RESEARCH ARTICLE

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Breast Cancer in Kazakhstan, 2004–2023: Successful Mortality Reduction Driven by Organized Screening and Stage Shift

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Abstract

Objective: To quantify two-decade national trends in the breast cancer burden in Kazakhstan and evaluate the performance of the organized mammography screening programme—including stage distribution and regional heterogeneity after its scale-up. **Methods:** We conducted a retrospective, population-based evaluation using national registry and screening data. Population indicators (incidence, mortality, years of potential life lost) were analysed for 2004–2023; screening performance (coverage, abnormal rate, cancer detection rate, positive predictive value, benign biopsy rate, number needed to screen, programme contribution) was assessed for 2010–2023. Trends were modelled with Joinpoint; staging followed TNM (I–II "early", III–IV "advanced"). **Results:** ASIR increased from 39.3 per 100,000 women in 2004 to 54.4 in 2023 (with a transient dip to 44.9 in 2020), whereas ASMR declined from 16.6 to 10.2 per 100,000 over the same interval; the mortality-to-incidence ratio decreased from 0.42 to 0.19. YPLL_75 fell from 175.1 per 100,000 in 2004 to a nadir of 76.0 in 2018, then measured 104.9 in 2023. The proportion diagnosed at stages I–II rose from 71.1% (2010) to 88.6% (2023), with corresponding declines in stage III (22.2% → 8.7%) and stage IV (6.8% → 5.1%). Following the expansion of eligibility to ages 40–70 (from 2018), screening throughput and coverage increased, but performance remained heterogeneous across regions, with variability in recall rates, detection yield, and downstream diagnostic pathways. **Conclusion:** Across 2004–2023, Kazakhstan experienced a favourable divergence between rising incidence and falling mortality, substantial reductions in premature mortality, and a marked shift toward earlier-stage diagnosis. These gains coincide with the maturation of the organised screening programme and broader system improvements. Consolidation will require targeted, region-specific quality-improvement bundles and resilience strategies to protect screening coverage and diagnostic capacity during system shocks.

Keywords: breast cancer - incidence - trends - geographical variation – Kazakhstan

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Introduction

Breast cancer is the most common malignancy among women worldwide and a leading cause of cancer mortality, with the fastest incidence growth occurring in low- and middle-income settings [1]. In Kazakhstan, breast cancer likewise represents the leading female cancer burden [2]. To promote earlier detection, a population-based, organised mammography programme was launched nationwide in 2008 and provided free of charge within the State Guaranteed Benefits Package. In its initial phase (2008–2017), the programme invited women aged 50-60 years (single-year cohorts at two-year intervals), reflecting prevailing evidence that the benefit–harm balance of mammographic screening is strongest from the early 50s in health systems with adequate diagnostic and treatment capacity [3]. This focus facilitated deliberate scale-up of infrastructure and workforce. By 2014, approximately 80% of mammography units had been digitised, improving image quality and enabling broader coverage [4].

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During the first decade, national cancer statistics indicated a favourable shift toward earlier stage at diagnosis [5] and a moderate decline in breast cancer mortality [6], suggesting that earlier detection paired with timely treatment was beginning to improve outcomes. On this basis, the Ministry of Health adopted Ministerial Order No. 995 (25 December 2017) to expand eligibility from 1 January 2018 to women aged 40–70 years, screened biennially [7]. The decision was guided by epidemiological analyses of breast cancer incidence in Kazakhstan, which revealed that a significant proportion of cases occurred in women younger than 60 [8-10]. Over the preceding 15 years, the incidence among women aged 45–49 years had risen sharply [11], yet these women were previously ineligible for screening. National cancer registry data show that incidence begins to increase noticeably by ages 40–44 and rises steeply by age 50, justifying the inclusion of women in their forties [8, 10]. Simultaneously, the upper age limit was extended to 70 years to capture a demographic with persistently high incidence and mortality: women aged 60–70 account for the highest age specific incidence [11], and the median age at death from breast cancer in Kazakhstan is 61 years [6]. Collectively, these data supported the need to screen the entire 40–70 year continuum, rather than delaying initiation until age 50.

In parallel, the government introduced additional measures to raise population coverage, aiming to reach 80–90% of eligible women by 2022 through improved outreach, mobile screening units, and strengthened primary care referral pathways [12].

