RESEARCH ARTICLE

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Study on Breast Cancer in Kazakhstan Using the Functional Time Series

Adiya Shertaeva[1], Dinara Ospanova[2], Andrej Grjibovsky[3], Alfia Shamsutdinova[4], Nurlan Rakhmetov[1], Zaure Dushimova[5], Bagdat Salimgereeva[6], Zhannym Yermentayeva[6], Indira Kaketaeva[6], Yerlan Kuandykov[7], Shynar Tanabayeva[1], Ildar Fakhradiyev[1]*, Samat Zharmenov[8]

Abstract

Aim: In Kazakhstan and Central Asia, breast cancer (BC) is the most common malignancy among women. However, no large-scale study on breast cancer using the functional time series approach has been carried out in Kazakhstan. **Methods:** A functional assessment of the age-period-cohort model (APC) and the survival rate (period 2017–2021) was used in the retrospective study. Clinical and demographic information on patients was analysed, including age, gender, region of residence, kind and stage of tumour, occupation, socioeconomic standing, nationality, and specifics of treatment and its outcomes. Additionally, the relationship between nationality, stage, and residency region and the survival rate of breast cancer patients was investigated too. **Results:** The data of n=22,736 breast cancer patients were analysed. The highest number of breast cancer cases reported was 4,945 (21.7%), in 2019. In 2021, n =4,939 (21.7%) cases were detected, while in 2020, n=4,222 (18.6%) cases were observed. The patients with breast cancer in stages I and Ia were recognized in 6,585 (29% of cases), while those in stages Ib and Ic were confirmed in 8687 (38.2% of cases). In n=10,147 (44.6%) cases, a malignant tumour of the upper outer quadrant of the breast (C50.4) was predominant. Kazakhs made up the majority (n=10,939, 48.1%) of patients with a primary validated diagnosis of breast cancer, followed by Russians (n=7527, 33.1%). Germans had the lowest survival rate overall (11.4 ± 1.7 months) ($p \leq 0.05$) (95% CI: 8.0-14.7 months). Uzbeks showed relatively high survival rates of 18.3 ± 1.6 months (95% CI: 15.1-21.5 months) ($p \leq 0.05$). The Aktobe region had the lowest breast cancer survival rates, measuring 12.1±0.9 months (95% CI: 10.3-13.9 months) ($p \leq 0.05$). The highest survival rates, 18.0±1.3 months (95% CI: 15.5-20.5 months) and 17.9±1.4 months (95% CI: 15.3-20.7 months), were seen in Shymkent and Zhambyl regions ($p \leq 0.05$), respectively. The prevalence of breast cancer increases after 37.5 years, according to the results of the APC analysis, with an indicator of 0.572 (95% CI: -0.41 - 1.56), maintaining a steady upward trend in the age range from 42.5 years to 62.5 years. **Conclusions:** Despite a slight drop in the disease's frequency, the incidence of breast cancer in women 37.5 years and older has been stable over the past five years. Additionally, it was shown that the country's northern regions had a higher incidence of breast cancer cases than the southern and western regions. Our results show the significance of demographic characteristics such as age and location for the development of preventive measures and effective treatment.

Keywords: Breast cancer- ethnicity- age- survival- epidemiology- prevalence

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Introduction

Breast cancer (BC) continues to be the main cause of cancer-related death in women worldwide (Wilkinson and Gathani, 2022). BC is the dominant malignant neoplasm among women in Kazakhstan (Beysebayev et al., 2015a).

There is a number of studies on breast cancer patient survival in relation to disease stage and geographic location (Rudolph et al., 2021). However, no such study has been carried out in Kazakhstan yet.

In 2008, a national breast cancer screening program was launched in Kazakhstan (Toguzbayeva et al., 2021). Nevertheless, the evaluation of the effectiveness of such a programme has been not carried out yet (Beysebayev

*[1]S.D. Asfendiyarov Kazakh National Medical University, Almaty, Republic of Kazakhstan. [2]Al-Farabi Kazakh National l University, Almaty, Republic of Kazakhstan. [3]Northern State Medical University, Arkhangelsk, Russian Federation. [4]Central Clinical Hospital, Almaty, Republic of Kazakhstan. [5]Kazakh Research Institute of Oncology and Radiology Almaty, Republic of Kazakhstan. [6]Kazakh-Russian Medical University, Almaty, Republic of Kazakhstan. [7]Khoja Akhmet Yassawi International Kazakh-Turkish University, Shymkent Medical Institute Postgraduate Studies Faculty, Shymkent, Republic of Kazakhstan. [8]Kazakhstan's Medical University "Kazakhstan School of Public Health", Almaty, Republic of Kazakhstan. *For Correspondence: fakhradiyev.i@kaznmu.kz*

et al., 2015b).

For instance, a regional epidemiological study of the prevalence of breast cancer was supposed to analyse the situation from 2009 to 2018 period of time. But it only provided comparative data for the studied period (Toguzbayeva et al., 2021) without comprehensive analysis (Beysebayev et al., 2015b). Moreover, the analysis was applied only for two years (2009 and 2018). In another study, data of only two years (1999 and 2013) were analysed (Beysebayev et al., 2015a).

Igissinov et al. conducted a study for an epidemiological assessment of breast cancer morbidity and mortality solely in two cities of Kazakhstan (Igissinov et al., 2019). So the study results were narrowed to the population of two cities only, and they cannot represent the country's situation.

