RESEARCH ARTICLE

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Epidemiology of Breast Cancer Mortality in Kazakhstan, trends and Geographic Distribution

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Abstract

Background: According to the International Agency for Research on Cancer, ongoing demographic changes will lead to an increase in the number of deaths from breast cancer (BC) per year in the vast majority of regions. In 2040 it is expected that 1.04 million people worldwide will die from this malignancy, including 2,380 women in Kazakhstan. **Methods:** The retrospective study (2009-2018) was done using descriptive and analytical methods of oncoepidemiology. The extensive, crude and age-specific incidence rates are determined according to the generally accepted methodology used in sanitary statistics. The data were used to calculate the average percentage change (APC) using the Joinpoint regression analysis to determine the trend over the study period. **Results:** During 10 years 12,958 women died from BC. An average age of the death was 61.6 years (95%CI=60.6-62.6) and tended to increase (APC=+0.6%, R2=0.6117). Age-specific rates had a bimodal increase with peak rates at 70-74 years – 76.7±5.5 (APC=+3.4%, R2=0.2656) and 80-84 years – 78.0±9.1 (APC=+3.7%, R2=0.0875). The age-standardized rate was 13.9 per 100,000 of female population, and the trend has decreased. When compiling thematic maps, mortality rates were determined on the basis of standardized indicators: low – up to 12.5, average – from 12.5 to 15.2, high – above 15.2 per 100,000. The results of the spatial analysis showed the regions with a higher levels of BC mortality rate per 100,000: Pavlodar (16.9), Almaty (19.2) and Astana cities (19.3). **Conclusions:** Age-standardized mortality rates had a strong downward trend (APC=−4.0%, R2=0.9218). The decrease mostly is due to a large coverage of the population by mammography screening and to an improvement in the effectiveness of breast cancer treatment.

Keywords: Breast cancer- mortality- trends- geographical variation- Kazakhstan

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Introduction

Breast cancer (BC) represents the most common cause of death among women, being the fifth leading cause of cancer death in the world, accounting for 2.3 million new cases (11.7% of all cases) and 684,996 deaths in 2020, with Asia contributing the highest, 1,026,684 (45.4%) of incident cases and 345,559 (50.4%) of deaths globally (Sung et al., 2021; Ferlay et al., 2022A).

The incidence of breast cancer in Kazakhstan is growing (Toguzbayeva et al., 2021; Igissinov et al., 2022). In the study of breast cancer in the ecological regions of Kazakhstan, a direct strong correlation was established between the degree of pollution by increased emissions of pollutants into the atmosphere from stationary sources and the incidence of breast cancer (r=0.77±0.15; p=0.026). These results indicate the growing importance of breast cancer in Kazakhstan and the etiological role of environmental pollution (Bilyalova et al., 2012). In 2019 alone, 4,896 new cases were estimated, with an incidence of 51.3 per 100 thousand women and 1,394 deaths, corresponding to a death risk of 14.6 per 100 thousand women. According to the IARC, ongoing demographic changes will lead to an increase in the number of deaths

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from BC per year in the vast majority of regions. The number of deaths from breast cancer is set to double by 2040 for most countries, suggesting an alarming increase in the future burden of BC, which needs more effective prevention programs against attributable risk factors, especially in countries with low SDI levels (Ferlay et al., 2021B; Li et al., 2019).

Mortality trends are associated with the level of effectiveness of cancer strategies in reducing the impact of cancer exposure over time (Ellis et al., 2014). Age-standardized mortality rates from the 1980s to 2020 declined by 40% in high-income countries, while a weak-to-moderate increase was observed in low-income countries (Hashim et al., 2016). Changes in mortality rates in different regions mostly are due to several screening and treatment programs in these regions and depends on race and access to hospitals and prevention programs, not on the pathogenetic characteristics of the tumor (Downing et al., 2007).

In Kazakhstan, mammography screening was conducted from 2008-2016, with the contingent of women 50 years and older (https://adilet.zan.kz/rus/docs/V1400010199). Although, since 2017, there has been a revision of the age, contingent of people, who undergoing mammography. From 2017 to the present, females who have reached the age of 40 go through mammography (https://adilet.zan.kz/rus/docs/V2000021572). Screening does not involve women who are diagnosed with breast cancer, as well as those with severe concomitant diseases that are highly likely to lead to death in the next 10 years, for example, myocardial infarction with congestive heart failure or diabetes mellitus.

Regular mammography screening is the most effective method for reducing mortality rates (Coleman, 2017). According to our research on breast cancer epidemiology in Kyrgyzstan, there is a significant increase in incidence rates (Igisinov et al., 2002; Igissinov et al., 2005; Chokoev et al., 2022). However, in countries like Kyrgyzstan where mammographic screening is not conducted, its absence may have a negative impact on breast cancer mortality in the future (Tabar et al., 2015).

The United States Prevention Services Task Force (USPSTF) recommends biennial mammography for women 50 years and older (Siu, 2016). Recommended double reading in breast cancer screening depends on both readers and their independence in examining the females' mammograms, and an effective system of arbitration of results (Duffy et al., 2021). The analysis of early detection and advanced stage rates demonstrates a positive trend in the proportion of patients diagnosed with stage I-II cancer and a decline in the proportion of patients with stage III-IV cancer in both Almaty and Astana. These epidemiological changes can be attributed to the successful implementation of anticancer measures, particularly the introduction of breast cancer screening in the Republic (Igissinov et al., 2019). In our study on the impact of screening on the incidence of breast cancer in Kazakhstan, the positive effect of mammological screening in the country was revealed (Toguzbayeva et al., 2021).

However, significant problems can become barriers to diagnosis, for example, fear of positive mammogram result, perception of being healthy, cost of mammogram, lack of transportation and lack of physician recommendation for a mammogram and cultural role, small amount of primary health care points in sparsely populated areas, which affects the use of mammography (Monticciolo et al., 2021; Alexandraki and Mooradian, 2010).

The American Cancer Society systematic review reported that screening mammography was associated with a decreased risk of breast cancer mortality in randomized controlled trials (Myers et., 2015). The incidence of breast cancers that will lead to death within 10 years of diagnosis was 50% lower in women who participated in both previous screening than in those who did not attend (Duffy et al., 2020).

The purpose of this study is to evaluate the spatial and temporal features of mortality from BC in Kazakhstan, taking into account the administrative-territorial division.

Materials and Methods

Registration of cancer mortality

Population-based mortality data from 2009 to 2018 were obtained from the Bureau of National Statistics of Republic of Kazakhstan (2018) for the 14 regions and cities of national significance - Almaty and Astana using the International Disease Code 10, code C50 (Bureau of National Statistics, 2022). Information on registration of the death of an oncological patient is transferred by the oncological dispensary to the electronic register of oncological patients no later than 10 days from the date of registration of the death by the civil registry office.