International guidance converges on biennial mammography for middle-aged women, with nuances by system capacity. The WHO prioritises organised screening for 50–69 years where the health system can ensure quality [3]. The USPSTF (2024) recommendation [3] and ACS advise initiating organised screening at 40 years reflecting contemporary evidence on earlier onset and equity considerations [13]. The UK NHS continues triennial screening from 50 years, with evaluations of potential extensions underway [14]. In this context, Kazakhstan's 2018 expansion to 40–70 years preceded recent changes in some high-income country recommendations, while remaining consistent with the principle that programmes should be tailored to national disease burden and system readiness.

Despite this progress, critical evidence gaps remain. Few peer-reviewed evaluations have: a) quantified two-decade trends in incidence, mortality, and years of potential life lost; b) characterised stage distribution and stage-specific incidence over time; c) assessed programme performance metrics (coverage, abnormal rate, cancer detection rate, positive predictive value, benign biopsy rate, number needed to screen, and programme contribution) and their temporal trends; and d) mapped regional heterogeneity across Kazakhstan's 16 regions. Evidence from Central Asia and other post-Soviet settings is particularly sparse, limiting international comparability and policy learning.

Study aims. To characterise the population impact of Kazakhstan's organised breast-cancer screening, we quantified 2004–2023 trends in incidence, mortality and years of potential life lost, temporal shifts in stage at diagnosis and stage-specific incidence, and 2010–2023 programme performance using Joinpoint regression. Second, we mapped regional heterogeneity across all indicators and benchmarked programme metrics against international quality standards to identify actionable targets for quality improvement.

Materials and Methods

Study design and reporting

We conducted a retrospective, population-based evaluation of Kazakhstan's organised breast cancer screening programme and national cancer burden. The analytic window was 1 January 2010 – 31 December 2023 for screening performance and 2004–2023 for population incidence, mortality, stage, and years of potential life lost. Reporting follows STROBE for observational studies and the IARC framework for quality indicators in population screening programmes.

Setting and programme evolution

Kazakhstan comprises 14 oblasts and the cities of Astana and Almaty (hereafter "regions"). Digital mammography was introduced nationally in 2008.

• 2008–2017: Biennial invitations to six single-year cohorts (50, 52, 54, 56, 58, 60 years), so each eligible woman was screened once every two years.

• From 1 January 2018: Eligibility broadened to 40–70 years in 16 single-year cohorts (40, 42, …, 68, 70) on a biennial cycle.

Data sources

Bureau of National Statistics of the Agency for Strategic Planning and Reforms of the Republic of Kazakhstan – Annual, de-identified counts by region and year: women eligible, screened, mammography assessments (BI-RADS), and biopsy histology. And incident invasive breast cancer (ICD-10 C50) and ductal carcinoma in situ (D05), stage at diagnosis (TNM), deaths from breast cancer, and female population denominators by region and year [15].

Case definitions and variables

• Screen-detected cancer: Histologically proven C50 or D05 diagnosed following a positive screening episode within the organised programme.

• Benign breast lesion: Histology coded D24, N60–N60.9, N63.

• Abnormal finding rate: Screening mammogram assessed BI-RADS 3/4/5.

• Stage groups: TNM stages were harmonised into I, II, III, IV; unknown stage is reported separately. For "early-stage" we used I–II; for "advanced-stage", III–IV.

Outcomes and indicators

Population indicators (registry-based)

Incidence and mortality	Annual age-standardised rates (Age standardized incidence rate – ASIR / Age standardized mortality rate – ASMR per 100,000), directly standardised to the WHO world standard population (2000–2025) [16].
Mortality-to-incidence ratio (M/I)	ASMR ÷ ASIR
Case-fatality rate (%)	Deaths in year ÷ women living with breast cancer at year-end × 100.
Years of potential life lost (YPLL)	YPLL up to age 75: For each breast-cancer death, max (0,75−age at death); summed annually; rate per 100,000 women. YPLL for ages 20-59: Sum of max(0,60−age at death) for deaths aged 20–59; rate per 100,000 women.
Stage indicators	Annual stage distribution (I, II, III, IV, unknown) and stage-specific incidence rates (I–II combined; III; IV).