Therefore, there was no national study on the epidemiology of breast cancer in Kazakhstan. This fact highlights the necessity to investigate incidence trends using various factors such as age, period of time, and place of residence (Holford, 1992). The study model has to demonstrate the prevalence or, conversely, the absence of the influence of age, period, and cohort trends on the severity and outcomes associated with cancer. The model must encompass the results and information from previous studies on malignant neoplasms around the world (Murphy and Yang, 2018). The cohort effect, also known as period changes in the risk of morbidity and mortality, can be extracted from cross-sectional data using the APC model, a traditional epidemiological method (Li et al., 2015).

Our study aimed at the analysis of breast cancer cases using a functional evaluation of the time series model (APC) and survival rate in Kazakhstan (2017 -2021 period).

Materials and Methods

Data collection

We collected patient data on newly diagnosed breast cancer cases over a 5-year period (2017 to 2021). The data were obtained from the Electronic Register of Patients with Oncological Diseases of the Ministry of Health of the Republic of Kazakhstan (www.erob.eicz.kz). The age, gender, place of residence, tumour stage, occupation, social status, nationality, type of cancer, as well as details of therapy and its results, were all methodically recorded in the Electronic Registry of Cancer Patients.

All morbidity and death rates are provided per 100 000 people and were standardized by sex, and age (2017 - 2021). The 10th revision of the International Classification of Diseases was used to code the medical records of patients with various types of breast cancer (ICD-10). Breast cancer "C50" (C50.0, C50.1, C50.2, C50.3, C50.4, C50.5, C50.6, C50.8, C50.9) in line with ICD-10 was one of the primary diagnoses included in the study (for the period from 2017 to 2021).

The following malignant neoplasms were categorized as breast cancer by ICD-10: C50.0-Nipple and areola, C50.1- Central part of the breast, C50.2- Upper outer quadrant of the breast, C50.5- Inferior outer quadrant of the breast, C50.6- Axillary posterior part of the breast, C50.8- Breast lesion extending beyond one or more of the above localizations, and C50.9- Mammary glands of unspecified part.

According to the International Standard Classification of Occupations (ISCO), patients were divided into ten groups (occupations), including: managers, professionals, technicians and associate professionals, clerical support workers, service and sales workers, skilled agricultural, forestry, and fishery workers, craft related trade workers, plant and machine operators, and assemblers, elementary occupations, and armed forces occupations; The non-workers group also includes students.

Patients were categorized into working, disabled, retirees, not working, and others based on their social position.

Statistical analysis

Statistical analysis was conducted using SPSS software (version 25.0, IBM SPSS Inc., Chicago, Illinois, USA). We utilized demographic information obtained from the Committee on Statistics of the Ministry of National Economy of the Republic of Kazakhstan on the total population of the Republic of Kazakhstan. Also, the app SEER*Prep was used to do statistical analysis (National Institute of Health).

For the APC analysis, breast cancer data (C50.0, C50.1, C50.2, C50.3, C50.4, C50.5, C50.6, C50.8, C50.9 codes according to ICD-10) and population were categorized by five consecutive years from 2017 to 2021 and 16 age groups from 16-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and 100+ years old. The purpose of the age, period, and cohort effects analysis is to assess the impact of age, period and cohort on demographic or morbidity rates. (Breslow and Day, 1987). Age-related effects represent different risks associated with different age groups; period effects represent changes in vital rates over time that are associated with all age groups simultaneously; cohort effects are associated with changes in indicators in groups of people with the same years of birth, that is, for successive age groups in successive periods of time (Fosse and Winship, 2019).

The Kaplan-Meier method was used to do a survival analysis. This analysis was carried out using the Age-Period-Cohort web tool (Biostatistics Branch, National Cancer Institute, NIH, Bethesda, Maryland.) (Rosenberg et al., 2014). «Local drifts» were obtained using log linear regression, the longitudinal age trend (age trend + period trend) and the cross age trend (age trend - period trend) was also estimated.

The web tool was used to calculate the relative frequency in any given calendar period (or birth cohort) compared to the reference period (or birth cohort), adjusted for age and non-linear effects of the cohort (or period). Also, Wald's statistical tests were used to evaluate the studied models.

Results

General characteristics of patients

The data of 22 736 patients with breast cancer were analysed. In 2017 and 2018, there were 4 329 (19%) and

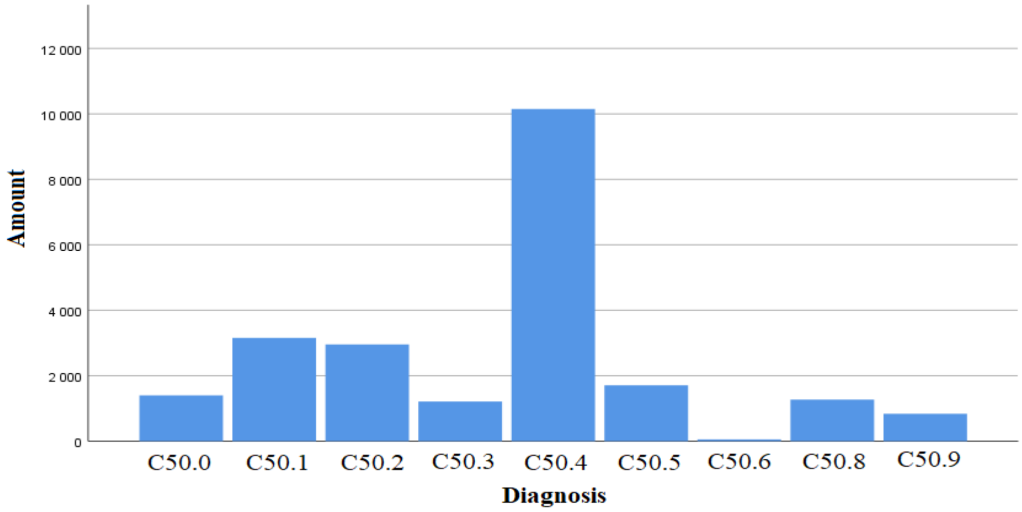

Figure 1. Characteristics of the Registered Cases of Breast Cancer According to the ICD-10 Classification