Statistical analysis

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

The extensive, crude and age-specific mortality 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) were calculated. Mean error in statistics usually refers to the average value of the differences between estimates and true values (Glanz, 1999). Student's criterion, also known as t-test is used to compare the means of two groups, and is based on the difference in means divided by an estimate of the standard error of the difference (Glanz, 1999). In addition, we have determined the level of approximation (R^2). The level of approximation in linear regression evaluates how close the linear model is to the original data. This indicator reflects how well the model matches the data and how accurately it predicts the values of the dependent variable based on the independent variables.

We were not smoothing 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; Glanz, 1999; dos Santos Silva, 1999). The mortality trend was studied for 10 years, while the incidence trend was determined by the least squares method and using the Joinpoint program (https://surveillance.cancer.gov/joinpoint/). The data were used to calculate the average percentage change (APC) using the Joinpoint regression analysis.

When compiling the thematic map, crude mortality rates (CMRs) and ASMRs were used for 10 years (2009-2018). The method of compiling thematic map proposed in 1974 by S.I. Igissinov was used, based on the determination of the standard deviation (σ) from the average (x). This method is a useful tool for visualizing spatial variability of data. It allows you to identify areas with deviations from the expected values and visually display differences in variability on a geographical map.

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. Data analysis was carried out in the statistical package SPSS Statistics version 28.0.1.0. The thematic maps were performed using the geographic information system QGIS version 3.18.

Ethics approval

The study included an analysis of publicly available administrative data and did not involve contacts with individuals. The Local Ethics Commission of the Central Asian Institute for Medical Research approved this study.

Results

During the study period (2009-2018), twelve thousand nine hundred and fifty-eight deaths from breast cancer among women were registered. In the age group of 50-74 years, the largest number of deaths from breast cancer was detected, that is, 8,526 deaths (65.8%), which is more than half of the cases. Of these, 1,757 cases (13.6%) in 50-54 years, 1983 cases (15.3%) in 55-59 years, 1,865 cases (14.4%) in 60-64 years, 1,361 cases (10.5%) in 65-69 years and 1,560 cases (12.0%) in 70-74 years (Table 1).

The average age of the death was 61.6 (95%CI=60.6-62.6) years and tended to increase slightly from 60.6 (95%CI=59.9-61.2) years in 2009 to 63.5 (95%CI=62.8-64.2) years in 2018. The average annual growth rate of the average age was APC=+0.6% (p=0.000; t=5.80; R^2=0.6117).

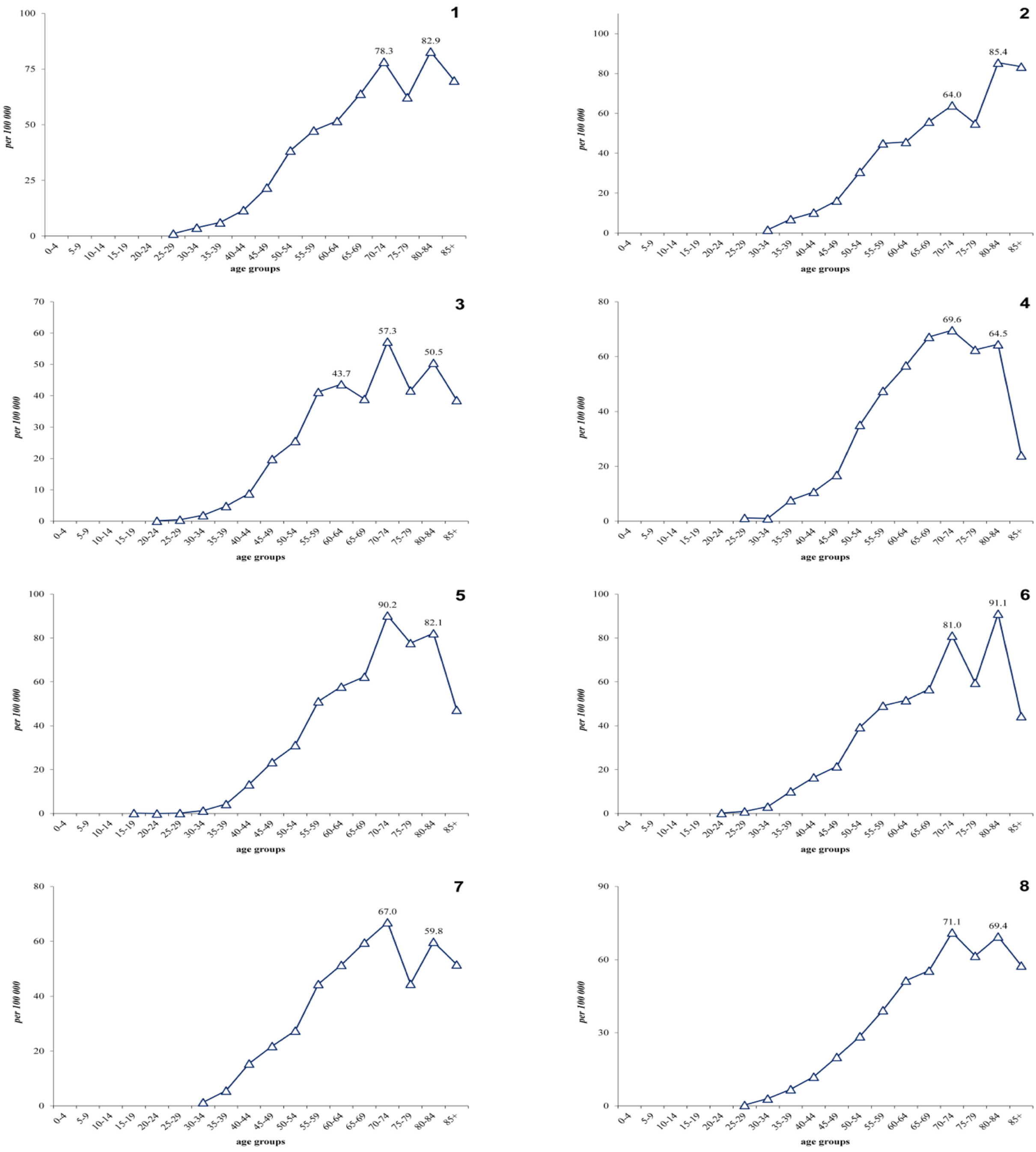
Crude rates of BC mortality among female population of Kazakhstan tended to decrease from 16.5 (95%CI=15.6-17.4) (2009) to 12.0 (95%CI=11.3-12.7) in 2018 per 100,000 of female population, the average annual mortality rate for the studied years was 14.7 (95%CI=13.7-15.8) per 100,000 of female population. The average annual rate of mortality decline by BC was significant (APC= -3.5%), as well as a high degree of reliability of the approximation (R^2=0.8924) proves a true reduction in mortality from this form of cancer in Kazakhstan. The standardized mortality rate for the country was 13.9 (95%CI=12.7-15.0) per 100,000 of female population. And the average annual rate of decline of ASMR was APC= -4.0% (R^2=0.9218).