Programme performance indicators (screening-based)

Coverage (%)	Screened ÷ Eligible × 100 (In years with values >100%, this functions as an attendance ratio due to cycle overlap/ denominator estimation; retained as reported and flagged in interpretation.)
Abnormal finding rate (% recall)	Abnormal ÷ Screened × 100
Cancer detection rate (CDR)	Screen-detected cancers ÷ Screened × 1,000
Benign biopsy rate (BBR)	Benign lesions ÷ Screened × 1,000
Positive predictive value (PPV_1)	Screen-detected cancers ÷ Abnormal × 100 (cancers among recalled)
Number needed to screen (NNS)	Screened ÷ Screen-detected cancers
Programme share of national incidence (%)	Screen-detected cancers ÷ All incident cancers × 100

Statistical analysis

Descriptive results are reported as means ± standard deviation. Trends in incidence, mortality, stage-specific incidence rates, and programme indicators (coverage, CDR, PPV, BBR, NNS, programme share) were modelled with the Joinpoint Regression Program v5.1.0 using log-linear models. The Weighted Bayesian Information Criterion was used as the primary method (current developer-recommended default); Monte Carlo permutation test (overall α=0.05) was run as a sensitivity analysis [17, 18]. Where multiple APCs were jointly tested (e.g., multi-segment mortality), Bonferroni adjustment was applied in the permutation framework.

Ethics approval

The study was based exclusively on aggregated, depersonalized administrative data. No individual patient consent was required. The research protocol complies with all relevant standards for ethical publication and data use. Ethical approval was granted by the Local Ethics Commission of the Central Asian Institute for Medical Research.

Results

National incidence and mortality trends (2004–2023)

Over 2005–2024, the period-averaged annual crude and standardized incidence rates were respectively of 45.2±1.3 per 100,000 and 41.8±0.9 per 100,000. Incidence rose steadily across the entire period with no joinpoints and a significant APC of +1.9% per year (95% CI 1.5–2.4; p<0.001). Mortality showed one joinpoint in 2010 (location 95% CI 2006-2018): it was essentially stable in 2004-2010 (APC −0.3%; 95% CI −2.2 to 5.1; p=0.795), followed by a significant decline in 2010-2023 (APC −3.6% per year; 95% CI −5.9 to −3.0; p=0.001). Thus, while incidence increased throughout, mortality decreased meaningfully from 2010 onward (Figure 1).

Over the study period, the population increased from 7.75 million to 10.12 million, while the number of women registered with breast cancer at year-end rose from 18,528 to 48,496. The incidence rate increased from 39.3 to 54.4 per 100,000, with a transient decline to 44.9 per 100,000 in 2020. In contrast, the mortality rate decreased from 16.6 to 10.2 per 100,000, with absolute deaths falling from 1,284 to 1,036. Both severity proxies improved: the case-fatality rate declined from 6.93 to 2.14, and the mortality-to-incidence ratio fell from 0.42 to 0.19 (Table 1).

Over the study window there were 80,490 incident cases and 25,290 deaths. Age specific incidence rate was negligible below age 25 and then rose steeply from 14.3 per 100,000 at 30-34 to a peak of 161.9 per 100,000 at 65–69, before declining at older ages (e.g., 149.6 at 70–74, 128.7 at 75–79, 111.5 at 80–84, 84.2 at ≥85). The mean age at diagnostic was of 57.4±0.2 years. Age specific mortality rates increased monotonically with age, from 0.6 per 100,000 at 25-29 to a maximum of 72.3 per 100,000 at 80-84 (then 62.7 at ≥85). By counts, the modal incidence occurred at 50-54 years (11,452; 14.2%) and 55-59 years (11,889; 14.8%), while deaths were most frequent at 55-59 years (3,668; 14.5%). Overall, women ≥50 years accounted for ~71% of incident cases and ~80% of deaths (Table 2).

Over 2004–2023, Years of potential life lost (YPLL) for 20-59 ages declined from 7,248 years (271.4 per 100,000) to 5,255 years (159.4 per 100,000), a 41% reduction in the rate; YPLL for ≤75 years fell from 20,318 (175.1 per 100,000) to 15,553 (104.9 per 100,000), a 40% reduction. Both series reached their lowest rates in 2018 (154.3 and 76.0 per 100,000, respectively), followed by a transient rise in 2019–2021 and partial re-convergence by 2023 (Table 3).