4 301 (18.9%) new cases of breast cancer, respectively. In 2019, there were n=4945 (21.7%) cases of breast cancer that were registered. In 2021, breast cancer was found in n=4939 (21.7%) patients, which was higher than in 2020 (n=4222 or 18.6%).

Table 1 shows the number of cases of breast cancer reported between 2017 and 2021, broken down by age group and calculated per 100 000 people. In 2017, 20–24-year-olds, 25–29-year-olds, and 30-34-year-olds were the age groups with the fewest cases of breast cancer, with 0.74, 3.28, and 11.77 cases per 100,000 people, respectively. The highest rates of registering breast cancer were found in people aged 60 to 64, with 161.78 cases per 100,000 people, and in people aged 70 to 74, with 175.35 cases per 100,000 people.

In 2018, there were 211 and 204 cases of breast cancer per 100,000 people in the 65–69 and 70–74 age groups, respectively. This was a high rate of breast cancer. From the age group of 85–89 years, there were 76 cases per 100 thousand people in 2018, but there were only 49 cases per 100 thousand people in the age group of 95 years and older. In 2019, it was found out that the number of people with breast cancer rose with age, reaching 229.46 per 100 000 people in the 70–74 age group. In the age group of 75–79 years, there were 124.10 cases of breast cancer for every 100,000 people. In the age group of 85–89

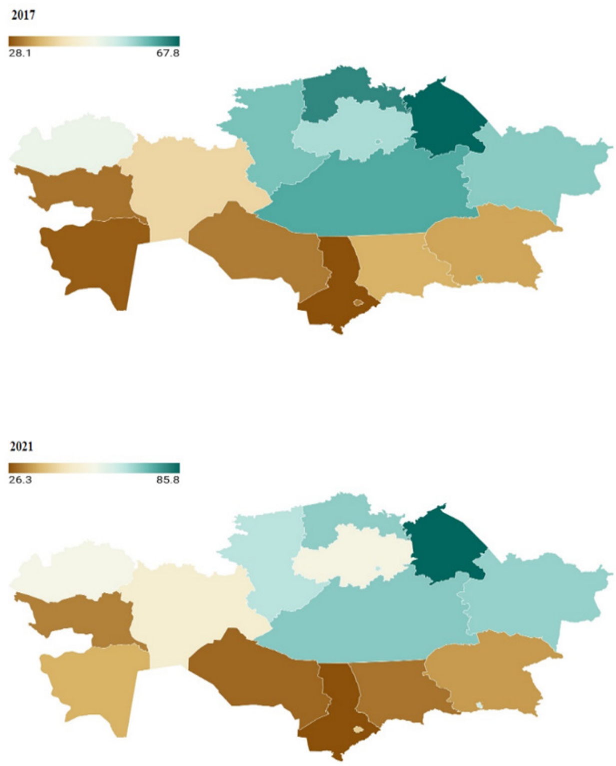

Figure 2. The Prevalence of Breast Cancer in 17 Regions of the Republic of Kazakhstan in Years 2017 and 2022 per 100 Thousand Population

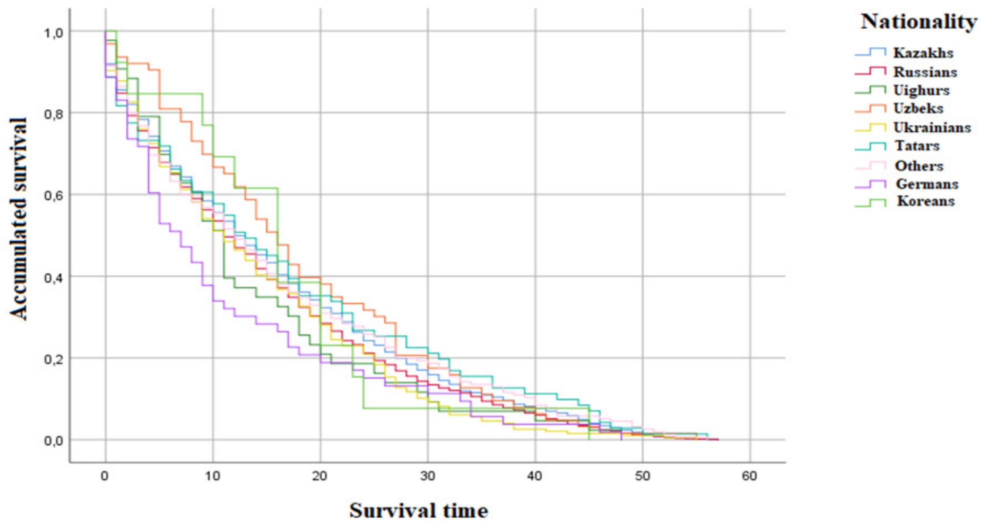

Figure 3. Survival Rates of Patients with Breast Cancer, Depending on Nationality

years, there were 79.80 cases of breast cancer for every 100,000 people.

