36.5%) regions, and the maximum increase was established in the Batken region (Δ_R=+721.4%). A pronounced growth in the combined impact of the risk of acquiring illness and the population number was found in in the Batken region (Δ_{PR}=+173.4%). Moreover, a pronounced decrease was found in Bishkek city (Δ_{PR}=−286.7%). Changes in the risk of acquiring illness and the age structure led to a sharp decrease in the number of patients in the Isıq-Kol region (Δ_{RA}=−125.6%), and the maximum increase was noted in the Chuy region (Δ_{RA}=+32.7%). The decrease in patients due to the combined influence of the risk of acquiring illness, population size, and age structure was the highest in the Isıq-Kol region (Δ_{RAP}=−17.0%) and in Bishkek city (Δ_{RAP}=−14.6%) compared to other regions (Table 5).

Therefore, the component analysis revealed geographical variability in the dynamics of the number of patients and the incidence of BC in Kyrgyzstan, which were associated with a difference in the influence of demographic factors (changes in population size and age structure) and the risk of acquiring the disease, that is, a combination of reasons that led to an increase, decrease, or stabilization of morbidity rates. In general, there is an increase in the incidence of BC in the republic.

Discussion

The incidence of BC and mortality from it increases with age until about the seventh decade, after which they tend to decrease, which is believed to mostly reflect low screening rates [21]. This pattern can also be seen in our study, since the peak incidence was found in the age group of 60–64 years and in the age group of 65 and older, the incidence was lower. During the study period in Kyrgyzstan, more than 34% of cases were registered in women over 60 years of age. According to research, more than 50% of BC cases in the world are diagnosed in patients over 60 years of [22], [23]. In clinical practice, the doctor observes larger tumors and nodular involvement in older women, probably due to a delay in diagnosis [24]. The risk of developing postmenopausal BC increases significantly with an increase in body mass index and abdominal obesity [25]. The prevalence of obesity is growing worldwide and more than 15% of adults in most countries are classified as obese [26], then, it is likely that the trends in increasing incidence in postmenopausal age are the result of the growing importance of obesity as a risk factor for cancer worldwide [27]. In addition, there are studies where it was found that people with a stable high level of education in relation to the father were more prone to low-grade cancer [28].

Among national organizations, mammography is the preferred imaging method for screening. Screening mammography reduces BC mortality by 19%

among women aged 40–69 years, but its usefulness is unknown for women over 70 years [29]. However, a Swedish study showed that the reduction in mortality as a result of screening, which includes patients over 60 years of age, was 34% in women aged 50 years and older [30]. According to the American Cancer Society (ACS), women between the ages of 40 and 49 should have a choice for annual screening mammography with the option of switching to 2-year screening before the age of 75. The ACS also recommends continuing screening mammography every 2 years if women are in good health and their life expectancy is more than 10 years [31]. Low socioeconomic status is associated with delayed detection of cancer and lower survival rates [32]. Therefore, screening recommendations should be adapted to the patient's age, goals, and life expectancy. With the increase in life expectancy and the growth of elderly population of Kyrgyzstan, it is paramount in BC research to pay more attention to the prevention, screening, and treatment of these patients. Age is no longer a limitation for the treatment of BC in the elderly. Studies have shown that the current insufficient cancer treatment reduces survival, but the situation is changing for the better to provide timely and complete medical care for the elderly. Most often, clinicians, and surgeons pay attention not only to the specific characteristics of a BC tumor but also to the functionality, tolerability, concomitant diseases, and life expectancy of patients in order to determine the best treatment [33].

The average age of diagnosis of BC in the world is 62 years, and, consequently, a significant proportion of women are diagnosed with invasive BC after 65 years [24]. The average age of BC patients in the republic for 2003–2017 was 53.8 years [34]. A lower average age indicator than that of patients all over the world indicates that in our republic women get sick mainly at an earlier age. The average annual growth rate in age groups (up to 30 years – T=+4.4% and 30–34 years – T=+3.7%) indicates that the incidence in young, pre-screening age increases annually. This means that there are more young women at high risk of acquiring the illness. However, this does not mean that it is necessary to involve all young women in screening, since radiation-induced cancers are more common in young women than in the elderly, due to the greater number of undifferentiated radiosensitive cells and a long lifespan, which gives time for the occurrence of life-threatening radiation-induced tumors [35]. Screening of young women can be useful only among selected high-risk women with adapted imaging strategies and methods [36]. Hence, personalized strategies for women at high risk of acquiring the illness will increase the effectiveness of early diagnosis in all age categories, especially in young women [37].

The results of the component analysis indicate that in the republic, the incidence of BC in the entire female population is increasing mainly due to changes in the age structure of the population ($\sum\Delta_A$=+2.08°/$_{0000}$), and the increase in patients due to growth of population number Δ_P=+71.8% and changes in the age structure of the population Δ_A=+35.5%. It is surprising that demographic indicators played the main role in the increase in the incidence of BC, while there was no impact of the risk of acquiring the illness. Consequently, doubts arise about the reliability of accounting and registration of patients. In addition, the identification of trends in decreasing incidence rates in the age groups exposed to screening and an increase in indicators in older age groups tells us that there is no timely diagnosis. This occurrence is most likely due to the fact that nationwide BC screening is not carried out in Kyrgyzstan.