Regional age-standardized incidence and mortality

Age-standardized incidence rates varied more than

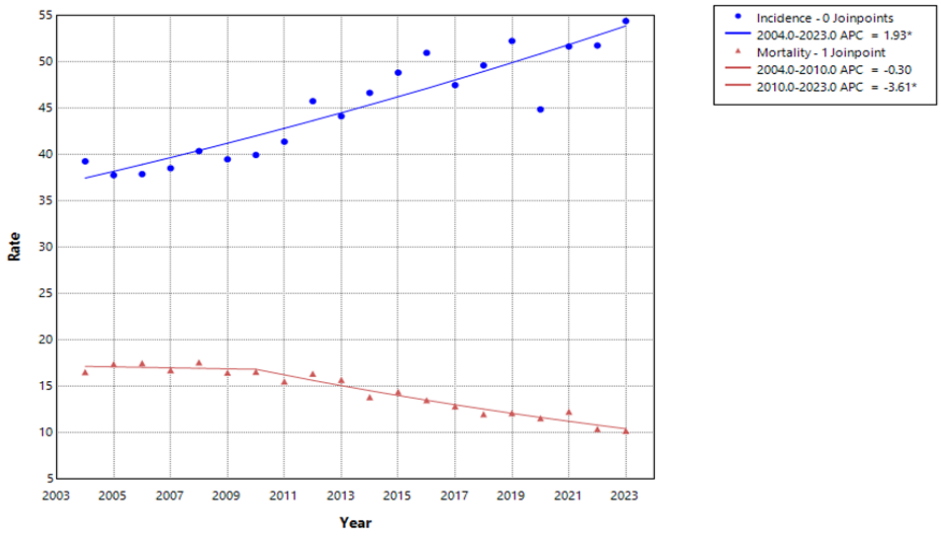

Figure 1. Trends in Breast-Cancer Incidence and Mortality, Kazakhstan, 2004–2023

proportion of stage I-II rose from 71.1% in 2010 to 88.6% in 2023 (+17.5 percentage points), exceeding 85% in every year from 2018 onward. Over the same period, stage III fell from 22.2% to 8.7% (−13.5 pp), and stage IV declined from 6.8% to 5.1% (−1.7 pp). Taken together, the share of advanced disease (III-IV) decreased from 29.0% in 2010 to 13.8% in 2023 – approximately a 52% relative reduction.

A short, pandemic-era perturbation was evident in 2020-2021, when the early-stage share dipped to 86.9% and 84.9%, with a temporary rise in stage IV to 5.0%, followed by recovery to the highest early-stage proportion by 2023 (88.6%). The fraction of unspecified stage remained very low throughout (≤1% in most years; isolated peaks of 1.34% in 2016 and 0.77% in 2021).

Trends in breast cancer incidence by stage and region (Table 5)

Across the study period, Kazakhstan exhibited a sustained stage shift toward earlier disease at diagnosis. The stage specific incidence rate of stage I–II cancer averaged 34.8 per 100,000 and increased significantly

Table 1. National Burden and Outcome Indicators for Breast Cancer, Kazakhstan, 2004–2023

Year	Female population (mid-year)	Prevalent cases at year-end	Incidence		Mortality		Case fatality rate	Mortality-to-incidence ratio
			Incident cases	ASIR* per 100,000 women	Deaths	ASMR** per 100,000 women		
2004	7752206	18528	3045	39.3	1284	16.6	6.93	0.42
2005	7817843	19276	2954	37.8	1362	17.4	7.07	0.46
2006	7894511	20468	2992	37.9	1384	17.5	6.76	0.46
2007	7987594	21623	3078	38.5	1340	16.8	6.2	0.44
2008	8079952	22965	3263	40.4	1423	17.6	6.2	0.44
2009	8283495	24276	3272	39.5	1368	16.5	5.64	0.42
2010	8395313	25522	3355	40	1394	16.6	5.46	0.42
2011	8515509	26639	3525	41.4	1324	15.5	4.97	0.38
2012	8632164	27137	3951	45.8	1415	16.4	5.21	0.36
2013	8751344	28277	3863	44.1	1376	15.7	4.87	0.36
2014	8876242	29796	4142	46.7	1230	13.9	4.13	0.3
2015	9002614	31352	4397	48.8	1299	14.4	4.14	0.3
2016	9128096	33053	4653	51	1235	13.5	3.74	0.27
2017	9249736	34877	4393	47.5	1191	12.9	3.41	0.27
2018	9366039	36817	4648	49.6	1126	12	3.06	0.24
2019	9482371	39648	4955	52.3	1152	12.1	2.91	0.23
2020	9597645	41350	4307	44.9	1114	11.6	2.69	0.26
2021	9719010	43187	5021	51.7	1196	12.3	2.77	0.24
2022	9989375	45728	5171	51.8	1041	10.4	2.28	0.2
2023	10119106	48496	5505	54.4	1036	10.2	2.14	0.19