Even though there were fewer cases of breast cancer being found in 2020, people aged 65–69 and 70–74 had high rates of getting breast cancer, at 170.7 and 168.2 per 100 000 of the population, respectively. In 2021, the age group of 65–69 years had the highest rate of breast cancer detection, at 188.65 per 100,000 people, and the age group of 70–74 years had the highest rate of breast cancer detection, at 188.32 per 100,000 people.

Compared to 2017, the number of breast cancer cases in people 20 to 24 years old went down by 0.1% in 2021, and the number of cases in people 25 to 29 years old went down by 0.5%. In 2021, compared to 2017, there were 5.3% more cases of breast cancer in the age group of 70–74 years old, but there were fewer cases in the age group of 65–69 years old. Table 2 shows information about the type and stage of breast cancer. In n=6585 (29.0%) of the cases, stages I and Ia were found, and in n=8687 (38.2%) of the cases, stages Ib and Ic were found. In n=4079 (17.9%) cases, people with breast cancer were given a disease stage of II, IIa, IIb, or II. In n=2239 (9.8%) patients, the stages of breast cancer were found to be III, IIIa, IIIb, and III. And stages IV, IVa, and IVb of breast cancer were found in n=1045 (4.6% of patients).

Figure 1 displays the characteristics of reported instances of breast cancer according to the ICD-10 classification. A malignant tumour of the nipple and areola of the breast (C50.0) was found in n=1399 (6.2%) patients, according to the ICD-10 classification. Malignant neoplasms in the upper inner quadrant of the breast (C50.2) were found in n=2957 (13.0%) patients, whereas those in the centre of the breast (C50.1) were found in n=3155 (13.9%) patients. The axillary posterior region of the breast neoplasm, n=53 (0.2%), was responsible for the fewest cases (C50.6). Patients had n=838 (3.7%) cases of malignant neoplasm of the nonspecific part of the mammary gland (C50.9) and n=10147 (44.6%) cases of malignant neoplasm of the upper outer quadrant of the breast (C50.4), respectively.

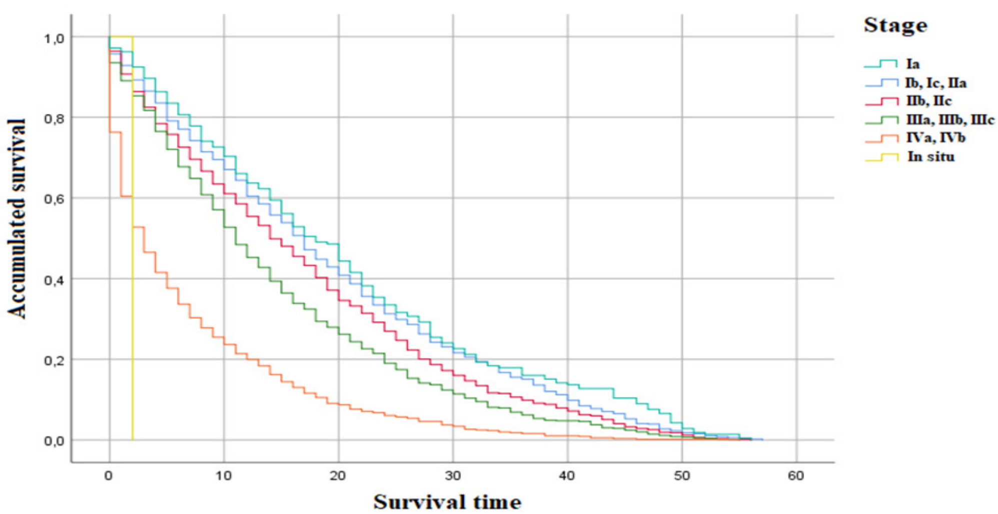

Figure 4. Survival Rates of Patients with Breast Cancer Depending on the Stage of the Disease

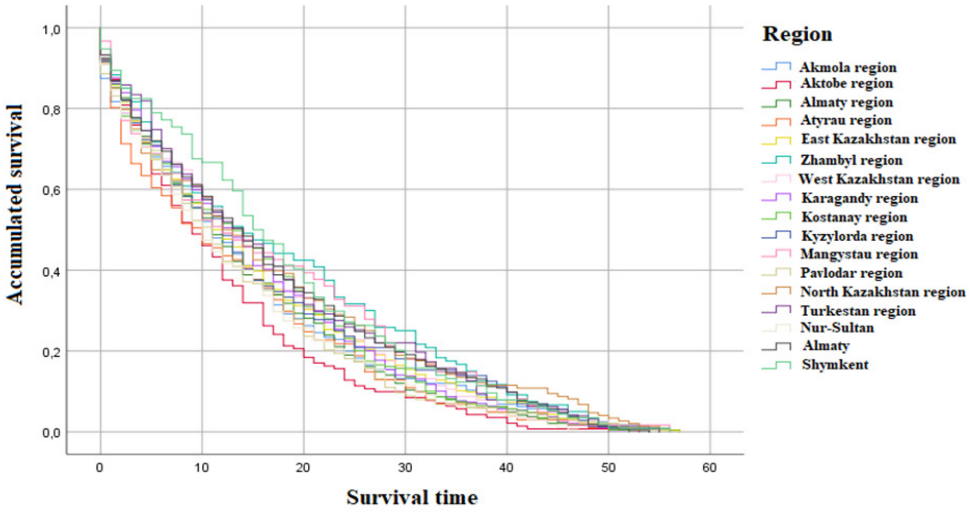

Figure 5. Survival Rates of Patients with Breast Cancer Depending on the Region of Residence

Table 3 and Figure 2 provide the distribution of registered cases of breast cancer standardised by sex per 100,000 populations by region for the period 2017-2021.