The highest mortality rates per 100,000 of female population were found in the age groups 70-74 years (76.7±5.5), 75-79 years (63.5±6.3), 80-84 years (78.0±9.1) and 85+ years (65.9±5.1). BC mortality had an upward trend only in three studied age groups: 65-69 years (APC=+1.0%), 70-74 years (APC=+3.4%) and in the

Table 1. The Average Age-Specific Mortality Rates of Breast Cancer in Kazakhstan for the Years 2009-2018

Age groups	Deaths (%)	ASMR, per 100,000		APC, %	R^2
		M±m	95% CI		
<30	46 (0.4)	0.1±0.0	0.1-0.1	−12.6	0.6077
30-34	145 (1.1)	2.2±0.4	1.4-3.0	−11.5	0.4874
35-39	372 (2.9)	6.1±0.6	4.9-7.4	−7.8	0.6671
40-44	657 (5.1)	11.6±1.0	9.7-13.4	−5.6	0.4863
45-49	1,152 (8.9)	20.5±1.8	17.1-24.0	−7.8	0.8977
50-54	1,757 (13.6)	33.0±2.4	28.3-37.6	−6.1	0.7969
55-59	1,983 (15.3)	44.7±3.3	38.3-51.2	−6.8	0.867
60-64	1,865 (14.4)	55.2±3.1	49.2-61.2	−5.3	0.9422
65-69	1,361 (10.5)	57.6±2.4	53.0-62.2	1	0.0857
70-74	1,560 (12.0)	76.7±5.5	65.8-87.5	3.4	0.2656
75-79	983 (7.6)	63.5±6.3	51.1-75.8	−8.9	0.8311
80-84	715 (5.5)	78.0±9.1	60.1-95.8	3.7	0.0875
≥85	362 (2.8)	65.9±5.1	55.8-75.9	−3.1	0.1344
Total/CMR	12,958 (100.0)	14.7±0.5	13.7-15.8	−3.5	0.8924
ASMR	−	13.9±0.6	12.7-15.0	−4.0	0.9218

ASpMR, age-specific mortality rate; CMR, crude mortality rate; ASMR, age-standardized mortality rate; M, median; m, error; CI, confidence interval; APC, average percentage change. R^2, the value of the approximation confidence.



Regions: 1. Akmola, 2. Aktobe, 3. Almaty, 4. Atyrau, 5. East-Kazakhstan, 6. Zhambyl, 7. West-Kazakhstan, 8. Karaganda

Figure 1A. Age-Specific Mortality Rate of Breast Cancer in Kazakhstan, 2009-2018

age of 80-84 years (APC=+3.7%). In other age groups, the leveled BC mortality was decreasing, with the most pronounced annual average downward rates in the age groups of up to 30 (APC=−12.6%), 30-34 (APC=−11.5%), and 75-79 years (APC=−8.9%) (Table 1).

Age-specific mortality rates from breast cancer had regional peculiarities: trimodal growth was observed in groups of 60-64, 70-74, 80-84 years in three regions: Almaty (43.7, 57.3, 50.5) (Figure 1A), Kyzylorda (53.0, 72.2, 69.0) and Mangystau (51.7, 58.5, 62.4) regions (Figure 1B).

Bimodal growth with peaks in the groups of 70-79 and 80-84 years was observed in Akmola (respectively 78.3, 82.9), Atyrau (respectively 69.6, 64.5), East Kazakhstan (respectively 90.2, 82.1), Zhambyl (respectively 81.0, 91.1), West Kazakhstan (respectively 67.0, 59.8) and Karaganda (respectively 71.1, 69.4) regions (Figure 1A).

At the same time, bimodal growth with peaks in groups of 60-64 and 80-84 years old was observed in Aktobe (respectively 64.0, 85.4) (Figure 1A), Kostanay

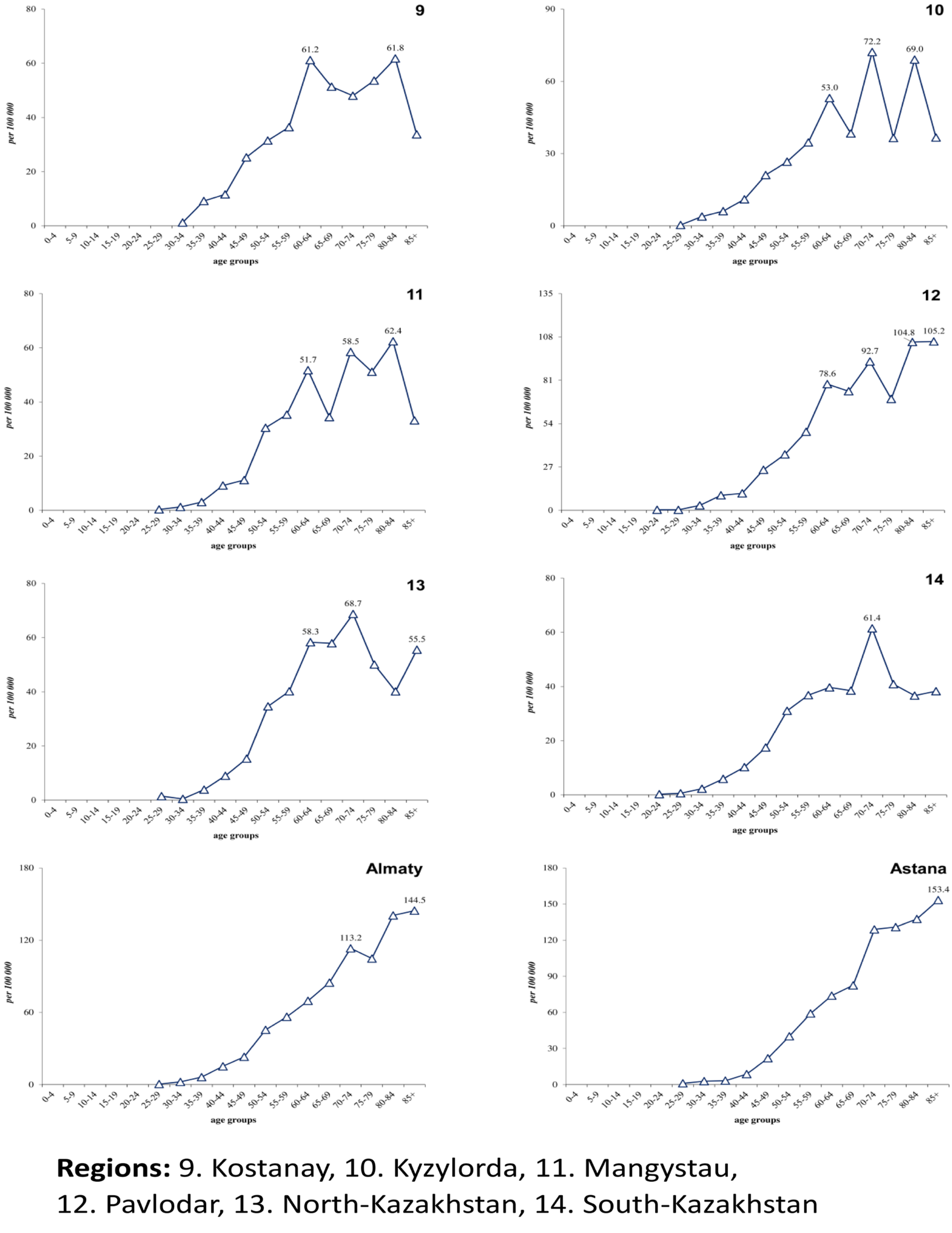


Figure 1B. Age-specific Mortality Rate of Breast Cancer in Kazakhstan, 2009-2018

(respectively 61.2, 61.8) (Figure 1B).