*ASIR, Age standardized incidence rate; **ASMR, Age standardized mortality rate

Table 2. Age-Specific Distribution of Breast-Cancer Incidence and Mortality in Kazakhstan, Cumulative 2004–2023. Incidence and mortality are shown as counts (percentage of all cases/deaths) and rates per 100,000 (±SE)

Age group (Years)	Incidence			Mortality		
	No. of cases	Percentage (%)	Age-specific rate per 100,000 (±SE)	No. of deaths	Percentage (%)	Age-specific rate per 100,000 (±SE)
0-4	0	0	0.0±0.0	0	0	0.0±0.0
5-9	0	0	0.0±0.0	0	0	0.0±0.0
10-14	0	0	0.0±0.0	1	0	0.0±0.0
15-19	21	0	0.1±0.1	1	0	0.0±0.0
20-24	119	0.1	0.8±0.2	10	0	0.1±0.0
25-29	540	0.7	3.8±0.3	82	0.3	0.6±0.1
30-34	1959	2.4	14.3±0.5	335	1.3	2.5±0.3
35-39	3857	4.8	31.1±0.9	753	3	6.2±0.4
40-44	6924	8.6	59.1±1.9	1451	5.7	12.5±0.8
45-49	9741	12.1	86.8±1.5	2453	9.7	21.9±1.4
50-54	11452	14.2	110.9±2.9	3364	13.3	33.3±1.9
55-59	11889	14.8	133.2±3.3	3668	14.5	43.4±2.9
60-64	10993	13.7	152.7±6.0	3356	13.3	51.0±2.9
65-69	9404	11.7	161.9±9.0	3081	12.2	55.2±2.3
70-74	6378	7.9	149.6±5.2	2778	11	67.6±4.2
75-79	4031	5	128.7±6.2	1917	7.6	62.7±4.1
80-84	2243	2.8	111.5±3.3	1377	5.4	72.3±6.0
≥ 85	939	1.2	84.2±3.8	663	2.6	62.7±4.4
Total	80490	100	-	25290	100	-

two-fold across regions, from 29.6 per 100,000 in Zhambyl to 57.7 per 100 000 in Almaty City and Astana City. In Joinpoint models, most regions showed monotonic increases with APC ≈ +1.0% to +1.7% per year. Atyrau recorded the steepest rise (+3.1%/year; p<0.001). Two territories exhibited biphasic trends: Zhambyl increased to 2017 (+2.0%/year; p=0.001) then declined thereafter (−3.2%/year; p=0.026), while Almaty City rose through 2016 (+2.4%/year; p=0.018) followed by non-significant downturn (−3.1%/year; 2016–2023; p=0.051). Mangystau showed a non-significant increase (+1.3%/year; p=0.174), and Akmola shifted from an early, short decrease (2004–2006) to a non-significant rise thereafter (Table 4).

Table 3. Years of Potential Life Lost from Breast Cancer, Kazakhstan, 2004–2023: total YPLL (years) and YPLL rates (per 100,000) for ages 20-59 and up to age 75.

Year	For ages 20-59		Up to 75 years old	
	Years	Per 100,000	Years	Per 100,000
2004	7248	271.4	20318	175.1
2005	7030	272.4	20550	165.6
2006	7625	279.7	21288	175.3
2007	6905	258.6	19933	155.2
2008	6760	265.1	20668	149.3
2009	6883	260.8	20920	147.5
2010	7065	257.6	20950	148.7
2011	6243	233.4	19255	129.3
2012	7105	253	21133	145.1
2013	6460	238.1	20130	130.5
2014	6003	218.7	18718	120.1
2015	6213	221.9	19233	123.4
2016	4088	170.7	14978	80.8
2017	3938	161.7	14370	77.6
2018	3855	154.3	13885	76
2019	5205	184.1	16803	102.9
2020	5560	180.8	16733	110.3
2021	5433	180.9	16978	108.2
2022	4780	154.5	14903	95.3
2023	5255	159.4	15553	104.9

Age-standardized mortality rates ranged from 10.5 (South Kazakhstan) to 18.5 (Almaty City) per 100,000, with widespread and significant declines over time. Continuous, single-segment decreases were observed in the majority of regions. Several areas showed marked post-joinpoint accelerations in mortality decline: Atyrau shifted from +3.7%/year (2004–2015) to −10.7%/year (2015–2023; p<0.001); Zhambyl moved from a flat trend to −6.6%/year (2013–2023; p<0.001); Akmola from stable to −6.4%/year (2012–2023; p=0.002); and Astana City from +1.7%/year (to 2016) to −6.9%/year (2016-2023; p=0.044). Karaganda experienced one of the sharpest sustained declines (−5.6%/year; p<0.001) (Table 4).