The Turkestan and Mangystau regions had the fewest breast cancer incidences in 2017, with indicators of 28.1 and 29.0 per 100,000 people, respectively. However, the number of occurrences of breast cancer registered in the Turkestan region fell to 26.3 instances per 100,000 people in 2021 as compared to 2017, while it rose to 36.4 cases per 100,000 people in the Mangystau region. The Pavlodar and North Kazakhstan regions had the highest rates of breast cancer diagnosis confirmation in 2017, with 67.8 and 64.8 instances per 100,000 people, respectively. In 2021, the Pavlodar region had the highest indicator for breast cancer diagnoses, at 85.8 instances per 100 000 people. The North Kazakhstan region also had one of the highest indicators for breast cancer diagnoses, at 71.3 cases per 100,000 people. The number of breast cancer incidences in the Zhambyl region fell from 34.9 to 30.0 per 100,000 people in 2021 as compared to 2017. Additionally, in the Kyzylorda region in 2021, 28.7 cases of breast cancer were discovered per 100,000 people, which was a decrease from the number of cases reported in 2017 (31.1 per 100,000 people). In contrast to 2017, breast cancer registration instances rose in 2021 in three republican-significant cities: Nursultan (from 58.5 to 66.5 cases per 100,000 people), Almaty (from 61.2 to 64.1), and Shymkent (31.0 to 40.7 cases per 100,000 people).

Table 1. The Amount of Registered Cases of Breast Cancer in the Context of 2017-2021 by Age Categories, Calculated per 100 Thousand Population.

Age	Year (n, by 100 thousand)										2017 vs 2021
	2017 year		2018 year		2019 year		2020 year		2021 year		
15-19	0	0	2	0	0	0	0	0	0	0	0
20-24	5	0.74	2	0	2	0.33	3	0.5	1	0.18	-0.1
25-29	27	3.28	29	4	24	3.12	25	3.4	30	4.29	-0.5
30-34	87	11.77	98	13	99	12.45	115	14.2	92	11.21	-0.8
35-39	190	30.09	189	29	195	29.72	226	33.5	207	29.79	-2.5
40-44	324	54.6	340	57	438	72.95	365	60.4	434	70.75	-0.9
45-49	464	84.46	437	78	533	94.49	448	78.5	514	89.58	1.2
50-54	664	120.56	521	97	553	103.87	469	88.9	591	111.55	1.5
55-59	727	139.56	546	102	670	123.04	592	108.1	628	116.45	-2.7
60-64	645	161.78	709	171	834	191.76	689	152.2	885	185.08	-2.7
65-69	488	157.03	686	211	739	219.36	597	170.7	672	188.65	-4.5
70-74	266	175.35	334	204	439	229.46	379	168.2	484	188.32	5.3
75-79	264	128.77	226	116	212	124.1	124	84.9	172	138.46	-2.2
80-84	130	136.66	132	122	157	125.45	139	100.5	168	116.17	-2.2
85-89	37	80.24	35	76	34	79.8	39	91.1	48	108.8	-1.6
90-94	10	73.67	14	99	15	97.39	11	74.3	12	72.27	0
95+	1	52.11	1	49	1	44.76	1	35.6	1	32.84	
Total	4329		4301		4945		4222		4939		

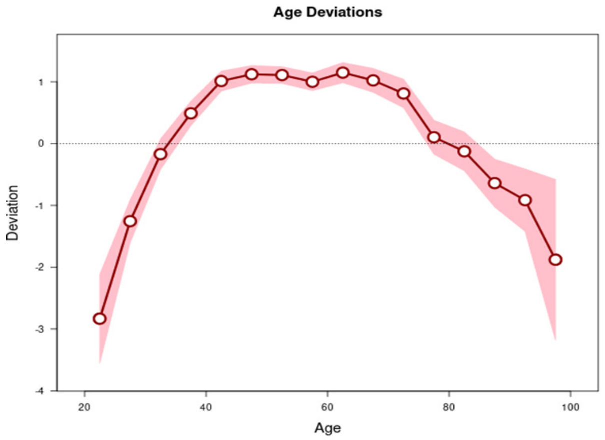

Figure 6. Longitudinal Age Curves of the Prevalence of Breast Cancer

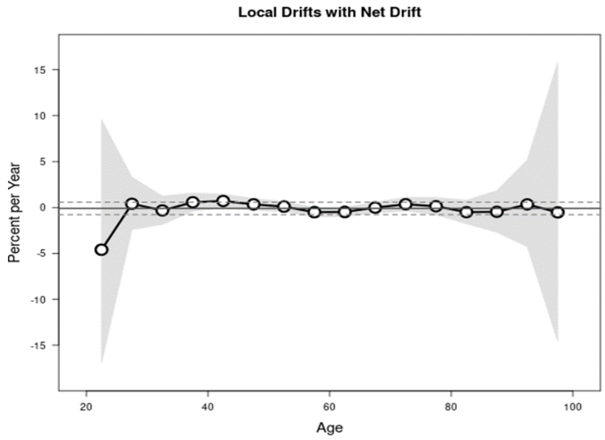

Figure 7. The Prevalence of Breast Cancer Depends on the Age Category

Table 2. Clinical Stages of Registered Cases of Breast Cancer

Stages	Number of cases (n,%)
I, Ia	6,585 (29.0)
I b, I c	8,687 (38.2)
II, IIa, II b, II c	4,079 (17.9)
III, IIIa, III b, III c	2,239 (9.8)
IV, IVa, IV b	1,045 (4.6)
Unknown	101 (0.4)
Total	22,736