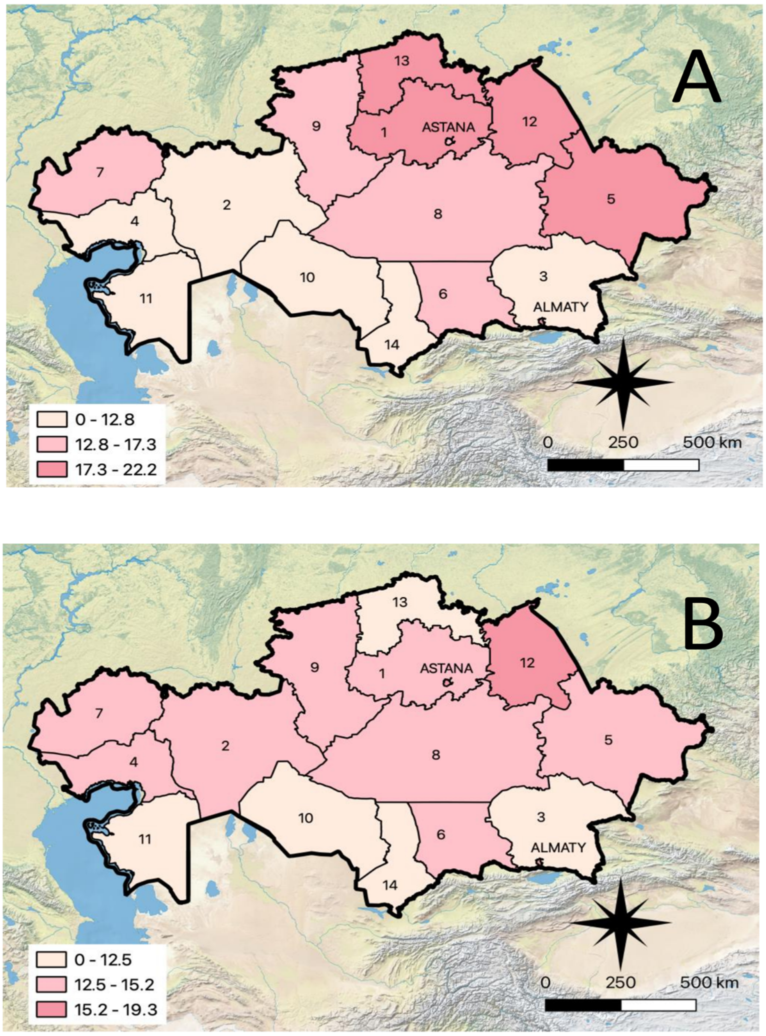
Unimodal growth in the 85+ year group was observed in the cities of Almaty (144.5), Astana (153.4) and South Kazakhstan region (61.4) (Figure 1B).

Based on the calculated average annual CMR and ASMR BC indicators, the thematic maps were compiled. The levels of BC CMR per 100,000 of female population based on the following criteria were determined: low – up to 12.8, average – from 12.8 to 17.3, high – above 17.3. As a result, the following groups of regions were revealed (Figure 2A):

1. Regions with the lowest indicators (up to 12.8 per 100,000 population of female): Mangystau (8.0), South Kazakhstan (8.3), Kyzylorda (9.9), Almaty (10.8), Atyrau (12.1), Aktobe (12.6).

2. Regions with average indicators (from 12.8 to 17.3 per 100,000 population of female): Zhambyl (14.1), Astana city (14.9), West Kazakhstan (15.1), Karaganda (16.7), Kostanay (17.1).

3. Regions with high indicators (17.3 and above per



Regions: 1. Akmola, 2. Aktobe, 3. Almaty, 4. Atyrau, 5. East-Kazakhstan, 6. Zhambyl, 7. West-Kazakhstan, 8. Karaganda, 9. Kostanay, 10. Kyzylorda, 11. Mangystau, 12. Pavlodar, 13. North-Kazakhstan, 14. South-Kazakhstan

Figure 2. The Thematic Map of Breast Cancer Mortality in Kazakhstan, 2009-2018 (A – CMR; B – ASMR)

100,000 population of female): North Kazakhstan (18.2), Akmola (18.9), East Kazakhstan (20.3), Almaty city (21.7), Pavlodar (22.2).

The levels of BC ASMR per 100,000 population of female based on the following criteria were determined: low – up to 12.5, average – from 12.5 to 15.2, high – above 15.2. As a result, the following groups of regions were determined (Figure 2B):

1. Regions with the lowest indicators (up to 12.5 per 100,000 population of female): Mangystau (10.5), South Kazakhstan (10.7), Almaty (10.8), Kyzylorda (11.8), North Kazakhstan (12.4).