The M/I ratio clustered around 0.3–0.4 in most regions, with a higher value in Zhambyl (0.5), consistent with the lower incidence and historically higher fatality there.

Trend of breast cancer cases according to the extension stage

The stage profile of newly diagnosed breast cancers shifted steadily toward earlier disease (Figure 2). The

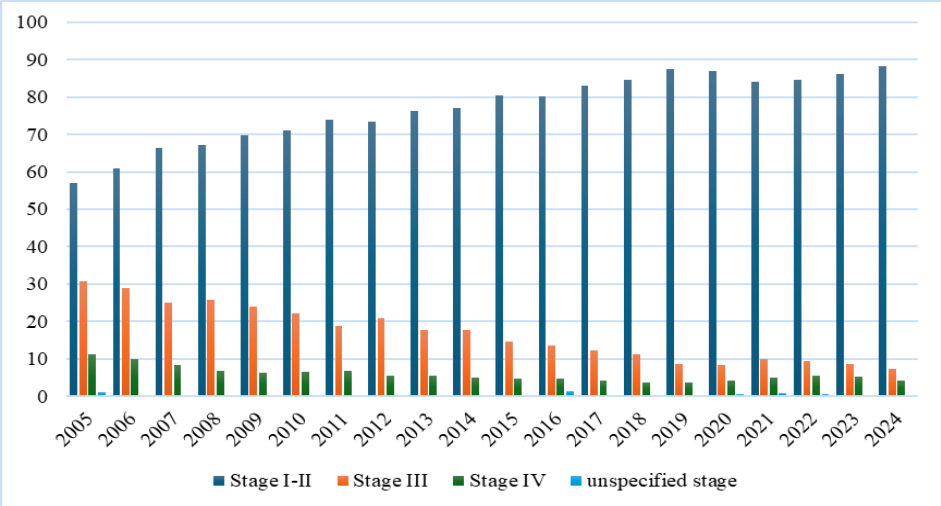

Figure 2. Dynamics of Indicators of Early Diagnosis (stage I–II) and Neglect (stage III and IV) of Breast Cancer in Kazakhstan

(APC=+3.8%/year; 95% CI 3.1-4.6; p<0.001). In contrast, stage III declined from a mean 6.1 per 100,000 with APC=−5.6%/year (95% CI −6.3 to −4.9; p<0.001), and stage IV fell more modestly (mean 2.3 per 100,000; APC=−2.4%/year; 95% CI −3.9 to −0.9; p<0.001).

Marked heterogeneity was observed across oblasts. For stage I–II, long-run stage-specific incidence rates were highest in Pavlodar (54.8), North Kazakhstan (52.7) and Almaty City (51.8), and lowest in Mangystau (18.4), South Kazakhstan (19.7) and Kyzylorda (22.1). Stage III was highest in Akmola (13.4) and Kostanay (10.0), and lowest in Atyrau (0.9), Kyzylorda (2.0) and South Kazakhstan (2.3). For stage IV, the highest means occurred in Karaganda (4.3) and Kostanay (3.6), whereas Zhambyl and South Kazakhstan were lowest (each 1.3). These differences – roughly three-fold for stage I-II and four-fold for stage III – underscore wide variation in diagnostic pathways and case-mix between regions.

Regional trends

• Stage I-II rose significantly in every region, with APCs ranging from +1.9%/year in Almaty City to +5.8%/year in Mangystau (all p≤0.01). Historically lower-incidence areas such as Kyzylorda (+5.0%), Aktobe (+5.5%) and Mangystau (+5.8%) posted steep gains, indicating substantial improvements in early detection.

• Stage III declined widely and steeply. Notable decreases included Atyrau (−12.4%/year), Kyzylorda (−10.3%), Mangystau (−9.3%), Astana City (−8.4%), Zhambyl (−8.4%) and Pavlodar (−8.3%) (all p<0.001). Kostanay was the principal exception (APC +0.5%/year, p=0.62). East Kazakhstan showed a biphasic pattern – an initial uptick to 2011 followed by a sharp decline (−9%/year thereafter; p<0.001).