The formation and influence of the above factors in the regions were not the same. Thus, the analysis of incidence by region in the entire female population showed that the "risk of acquiring the illness" component affected the overall decrease in incidence in the following regions: The city of Bishkek ($\sum\Delta_R$=−9.14°/$_{0000}$), Isıq-Kol region ($\sum\Delta_R$=−4.17°/$_{0000}$), Batken region ($\sum\Delta_R$=−3.58°/$_{0000}$), and Chuy region ($\sum\Delta_R$=−1.72°/$_{0000}$).

Along with this, there are regions where the increase in incidence was due to the influence of the "risk of acquiring the disease" component. Thus, in Jalal-Abad ($\sum\Delta_R$=+5.38°/$_{0000}$) and Osh ($\sum\Delta_R$=+3.71°/$_{0000}$) regions, the increase was due to the influence of the risk of acquiring the illness, that is, the contribution to the formation of the indicator was more than 40.0%.

Thus, the results of the study indicate the need to create a single cancer registry for monitoring and evaluating new breast cases and organizing targeted anti-cancer measures.

Author contribution statement

AC, ZT, ES, and GN – Collection and preparation of data, primary processing of the material and their verification.

AC, NI, ZT, and ES – Statistical processing and analysis of the material, writing the text of the article (material and methods, results).

AC, ZT, SA, and GN – Writing the text of the article (introduction and discussion).

AC, NI, and EM – Concept, design and control of the research, approval of the final version of the article.

All authors approved the final version of the manuscript.

Acknowledgments

The authors greatly appreciate the contribution of the Ministry of Health of the 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.

References

1. Ferlay J, Ervik M, Lam F. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer; 2020. Available from: https://www.gco.iarc.fr/today
2. Oliveira NP, Santos Siqueira CA, Lima KY, de Camargo Cancela M, Souza DL. Association of cervical and breast cancer mortality with socioeconomic indicators and availability of health services. Cancer Epidemiol. 2020;64:101660. https://doi.org/10.1016/j.canep.2019.101660
   PMid:31877471
3. Sharma R. Breast cancer incidence, mortality and mortality-to-incidence ratio (MIR) are associated with human development, 1990-2016: Evidence from Global Burden of disease study 2016. Breast Cancer. 2019;26(4):428-45. https://doi.org/10.1007/s12282-018-00941-4
   PMid:30604398
4. Cintolo□Gonzalez JA, Braun D, Blackford AL, Mazzola E, Acar A, Plichta JK, *et al*. Breast cancer risk models: A comprehensive overview of existing models, validation, and clinical applications. Breast Cancer Res Treat. 2017;164(2):263□84. https://doi.org/10.1007/s10549-017-4247-z
   PMid:28444533
5. Lee TC, Reyna C, Shaughnessy E, Lewis JD. Screening of populations at high risk for breast cancer. J Surg Oncol. 2019;120(5):820-30. https://doi.org/10.1002/jso.25611
   PMid:31286529
6. Cifu G, Arem H. Adherence to lifestyle-related cancer prevention guidelines and breast cancer incidence and mortality. Ann Epidemiol. 2018;28(11):767-73.e1. https://doi.org/10.1016/j.annepidem.2018.09.002
   PMid:30309689
7. Freudenheim JL. Alcohol's effects on breast cancer in women. Alcohol Res. 2020;40(2):11. https://doi.org/10.35946/arcr.v40.2.11
   PMid:32582503
8. Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA. Breast cancer screening in women at higher-than-average risk: Recommendations from the ACR. J Am Coll Radiol. 2018;15(3):408-14. https://doi.org/10.1016/j.jacr.2017.11.034
   PMid:29371086
9. Monticciolo DL, Malak SF, Friedewald SM, Eby PR, Newell MS, Moy L, *et al*. Breast cancer screening recommendations inclusive of all women at average risk: Update from the ACR and society of breast imaging. J Am Coll Radiol. 2021;18(9):1280-8. https://doi.org/10.1016/j.jacr.2021.04.021
   PMid:34154984
10. Toguzbayeva A, Telmanova Z, Khozhayev A, Jakipbayeva A, Aimbetova G, Zhantureyeva A, *et al*. Impact of screening on breast cancer incidence in Kazakhstan: Results of component analysis. Asian Pac J Cancer Prev. 2021;22(9):2807-17. https://doi.org/10.31557/APJCP.2021.22.9.2807
    PMid:34582649
11. National Statistical Committee of the Kyrgyz Republic. Statistical yearbook of the Kyrgyz Republic. Kyrgyzstan: National Statistical Committee of the Kyrgyz Republic; 2017.
12. National Statistical Committee. Available from: https://www.stat.kg
13. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJ, Lozano R, Inoue M, *et al*. Age Standardization of Rates: A new who standard. GPE Discussion Paper Series: No.31 EIP/GPE/EBD. Geneva: World Health Organization; 2019.
14. Merkov AM, Polyakov LE. Sanitary Statistics. Leningrad: Medicine; 1974. p. 384.
15. Glanc S. Biomedical Statistics. Moscow: Practice; 1999. p. 460.
16. dos Santos Silva I. Cancer Epidemiology: Principles and Methods. Lyon, France: IARC; 1999. p. 442.
17. Dvoyrin VV, Aksel EM. Component Analysis of the Dynamics of Malignant Neoplasms: Guidelines. Moscow: Medicine; 1987. p. 130.
18. Online Statistical Calculator. Available from: https://www.medstatistic.ru/calculators/averagestudent.html
19. Law of the Kyrgyz Republic. About Official Statistics. Kyrgyzstan: Law of the Kyrgyz Republic; 2019.
20. WMA Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects; 2013. Available from: https://www.wma.net
21. Howlader N, Noone AM, Krapcho M. SEER Cancer Statistics Review, 1975-2012. Bethesda, MD: National Cancer Institute; 2015.
22. Inwald EC, Ortmann O, Koller M, Zeman F, Hofstädter F, Evert M, *et al*. Screening-relevant age threshold of 70 years and older is a stronger determinant for the choice of adjuvant treatment in breast cancer patients than tumor biology. Breast Cancer Res Treat. 2017;163(1):119-30. https://doi.org/10.1007/s10549-017-4151-6
    PMid:28205042
23. Cancer of the Breast (Female)-cancer Stat Facts. Available from: https://www.seer.cancer.gov/statfacts/html/breast.html [Last accessed on 2017 Oct 08].
24. Desai P, Aggarwal A. Breast cancer in women over 65 years-a review of screening and treatment options. Clin Geriatr Med. 2021;37(4):611-23. https://doi.org/10.1016/j.cger.2021.05.007
    PMid:34600726
25. Neuhouser ML, Aragaki AK, Prentice RL, Manson JE, Chlebowski R, Carty CL, *et al*. Overweight, obesity, and postmenopausal invasive breast cancer risk: A secondary analysis of the women's health initiative randomized clinical trials. JAMA Oncol. 2015;1(5):611-21. https://doi.org/10.1001/jamaoncol.2015.1546
    PMid:26182172
26. GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med. 2017;377(1):13-27. https://doi.org/10.1056/NEJMoa1614362
    PMid:28604169
27. Heer E, Harper A, Escandor N, Sung H, McCormack V, Fidler-Benaoudia MM. Global burden and trends in premenopausal and postmenopausal breast cancer: A population-based study. Lancet Glob Health. 2020;8(8):e1027-37. https://doi.org/10.1016/s2214-109x(20)30215-1
    PMid:32710860
28. Gupta A, Jones K, Deveaux A, Bevel M, Salako O, Daramola A, *et al*. Association of life-course educational attainment and breast cancer grade in the mend study. Ann Glob Health. 2021;87(1):59. https://doi.org/10.5334/aogh.3142
    PMid:34277361
29. Walter LC, Schonberg MA. Screening mammography in older women: A review. JAMA. 2014;311(13):1336-47. https://doi.org/10.1001/jama.2014.2834
    PMid:24691609