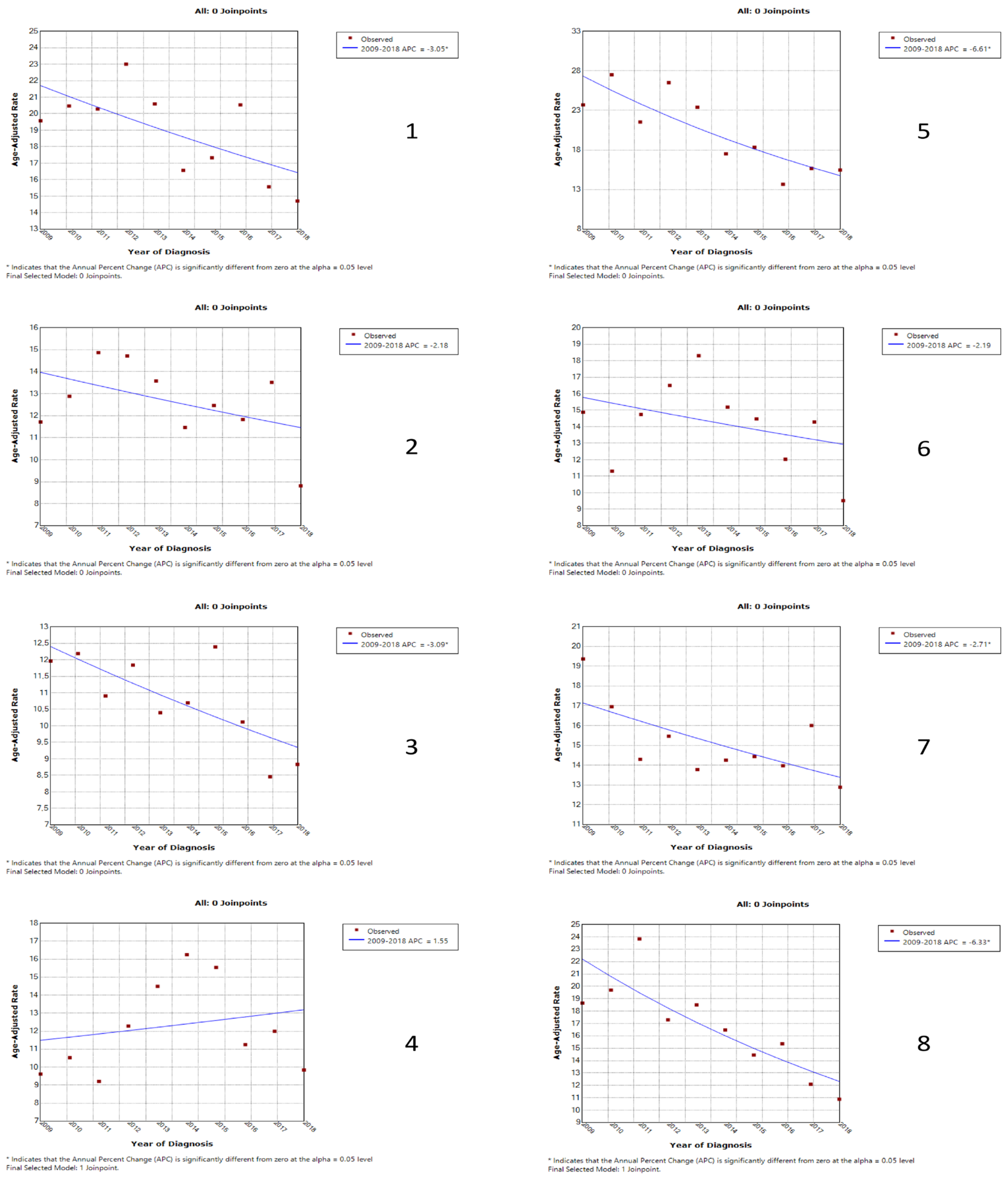
2. Regions with average indicators (from 12.5 to 15.2 per 100,000 population of female): Kostanay (12.7), Aktobe (12.8), West Kazakhstan (12.9), Karaganda (12.9), Atyrau (13.7), Akmola (14.6), East Kazakhstan (14.8), Zhambyl (15.0).

3. Regions with high indicators (15.2 per 100,000 population of female and above): Pavlodar (16.9), Almaty city (19.2) and Astana city (19.3).

Thus, the mortality thematic maps more clearly reflect the spatial distribution of BC in the republic, while the discrepancy between the theoretical and actual distribution of BC mortality by regions and cities is small, the Pearson criterion (χ^2) equals 2.0 and 3.8 (for a crude and age-standardized indicator, respectively).

Trends in the aligned mortality rates from BC lowered in almost all regions of the country, apart from the Atyrau region, where there was an increase (APC=+1.55%; R^2=0.0674). The highest rates of decline were found in Karaganda (APC=−6.33%, R^2=0.7792) and East Kazakhstan (APC=−6.61%, R^2=0.7707), while the values of the approximation confidence were appreciable (Figure 3A).

In all regions there is a decrease in the mortality rate, while the downward trends and their degrees of approximation are expressed in East Kazakhstan (APC=−6.61%, R^2=0.7707), Karaganda (APC=−6.33%,



Regions: 1. Akmola, 2. Aktobe, 3. Almaty, 4. Atyrau, 5. East-Kazakhstan, 6. Zhambyl, 7. West-Kazakhstan, 8. Karaganda

Figure 3A. Trends of Age-Standardized Mortality Rates of Breast Cancer in Kazakhstan, 2009-2018.

R^2=0.7792), Almaty (APC=−3.09%, R^2=0.6690), West Kazakhstan (APC=−2.71%, R^2=0.6294) (Figure 3A) regions, and Almaty city (APC=−4.27%, R^2=0.7005) (Figure 3B), which suggests that this trend will be stable in the coming years.

Discussion

Despite the fact that mortality rates are decreasing in Kazakhstan, our republic belongs to the region with average mortality rates (13.8-16.6 per 100,000 population). The standardized death rate was 13.6 per 100,000 population. According to IARC, the highest standardized mortality rates are observed in Africa: Nigeria (25.5), Chad (25.2), Ethiopia and Namibia (24.1), Central African Republic (24.4), as well as in Barbados (42.2), Serbia (23.9), Iraq (23.3), Malaysia (20.7), Georgia (23.5), Egypt (20.4). The lowest standardized mortality rates are observed in Bhutan (2.6), Mongolia (3.9), Korea (6.4), Kyrgyzstan (8.1) (Ferlay et al., 2019A).

Mortality from breast cancer in Kazakhstan has a global trend, as in the rest of the world, the rate is low