By nationality, most (n=10939, 48.1%) of the breast cancer patients with a primary confirmed diagnosis were Kazakhs, and (n=7527, 33.1%) were Russians. Tatars had n=529 (2.3%), Ukrainians had n=1178 (5.2%) breast cancer diagnoses. There was a small number of Uighurs, Uzbeks, Germans, and Koreans among breast cancer patients with indicators of n=368 (1.6%), n=441 (1.9%), n=408 (1.8%), and n=262 (1.2%).

According to occupation, there were 1,485 (6.5%) professionals and 2,685 (11.8%) workers in elementary vocations among breast cancer patients with documented instances. While skilled workers in the agricultural, forestry, and fishing industries, as well as in craft-related crafts, plant and machine operators, and assemblers, made up 0.5% of the total. Managers and jobs in the armed forces made up a small portion, with n=159 (0.7%) and n=159 (0.2%), respectively. There was n=256 (1.2%) technicians and associate professionals, and n=301 (1.3%) clerical support workers.

Only 364 (1.6% of patients with a confirmed diagnosis of breast cancer were service or sales professionals; the majority, 17,108 (75.2%), were not employed.

Table 3. Distribution of Registered Cases of Breast Cancer Standardized by Gender Per 100 Thousand Population Depending on the Region in the Context of 2017-2021.

Region n, (by 100 thousand)	2017 year	2018 year	2019 year	2020 year	2021 year
Akmola region	214 (56.3)	196 (51.5)	212 (55.9)	179 (47.3)	206 (54.3)
Aktobe region	172 (39.1)	195 (43.8)	247 (54.7)	160 (35.0)	228 (49.8)
Almaty region	343 (33.9)	343 (33.5)	353 (34.1)	342 (32.7)	355 (34.0)
Atyrau region	95 (30.5)	118 (37.1)	125 (38.6)	115 (34.8)	104 (31.4)
East Kazakhstan region	164 (49.3)	212 (63.3)	215 (63.8)	149 (44.0)	189 (55.6)
Zhambyl region	198 (34.9)	193 (33.9)	188 (32.9)	160 (27.8)	173 (30.0)
West Kazakhstan region	450 (61.9)	516 (71.2)	568 (78.5)	440 (60.9)	520 (71.9)
Karagandy region	274 (59.4)	283 (61.6)	333 (72.8)	250 (55.0)	306 (67.1)
Kostanay region	121 (31.1)	106 (26.9)	118 (29.6)	101 (25.1)	116 (28.7)
Kyzylorda region	95 (29.0)	104 (31.0)	84 (24.3)	67 (18.8)	130 (36.4)
Mangystau region	270 (67.8)	269 (67.7)	371 (93.6)	278 (70.3)	340 (85.8)
Pavlodar region	190 (64.8)	232 (79.9)	209 (72.6)	230 (80.7)	204 (71.3)
North Kazakhstan region	274 (28.1)	94 (9.6)	276 (28.0)	230 (23.0)	263 (26.3)
Turkestan region	424 (58.4)	426 (59.0)	500 (69.6)	429 (60.1)	504 (70.5)
Nur-Sultan	304 (58.5)	338 (61.7)	353 (61.3)	341 (56.5)	402 (66.5)
Almaty	591 (61.2)	553 (55.7)	597 (58.4)	590 (56.0)	676 (64.1)
Shymkent	150 (31.0)	123 (24.2)	196 (36.9)	161 (29.5)	223 (40.7)

Figure 8. Age Cohort Analysis of Breast Cancer Frequency

Survival analysis

Figure 3 displays patient survival rates according to nationality. Germans had the lowest survival rate of 11.4±1.7 months, according to nationality. (95% CI: 8.0-14.7) months. Additionally, Uighurs and Ukrainians had low survival rates, with rates of 13.6±1.8 months (95% CI: 10.0-17.2 months) and 13.8±0.8 months (95% CI: 12.2-15.4 months), respectively.

Uzbeks had quite good survival rates, with rates of 18.3±1.6 months (95% CI: 15.1-21.5 months). The median time to death for Tatars was 13.0± 2.5 months, whereas the median time to death for Germans was 7.0± 1.6 months. The connection between nationality and survival was statistically significant (p=0.02) according to the long-rank Mantel-Cox test.

Figure 4 displays patient survival rates according to the clinical stage of breast cancer. The best survival for patients with stage I and stage I a breast cancer was found to be 20.5± 1.0 months (95% CI: 18.5-22.5 months). A higher patient survival rate of 19.0± 0.5 months (95% CI: 18.1-20.0 months) was also found in the group of patients with breast cancer stages Ib, Ic, II, and IIa. The survival rate for breast cancer in stages IIb and IIc was 16.9± 0.5 months (95% CI: 15.9-17.9 months). Patients' median survival in the clinical stages of breast cancer 9-III, III a, III b, and III c was 14.3± 0.4 months (95% CI: 13.4-15.2 months). Additionally, individuals with breast cancer in stages IV, IV a, and IV b had the lowest survival rates, with median survival times of just 6.8 ±0.4 months (95% CI: 6.0-7.5 months) ($p \leq 0.001$).