• Stage IV generally moved downward, with significant decreases in Zhambyl (−7.8%/year), Pavlodar (−5.0%), West Kazakhstan (−5.0%), Kostanay (−4.3%), Astana City (−4.1%/year), (all p≤0.015). Akmola showed a non-significant increase (+3.3%/year; p=0.074). East and North Kazakhstan exhibited post-joinpoint upturns in stage IV in recent years, warranting close surveillance of late-stage presentations.

National screening coverage (2010–2023)

National annual coverage of the eligible female population is presented in Figure 3. Between 2010 and

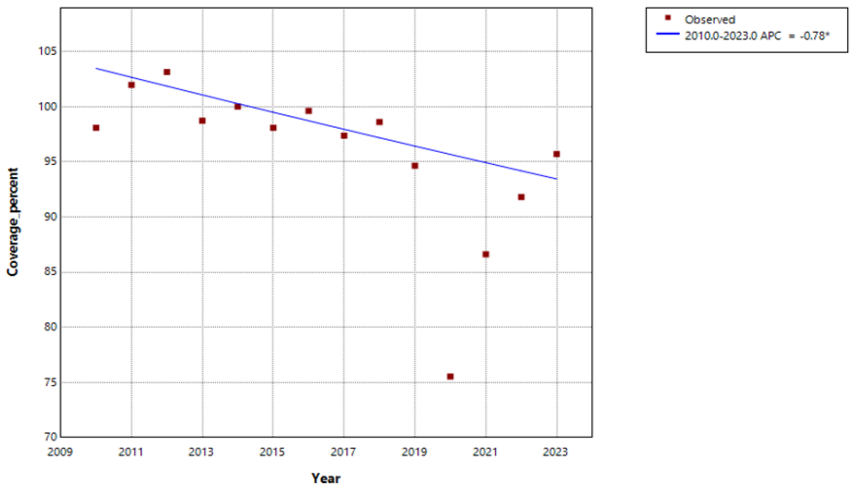

Figure 3. Temporal Trends in National Breast Cancer Screening Coverage in Kazakhstan, 2010–2023.

Table 4. Age-Standardized Incidence, Mortality, and Mortality-to-Incidence Ratio for Breast Cancer by Region, Kazakhstan, 2004–2023

No	Region	ASIR*				ASMR**				M/I******
		per 100,000	APC***, %	CI 95%****	p*****	per 100,000	APC***, %	CI 95%****	p*****	
1	Zhambyl	29.6±0.8	2004-2017=+2.0	[1.0; 5.6]	0.001	13.5±0.7	2004-2013=+2.3	[−0.7; 9.9]	0.117	0.5
			2017-2023=−3.2	[−11.4; −0.3]	0.026		2013-2023=−6.6	[−13.1; −4.1]	< 0.001	
2	South-Kazakhstan	29.7±0.9	2004-2023=+1.5	[0.5; 2.6]	0.002	10.5±0.4	2004-2023=−1.7	[−3.0; −0.4]	0.014	0.4
3	Kyzylorda	29.9±0.9	2004-2023=+1.5	[0.6; 2.6]	0.001	10.8±0.6	2004-2023=−2.4	[−4.3; −0.5]	0.013	0.4
4	Mangystau	32.5±1.7	2004-2023=+1.3	[−0.6; 3.8]	0.174	11.3±1.0	2004-2023=−4.2	[−6.2; −2.1]	< 0.001	0.3
5	Almaty	32.9±1.2	2004-2023=+1.4	[0.4; 2.6]	0.014	10.9±0.5	2004-2023=−2.9	[−3.8; −2.0]	< 0.001	0.3
6	Atyrau	33.0±1.7	2004-2023=+3.1	[1.8; 4.8]	< 0.001	12.0±0.7	2004-2015=+3.7	[0.8; 9.0]	0.017	0.4
							2015-2023=−10.7	[−18.7; −6.8]	< 0.001	
7	Aktobe	38.2±1.4	2004-2023=+1.6	[0.4; 3.0]	0.01	12.3±0.9	2004-2023=−4.7	[−6.7; −2.9]	< 0.001	0.3
8	Akmola	41.3±1.2	2004-2006=−13.2	[−21.1; 1.9]	0.174	13.7±0.8	2004-2012=−0.3	[−3.0; 9.1]	0.991	0.3
			2006-2023=+1.7	[-11.1; 9.5]	0.08		2012-2023=−6.4	[−13.8; −4.6]	0.002	
9	West-Kazakhstan	41.7±1.4	2004-2023=+1.5	[0.5; 2.5]	0.005	13.0±0.8	2004-2023=−4.1	[−5.0; −3.4]	< 0.001	0.3
10	Kostanay	42.5±1.5	2004-2023=+1.6	[0.7; 2.6]	0.001	12.5±0.8	2004-2023=−4.2	[−5.4; −3.1]	< 0.001	0.3
11	East-Kazakhstan	45.3±1.2	2004-2023=+1.5	[0.7; 2.4]	< 0.001	14.3±0.8	2004-2023=−3.2	[−4.4; −2.2]	< 0.001	0.3
12	North-Kazakhstan	45.5±1.4	2004-2023=+1.6	[0.7; 2.6]	0.001	12.9±0.9	2004-2023=−3.7	[−5.6; −2.1]	< 0.001	0.3
13	Karaganda	48.3±1.4	2004-2023=+1.7	[0.8; 2.7]	< 0.001	13.4±1.1	2004-2023=−5.6	[−6.6; −4.8]	< 0.001	0.3
14	Pavlodar	52.2±1.4	2004-2023=+1.0	[0.0; 2.1]	0.046	16.6±1.0	2004-2023=−3.6	[−5.1; −2.3]	< 0.001	0.3
15	Almaty city	57.7±1.8	2004-2016=+2.4	[0.8; 12.5]	0.018	18.5±0.9	2004-2023=−3.1	[−4.3; −2.0]	< 0.001	0.3
			2016-2023=−3.1	[−14.0; 0.0]	0.051					
16	Astana city	57.7±2.0	2004-2023=+1.3	[0.2; 2.7]	0.021	16.5±0.9	2004-2016=+1.7	[−2.5; 44.3]	0.252	0.3
							2016-2023=−6.9	[−36.0; −0.3]	0.044	