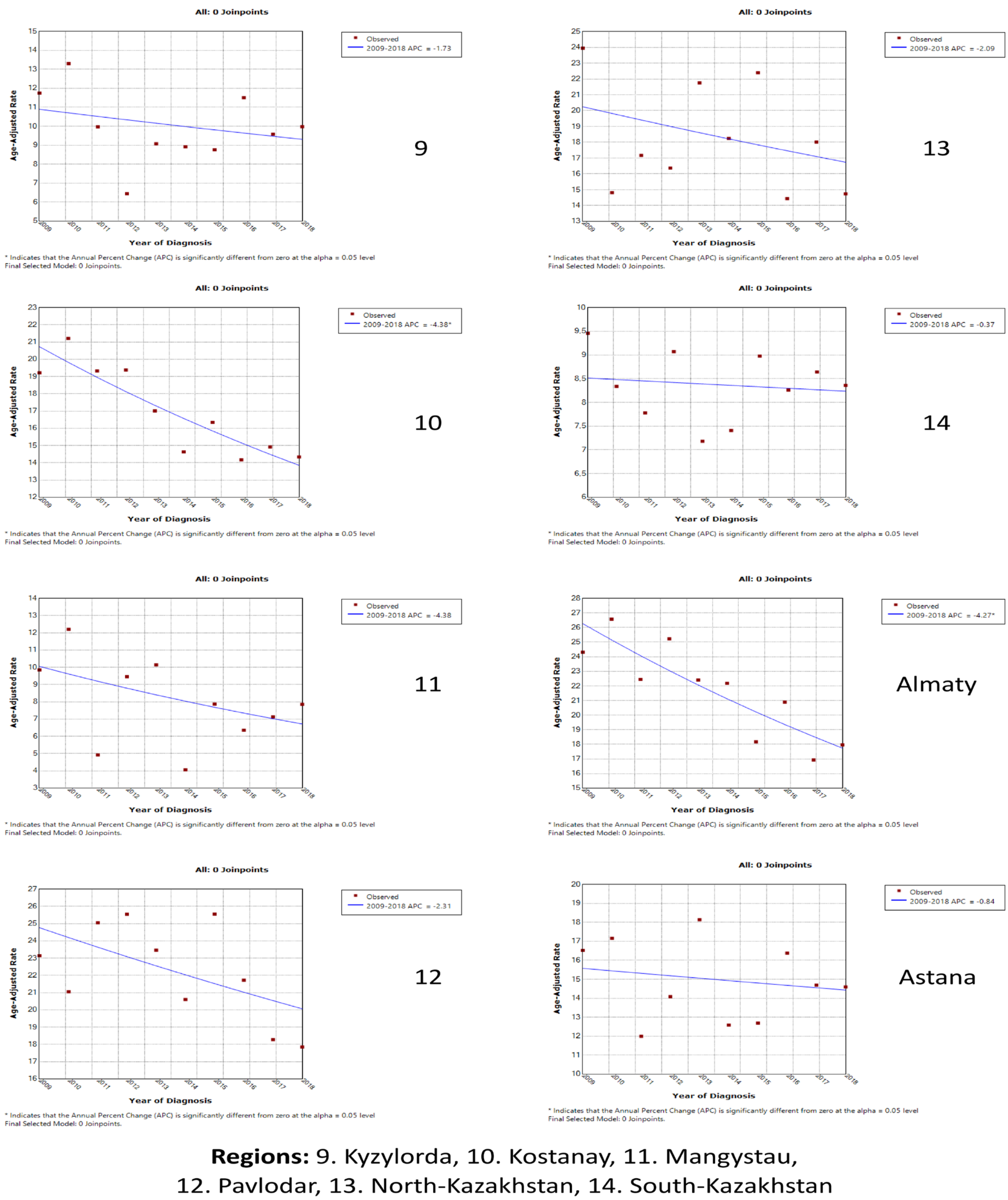


Figure 3B. Trends of Age-Standardized Mortality Rates of Breast Cancer in Kazakhstan, 2009-2018.

under the age of 50 (up to 50 years – 4.00/0000), but strongly increases with age (from 50 years and older – 52.10/0000). The trend can be traced in the USA (up to 50 years – 3.10/0000, from 50 years and older – 49.90/0000), in China (up to 50 years – 2.00/0000, from 50 years and older – 41.70/0000), and in Japan (under 50 – 2.80/0000, 50 and older – 38.60/0000) (Ferlay et al., 2019A; Azamjah et al., 2019). About 89% of breast cancer deaths in the United States in 2017 occurred in the age group over 50 (Desantis et al., 2017). Higher mortality rates are observed in older Chinese, Indian and Pakistani women (Mubarik et al., 2020). This indicates that older women made the greatest contribution to the increase in breast cancer mortality rates. The transition from unimodal ASMR to bimodal with peak rates predominantly in the group over 50 years old may indicate mortality corresponding to postmenopausal tumors. In women over 75 years of age, cancer can be diagnosed at an earlier stage, but it cannot be responsible for the reduction in mortality, in part due to shorter life expectancy (Smith-Bindman et al., 2000; Braithwaite et al., 2016).

An increase in the Universal Health Coverage (UHC) Index is associated with a decline in age-standardized mortality rates. Moreover, it was found that with an increase in UHC, the ASMR decreases by 0.12 units, and each established cancer center (per 10,000 people) reduces the indicator by 0.23 units (Duggan et al., 2021). However, with an increase in the human development index, there is an increase in the incidence of breast cancer, which in higher-income countries is associated with a "westernization" of lifestyle, while the indicator in countries with a low HDI is associated with a low level of health care and limited access to health services (Porter, 2008; Bray et al., 2018).

The epidemiological indicators derived from our study need to be associated with breast cancer risk factors, which are ubiquitously increasing mortality rates (Momenimovahed and Salehiniya, 2019). Reproductive factors, including decreased fertility rates, age of menopause, low prevalence of breastfeeding, and the prevalence of pregnancies at mature age (especially in the cities of republican significance – Astana and Almaty), can have a significant impact on the increase in ASMR (Laamiri et al., 2016; Kim et al., 2015). The decline in fertility in the United States, late maternal age, breastfeeding, use of oral contraceptives and hormone therapy in Korea are associated with increase in breast cancer incidence, and a corresponding increase in the risk of death (Krueger and Preston, 2008; Wang et al., 2018).

The levels of ASMR and CMR in our country have geographic variability, the lowest rates are observed in the southern regions, the highest in the eastern regions. Presumably, this is due to the ethnic composition of the population, changes in the age structure and characteristics of lifestyle and social behavior. The incidence of breast cancer varies, showing large differences across ecological regions, with a strong correlation with air emissions, indicating an etiological role (Bilyalova, 2012). Epidemiological studies of breast cancer have shown that there is an ethnic difference in the average age of patients (Bilyalova, 2012), with the average age of Kazakh patients being 50 years old, and Russian patients being 60 years old, which explains the increased prevalence of postmenopausal tumors in the northern regions. Ethnicity has been found to be an important etiological factor in breast cancer. Some ethnic groups, such as blacks had 21% higher risk of breast cancer-specific death (HR, 1.21; 95% CI, 1.00 to 1.45), which is related to the characteristics of the tumor and the stage of diagnosis, as well as the body mass index (Warner et al., 2015).

Women at average risk should be counseled about breast self-examinations and encouraged to notify their health care provider if they notice a change in sensation. Moreover, healthcare providers should periodically assess the risk of breast cancer by reviewing the patient's medical history.

Early detection and different risk factors may explain the differences in breast cancer mortality worldwide. Screening had a positive effect on epidemiological indicators in European countries, a decrease in mortality rates among women aged 50-69 was found to be −6.3% and −8.2%, respectively, compared to −5.6% and −7.1 % for younger women (Wojtyla et al., 2021). The importance of screening was confirmed in a prospective 13-year study, and it was found that annual screening using MRI and mammography is associated with a 20-year probability of not dying in this period (Warner et al., 2020). A 20-year cohort study found that with continued invitations to mammography screening up to age 74, breast cancer detection was 20% more effective than invitations up to age 69 (Zheng et al., 2020). The results of regression analysis based on data from European countries confirm the positive effect of the introduction of screening on reducing mortality from breast cancer (Iwamoto et al., 2019). According to the UK National Survey, when a woman visits at least one mammography screening, there is an overall 38% reduction in the risk of dying from breast cancer for women (Maroni et al., 2021). Mammographic screening will have a meaningful effect if it involves a large segment of the target population, and the positive effect will be reflected in epidemiological indicators for more than 10 years (Duffy et al., 2021). However, with the current epidemiological situation in 2019-2021, women have not been able to participate in mammography screening, which may affect the rates of morbidity and mortality in the next few years (Alagoz et al., 2021). Moreover, lack of awareness, higher diagnostic costs may partly explain higher mortality (Solikhah et al., 2019; Capri and Russo, 2017). Connor et al. stated that there is a significant association between individual race and racial economic segregation, with an increase in mortality among women living in less privileged areas (Avonne et al., 2022). Optimized screening programs will increase mortality and morbidity as a result of more frequent breast cancer detection, as many women who have not previously received secondary prevention will be diagnosed at terminal stages. However, this trend will be temporary and will be followed by a decrease in epidemiological indicators. Given the high degree of approximation in our study, as well as the reiteration of the ASMR and CMR curves, it is fair to assume that this trend will be persistent over the next years. Presumably, in our country, it is advisable to change the age of screening, taking into account the reproductive history and average life expectancy. Inadequate screening coverage and delayed treatment can be major barriers to lower mortality rates.