Figure 5 displays the survival rates for breast cancer patients according to their place of residence. The Aktobe region had the lowest breast cancer survival rates, at 12.1±0.9 months (95% CI: 10.3-13.9 months) ($p \leq 0.05$). Additionally, Atyrau, Pavlodar, and Nur-Sultan had low survival rates of 13.1±1.2 months (95% CI: 10.7-15.6 months), 13.6±0.8 months (95% CI: 12.1-15.2 months), and 13.4±0.9 months (95% CI: 11.6-15.2 months), respectively.

The highest survival rates, 18.0±1.3 months (95% CI: 15.5-20.5 months) and 17.9±1.4 months (95% CI: 15.3-20.7 months), respectively, were seen in the oblasts of Shymkent and Zhambyl. No statistically significant differences were discovered based on the results of the Wald tests on the influence of cohorts (All Cohort RR = 1; X^2 - 15.9; Df-19; p = 0.66), the influence of periods (All Period RR = 1; X^2 - 29.4; Df- 4; p = 0), and the influence of local drift (All Local Drifts = Net Drift; X^2 -13.97; Df-16; p =0)

According to an analysis of the data on the longitudinal age curves of the prevalence of breast cancer, the disease becomes more common after 37.5 years (Dv 0.49, 95% CI: 0.29 - 0.68), according to Figure 6. A consistent increase trend in the prevalence of breast cancer was found from the age of 42.5 years (Dv 1.01, 95% CI: 0.85 - 1.17) to 62.5 years (Dv 1.15, 95% CI: 0.98 - 1.31) but without peak values. The prevalence of the disease then gradually decreased until the age of 82.5 years (Dv -0.12, 95% CI: -0.43 - 0.19), which was then replaced with an abrupt reduction in the prevalence of breast cancer as patients' ages increased (Dv 0.81, 95% CI: 0.58 - 1.04).

Figure 7 displays the annual percentage change in breast cancer according to age group. The results indicate that the local drift values tended to be positive at the age of 27.5 years, with a percentage per year equal to 0.401 (95% CI: -2.4 - 3.28). Additionally, a negative trend equivalent to -0.321 (95% CI: -1.85 - 1.23), in women with breast cancer, was found at the age of 32.5. The value of the annual percentage change prevalence of breast cancer showed a favourable trend from the age of 37.5 years with a percentage per year of 0.572 (95% CI: -0.41 - 1.56) to 52.5 years of age with a percentage per year of 0.094 (95% CI: -0.45 - 0.65) as well. At the age of 82.5 years, the maximum negative value was found to be -0.506 (95% CI: -1.78 - 0.78) percent per year.

The age-cohort analysis of the incidence of breast cancer over the 5-year period (2017–2021) revealed that, compared to 2017, when the indicators were RR 0.93 (95% CI: 0.85–1.02), in 2018 there was a decrease in PCa prevalence, with an RR of 0.89 (95% CI: 0.83–0.97), and with a gradual increase until 2019, when this indicator was equal to RR 1 (95% CI: 1–1). Additionally, there was a significant drop in the prevalence of breast cancer in 2020, with indicators at RR 0.83 (95% CI: 0.77-0.9), and following this drop, a steady rise to RR 0.94 (95% CI: 0.86-1.03) was recorded in 2021 (Figure 8).

Discussion

The APC model was used to examine the trend in the prevalence of breast cancer in the setting of 2017–2021 in this study, which is the first national study of breast cancer in the Republic of Kazakhstan.

At present, the frequency and incidence of breast cancer are rising globally despite a minor decline in mortality rate (Banas et al., 2016). In this study, we observed the highest number of breast cancer cases in 2021, while the lowest number was detected in 2020. In fact, some authors have forecasted the global decline in breast cancer registration cases (Figueroa et al., 2021; Cairns et al., 2022). Such a forecast has been based on the implementation of restrictive measures, the mandatory re-profiling of medical institutions into infectious hospitals in 2020 (Zhussupov et al., 2022) as a result of COVID-19 pandemic.

Age, ethnicity, tumour type and size, and others are known key prognostic factors impacting the survival of patients with breast cancer (Tan et al., 2021). The late detection and a lack of access to high-quality medical care are the main causes of low breast cancer survival rates (Cumber et al., 2017). Women in this study were more likely to be diagnosed with early-stage breast cancer than late-stage breast cancer, in contrast to prior studies (Yoo et al., 2002; Fouladi et al., 2012). Additionally, based on our findings, patients with clinical stage 1 breast cancer had a greater rate of survival. Additionally, the correlation between breast cancer survival and clinical stages was statistically significant ($p = 0.001$). According to some studies, good screening programs may be to blame for the high frequency of early-stage malignancies and the low incidence of later-stage cancers (Ferraz and Moreira-Filho, 2017).

Most frequently, breast cancer cases with the malignant process localized in the upper outer quadrant of the mammary gland were reported by 44.6% of those who were brought to the pharmacy (C50.4 according to ICD-10). These findings are in line with findings from previous studies, including one conducted in Saudi Arabia (Pérez-Rodríguez, 2015), where breast cancer with localization in the upper outer quadrant was the most prevalent type (Alotaibi et al., 2018). The existence of the greatest quantity of glandular tissue in the upper outer quadrant of the breast is occasionally linked as a potential explanation for the frequent localization of breast cancer.