30. Paesmans M, Ameye L, Moreau M, Rozenberg S. Breast cancer screening in the older woman: an effective way to reduce mortality? Maturitas. 2010;66(3):263-7. https://doi.org/10.1016/j.maturitas.2010.03.016

PMid:20451335

31. Oeffinger KC, Fontham ET, Etzioni R, Herzig A, Michaelson JS, Shih YC, *et al*. Breast cancer screening for women at average risk: 2015 guideline update from the American cancer society. JAMA. 2015;314(15):1599-614. https://doi.org/10.1001/jama.2015.12783

PMid:26501536

32. Hassanipour S, Maghsoudi A, Rezaeian S, Arab-Zozani M, Mokhtari AM, Abdzadeh E, *et al*. Survival rate of breast cancer in eastern Mediterranean region countries: A systematic review and meta-analysis. Ann Glob Health. 2019;85(1):138. https://doi.org/10.5334/aogh.2521

PMid:31857944

33. Varghese F, Wong J. Breast cancer in the elderly. Surg Clin North Am. 2018;98(4):819-33. https://doi.org/10.1016/j.suc.2018.04.002

PMid:30005776

34. Chokoev A, Igissinov N. Breast cancer incidence trends in Kyrgyzstan. Medicina (Kaunas). 2020;56(1):166.

35. Yaffe MJ, Mainprize JG. Risk of radiation-induced breast cancer by mammographic screening. Radiology. 2011;258(1):98-105. https://doi.org/10.1148/radiol.10100655

36. Siu AL, U.S. Preventive Services Task Force. Screening for breast cancer: U.S. preventive services task force recommendation statement. Ann Intern Med 2016;164(4):279-96. https://doi.org/10.7326/M15-2886

PMid:26757170

37. Desreux JAC. Breast cancer screening in young women. Eur J Obstet Gynecol Reprod Biol. 2018;230:208-11. https://doi.org/10.1016/j.ejogrb.2018.05.018

PMid:29804884