Breast cancer can be slow-growing or aggressive and deadly since it grows and spreads rapidly, mammograms may not be sensitive to fast-growing cancers (Welch and Black, 2010; Huang et al., 2017; Tagliafico et al., 2020; De Marchi et al., 2021). This leads to interval cancers that were not seen on the last mammogram. Women with interval cancer may delay seeking care due to a false negative result. In the European Region, the risk of false-positive results was 20%, therefore, the risk of biopsy was increased (Hofvind et al., 2012). False positive results lead to additional financial costs and deterioration in the psychological well-being of women (Long et al., 2019). Mammographic screening conducts to overdiagnosis due to the tendency to detect cancers that are unlikely to be malignant and would not be clinically diagnosed in a lifetime, so over-treatment can lead to increased mortality due to the side effects of therapy (Houssami, 2017).

One of the main reasons that maintains high mortality rates in our country may be the insufficient and incomplete management of patients with breast cancer. After a woman receives a positive mammography result, possibly due to insufficient support from medical staff, she does not visit an oncologist and undergo further diagnostic procedures. Which in the future may lead to neglect of the disease (transition to later stages), ineffectiveness of treatment and an increase in mortality from breast cancer.

Other causes, such as death from cardiovascular diseases - coronary heart disease, acute coronary syndrome, as well as other chronic diseases and injuries, could affect the registration of deaths. This was confirmed in a population-based study in the United States, as heart disease was 10%, then cerebrovascular disease 2.4% and chronic obstructive pulmonary disease 2%, in addition to these causes – septicemia, Alzheimer's disease, suicide and other cancers became cause of death after one year of breast cancer diagnosis (Afifi et al., 2020).

The study of mortality trends from breast cancer has theoretical and practical significance: monitoring and evaluation of the effectiveness of early detection and treatment of the detected pathology. Health authorities should take into account the results obtained when organizing anti-cancer measures.

Author Contribution Statement

AT, ZhT, RT, YK – Collection and preparation of data, primary processing of the material and their verification.

DT, DB, DK, VD – Statistical processing and analysis of the material, writing the text of the article (material and methods, results). IK, NS, DK, GO, KR – Writing the text of the article (introduction, discussion). NI, ZK, ZB, GI – Concept, design and control of the research, approval of the final version of the article. All authors approved the final version of the manuscript.

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References

Afifi AM, Saad AM, Al-Husseini MJ, et al (2020). Causes of death after breast cancer diagnosis: A US population-based analysis. *Cancer*, **126**, 1559-67.

Ahmad O, Boschi-Pinto C, Lopez A, et al (2001). Age standardization of rates: a new who standard. GPE Discussion Paper Series: No.31 EIP/GPE/EBD World Health Organization.

Alagoz O, Lowry K, Kurian A, et al (2021). Impact of the COVID-19 Pandemic on Breast Cancer Mortality in the US: Estimates From Collaborative Simulation Modeling. *J Natl Cancer Inst*, **113**, 1484-94.

Alexandraki I, Mooradian A (2010). Barriers related to mammography use for breast cancer screening among minority women. *J Natl Med Assoc*, **102**, 206–18.

Avonne E Connor, Maneet K, Kate E Dibble, et al (2022). Racialized Economic Segregation and Breast Cancer Mortality among Women in Maryland. *Cancer Epidemiol Biomarkers Prev*, **31**, 413–21.

Azamjah N, Soltan-Zadeh Y, Zayeri F (2019). Global Trend of Breast Cancer Mortality Rate: A 25-Year Study. *Asian Pac J Cancer Prev*, **20**, 2015–20.

Bilyalova Z (2012). Environmental epidemiology of breast cancer in Kazakhstan. Dissertation for the degree of Doctor of Philosophy. *Asian Pac J Cancer Prev*, **13**, 2341-4.

Bilyalova Z, Igissinov N, Moore M, et al (2012). Epidemiological evaluation of breast cancer in ecological areas of Kazakhstan--association with pollution emissions. *Asian Pac J Cancer Prev*, **13**, 2341-4.

Braithwaite D, Demb J, Henderson L (2016). Optimal breast cancer screening strategies for older women: current perspectives. *Clin Interv Aging*, **11**, 111–25.

Bray F, Ferlay J, Soerjomataram I, et al (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin, **68**, 394–424.

Capri S, Russo A (2017). Cost of breast cancer based on real-world data: a cancer registry study in Italy. *BMC Health Serv Res*, **17**, 84.

Chokoev A, Akhunbaev S, Kudaibergenova I, et al (2022). Breast Cancer Incidence in Kyrgyzstan: Report of 15 Years of Cancer Registry. *Asian Pac J Cancer Prev*, **23**, 1603-10.

Coleman C (2017). Early Detection and Screening for Breast Cancer. *Semin Oncol Nurs*, **33**, 141–55.

De Marchi T, Pyl PT, Sjöström M, et al (2021). Proteogenomic Workflow Reveals Molecular Phenotypes Related to Breast Cancer Mammographic Appearance. *J Proteome Res*, **20**, 2983–3001.

Desantis C, Ma J, Goding Sauer A, et al (2017). Breast cancer statistics, 2017, racial disparity in mortality by state. *CA Cancer J Clin*, **67**, 439-48.

Dos Santos Silva I (1999). Cancer epidemiology: principles and methods. Lion, France: IARC, p 441.

Downing A, Prakash K, Gilthorpe M, et al (2017). Socioeconomic background in relation to stage at diagnosis, treatment and survival in women with breast cancer. *Br J Cancer*, **96**, 836–40.

Duffy S, Tabár L, Yen A, et al (2021). Beneficial Effect of Consecutive Screening Mammography Examinations on Mortality from Breast Cancer: A Prospective Study. *Radiology*, **299**, 541–7.

Duffy S, Tabár L, Yen A, et al (2020). Mammography screening reduces rates of advanced and fatal breast cancers: Results in 549,091 women. *Cancer*, **126**, 2971–9.