The Pavlodar and North Kazakhstan regions, which are in the northern and north-eastern parts of Kazakhstan, were determined to have the highest number of breast cancer registrations in 2021, just as they were in 2017. In addition, despite a minor increase in the number of cases of breast cancer reported in 2021, cities and areas in Kazakhstan's eastern and southern regions had low rates of breast cancer diagnosis during the study period. This may be due to the favourable predominance of the protective reproductive factor in women in these regions (relatively younger puerperal age, higher fertility, as well as a slightly higher prevalence of breastfeeding among women who have given birth) (Giorgi Rossi et al., 2020). It may also be due to some cultural and behavioural peculiarities of the territorial nature. As is well known, numerous births can also lower the risk of contracting this illness (Horn-Ross et al., 2004), as does childbirth, particularly at full-term pregnancy, encouragement of nursing, and prevention of breast cancer (Daling et al., 2003). Given that the population of Kazakhstan's western and southern areas has a higher birth rate, according to figures for 2021, the regions with the highest birth rates were Shymkent (32.35 births per 1,000 people), Mangistau (31.98), and Turkestan (31.58). The regions of North Kazakhstan (12.01), Kostanay (12.97), and Pavlodar (15.58) had the lowest birth rates (Bureau of National Statistics of the Agency for Strategic Planning and Reforms of the Republic of Kazakhstan, 2021). This situation is somewhat consistent with other studies. For instance, a previously published study in Italy found that the southern regions had a lower incidence of breast cancer than the northern regions, but there were predictions that this difference in prevalence and incidence may soon vanish due to certain circumstances (Giorgi Rossi et al., 2020).

According to nationality, breast cancer was found more frequently among Kazakhs (48.1 %) and Russians (33.1 %). In fact, both ethnicities are the main ethnic groups in Kazakhstan (data of Bureau of National Statistics of the Agency for Strategic Planning and Reforms of the Republic of Kazakhstan, 2000).

Given that women in Kazakhstan can begin to retire at age 63, the vast majority of patients with breast cancer did not hold any form of employment. As a result, in this group of older women, the development of this illness may also be attributed to hormonal variables originating in premenopause that are linked to estrogen oversaturation (Balekouzou et al., 2016).

The Germans had the lowest survival rate, which was judged to be 11.4 1.7 months based on the results of the survival analysis. Additionally, there was a statistically significant association between nationality and survival ($p=0.02$). Patients from the southern regions, specifically the Zhambyl region (17.9 1.4 months) and the city of Shymkent (18.0 1.3 months), had the best survival rates.

The prevalence of breast cancer was found to increase after 37.5 years, with a consistent rising trend in the age range of 42.5 years to 62.5 years, but without peak values. Only in the age category of 72.5 years was a decline in the growth of cases noticed. For instance, breast cancer in women is strongly correlated with age in China, where the incidence rate is fairly low in those under the age of 30 and rises quickly, peaking around 50 years old (Chen et al., 2013). Besides, a similar peak incidence was not seen in women aged 70 and older in a Danish retrospective review of breast cancer patients (Jensen et al., 2016).

These findings are in line with the results of previous studies. It was demonstrated that educating women 40 years of age and older (routine mammography screening and monitoring) is one of the key factors for lowering breast cancer-related mortality (DeSantis et al., 2011). Additionally, another study showed that 91.6% of breast cancer cases diagnosed after the age of 35 and 8.4% diagnosed before the age of 35 underlines the significance of routine breast exams for women over the age of 35 (Yu et al., 2012).

The results acquired demonstrate that the incidence of breast cancer among women aged 37.5 years and older has been consistent over the past five years in Kazakhstan, despite a minor decline in the frequency of the disease. Additionally, it was discovered that the northern sections of the country had a higher incidence of cases of breast cancer compared to the southern and western regions.

Our findings indicate the necessity of the development of new strategies to improve diagnostics and treatment. It must encompass the information about age, place of residence and other demographic data.

Study limitations

This research has a few limitations. One issue was the absence of data on additional variables that might be related to breast cancer incidence, tumour histology, treatment options, and death. Apart from that, there was a lack of information about the socioeconomic situation of the patient, access to healthcare, heredity, and hormonal and reproductive factors.

Author Contribution Statement

Conceptualisation: Adiya Shertaeva and Dinara Ospanova, data curation: Dinara Ospanova and Andrey Grzhibovsky; formal analysis: Nurlan Rakhmetov, Dinara Ospanova, Zaure Dushimova and Bagdat Salimgereeva; investigation: Zhannym Yermentayeva, Indira Kaketaeva, Shynar Tanabayeva and Ildar Fakhradiyev; methodology: Adiya Shertaeva, Ildar Fakhradiyev; project administration: Adiya Shertaeva; resources: Dinara Ospanova; validation: Yerlan Kuandykov; visualisation: Andrey Grzhibovsky; writing – original draft, and writing–review & editing: Adiya Shertaeva, Dinara Ospanova, Ildar Fakhradiyev, and Nurlan Rakhmetov.

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Ethical Declaration
For this study, anonymous information from the electronic register of cancer patients was utilized. The study was conducted in accordance with the ethical standards of the state and national research committee. Due to the retrospective nature of the study, the ethical approval was considered to be waived by Institutional Review Board. Data records were anonymous, so informed consent also was exempted.

Data Availability
The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Conflict of interest
The authors declare no conflict of interest.

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