Duggan C, Trapani D, Ilbawi A, et al (2021). National health system characteristics, breast cancer stage at diagnosis, and breast cancer mortality: a population-based analysis. *Lancet Oncol*, **22**, 1632–42.

Ellis L, Woods L, Estève J, et al (2014). Cancer incidence, survival and mortality: explaining the concepts. *Int J Cancer*, **135**, 1774–82.

Ferlay J, Ervik M, Lam F, et al (2021). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer [cited 2021 Feb 25]. Available from: https://gco.iarc.fr/today.

Ferlay J, Laversanne M, Ervik M, et al (2021). Global Cancer Observatory: Cancer Tomorrow. Lyon, France: International Agency for Research on Cancer [cited 2021 Feb 25]. Available from: https://gco.iarc.fr/tomorrow.

Glanz S (1998). Biomedical statistics. Moscow: Practice, p 459.

Hashim D, Boffetta P, La Vecchia C, et al (2016). The global decrease in cancer mortality: trends and disparities. *Ann Oncol*, **27**, 926–33.

Hofvind S, Ponti A, Patnick J, et al (2012). False-positive results in mammographic screening for breast cancer in Europe: a literature review and survey of service screening programmes. *J Med Screen*, **19**, 57–66.

Houssami N (2017). Overdiagnosis of breast cancer in population screening: does it make breast screening worthless?. *Cancer Biol Med*, **14**, 1–8.

Huang Y, Yang L, Song F, Chen K (2017). Overdiagnosis in mammography screening for breast cancer. *Chin J Epidemiol*, **38**, 1574–8.

Igisinov S, Soodonbekov E, Igissinov 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 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.

Igissinov N, Toguzbayeva A, Telmanova Z, et al (2022). Evaluation of Breast Cancer Incidence Trends in the Karaganda Region of Kazakhstan. *Iran J Public Health*, **51**, 2308-16.

Igissinov N, Toguzbayeva A, Turdaliyeva B, et al (2019). Breast Cancer in Megapolises of Kazakhstan: Epidemiological Assessment of Incidence and Mortality. *Iran J Public Health*, **48**, 1257-64.

Iwamoto Y, Kaucher S, Lorenz E, et al (2019). Development of breast cancer mortality considering the implementation of mammography screening programs - a comparison of western European countries. *BMC Public Health*, **19**, 823.

Kim Y, Yoo K, Goodman M (2015). Differences in incidence, mortality and survival of breast cancer by regions and countries in Asia and contributing factors. *Asian Pac J Cancer Prev*, **16**, 2857–70.

Krueger P, Preston S (2008). Cohort fertility patterns and breast cancer mortality among U.S. women, 1948-2003. *Demographic Res*, **18**, 263-84.

Laamiri F, Hasswane N, Kerbach A, et al (2016). Risk factors associated with a breast cancer in a population of Moroccan women whose age is less than 40 years: a case control study. *Pan Afr Med J*, **24**, 19.

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.

Long H, Brooks JM, Harvie M, et al (2019). How do women experience a false-positive test result from breast screening? A systematic review and thematic synthesis of qualitative studies. *Br J Cancer*, **121**, 351–8.

Maroni R, Massat N, Parmar D, et al (2021). A case-control study to evaluate the impact of the breast screening programme on mortality in England. *Br J Cancer*, **124**, 736–43.

Merkov A, Polyakov L (1974). Health Statistics. Leningrad: Medicine, p 384.

Momenimovahed Z, Salehiniya H (2019). Epidemiological characteristics of and risk factors for breast cancer in the world. *Breast Cancer (Dove Medical Press)*, **11**, 151–64.

Monticciolo D, Malak S, Friedewald S, et al (2021). Breast Cancer Screening Recommendations Inclusive of All Women at Average Risk: Update from the ACR and Society of Breast Imaging. *J Am Coll Radiol*, **18**, 1280–8.

Mubarik S, Wang F, Fawad M, et al (2020). Trends and Projections in Breast Cancer Mortality among four Asian countries (1990-2017): Evidence from five Stochastic Mortality Models. *Sci Rep*, **10**, 5480.

Myers E, Moorman P, Gierisch J, et al (2015). Benefits and Harms of Breast Cancer Screening: A Systematic Review. *JAMA*, **314**, 1615–34.

Online Statistical Calculator. https://medstatistic.ru/calculators/averagestudent.html

Porter P (2008). "Westernizing" women's risks? Breast cancer in lower-income countries. *N Engl J Med*, **358**, 213-6.

Siu A , 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-Bindman R, Kerlikowske K, Gebretsadik T, Newman J (2000). Is screening mammography effective in elderly women?. *Am J Med*, **108**, 112–9.

Solikhah S, Promthet S, Hurst C (2019). Awareness Level about Breast Cancer Risk Factors, Barriers, Attitude and Breast Cancer Screening among Indonesian Women. *Asian Pac J Cancer Prev*, **20**, 877–84.

Sung H, Ferlay J, Siegel RL, et al (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*, **71**, 209–49.

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.

Tagliafico AS, Piana M, Schenone D, et al (2020). Overview of radiomics in breast cancer diagnosis and prognostication. *Breast J (Edinburgh, Scotland)*, **49**, 74–80.

The Law of the Republic of Kazakhstan No. 174/2020 of October 30, 2020 "Target groups subject to screening examinations, as well as the rules, scope and frequency of these examinations". https://adilet.zan.kz/rus/docs/V2000021572

The Law of the Republic of Kazakhstan No. 685 of November 10, 2009 "Rules for conducting preventive medical examinations of target population groups". https://adilet.zan.kz/rus/docs/V1400010199.

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.

Wang J, Lv H, Xue Z, et al (2018). Temporal Trends of Common Female Malignances on Breast, Cervical, and Ovarian Cancer Mortality in Japan, Republic of Korea, and Singapore: Application of the Age-Period-Cohort Model. *Biomed Res Int*, **2018**, 5307459.

Warner E, Tamimi R, Hughes M, et al (2015). Racial and Ethnic Differences in Breast Cancer Survival: Mediating Effect of Tumor Characteristics and Sociodemographic and Treatment Factors. *J Clin Oncol*, **33**, 2254–61.

Warner E, Zhu S, Plewes D, et al (2020). Breast Cancer Mortality among Women with a BRCA1 or BRCA2 Mutation in a Magnetic Resonance Imaging Plus Mammography Screening Program. *Cancers*, **12**, 3479.

Welch HG, Black WC (2010). Overdiagnosis in cancer. *J Natl Cancer Inst*, **102**, 605-13.

Wojtyla C, Bertuccio P, Wojtyla A, La Vecchia C (2021). European trends in breast cancer mortality, 1980-2017 and predictions to 2025. *Eur J Cancer*, **152**, 4–17.

Zheng M, Lennarth N, Håkan J (2020). Effectiveness of Population-Based Service Screening with Mammography for Women Aged 70–74 Years in Sweden. *Cancer Epidemiol Biomarkers Prev*, **29** , 2149–56.