*ASIR, Age standardized incidence rate; **ASMR, Age standardized mortality rate; ***APC, Annual percentage change; ****CI, Confidence interval; *****p, level of significance; ****** M/I, mortality-to-incidence ratio.

Table 5. Trends of Breast Cancer Incidence by Stage and Region, 2004-2023

No	Region	Stage I-II				Stage III				Stage IV			
		per 100,000	APC*, %	CI 95%**	p***	per 100,000	APC*, %	CI 95%**	p***	per 100,000	APC*, %	CI 95%**	p***
1	Akmola	34.2±2.4	2004-2023=+4.5	[3.0; 6.4]	< 0.001	13.4±1.2	2004-2023=−3.6	[−6.3; −1.3]	0.004	2.9±0.4	2004-2023=+3.3	[−0.4; 7.8]	0.074
2	Aktobe	28.0±2.4	2004-2023=+5.5	[3.8; 7.9]	< 0.001	7.1±0.6	2004-2023=−5.9	[−8.2; −3.9]	< 0.001	2.1±0.1	2004-2023=−3.9	[−6.8; −1.2]	0.005
3	Almaty	25.2±1.5	2004-2023=+3.9	[2.9; 5.3]	< 0.001	5.4±0.4	2004-2023=−3.8	[−6.2; −1.5]	0.002	2.0±0.1	2004-2023=+0.03	[−2.0; 2.3]	0.928
4	Atyrau	27.2±1.9	2004-2023=+4.6	[3.2; 6.7]	< 0.001	0.9±0.2	2004-2023=−12.4	[−18.7; −8.3]	< 0.001	1.9±0.2	2004-2023=+4.6	[−2.2; 8.1]	< 0.001
5	East-Kazakhstan	46.8±2.7	2004-2023=+4.1	[3.2; 5.0]	< 0.001	9.0±0.9	2004-2011=+4.6	[0.6; 11.3]	0.028	2.9±0.3	2004-2017=−8.1	[−24.8; −3.8]	0.002
							2011-2023=−9.0	[−12.3; −7.1]	< 0.001		2017-2023=+21.6	[3.8; 91.4]	0.008
6	Zhambyl	22.4±1.6	2004-2023=+4.3	[2.0; 7.2]	< 0.001	3.1±0.5	2004-2023=−8.4	[−11.4; −6.5]	< 0.001	1.3±0.1	2004-2023=−7.8	[−12.0; −4.8]	< 0.001
7	West-Kazakhstan	40.4±2.6	2004-2023=+4.1	[2.7; 5.8]	< 0.001	4.4±0.5	2004-2023=−7.4	[−10.1; −5.6]	< 0.001	1.5±0.3	2004-2023=−5.0	[−10.0; −1.1]	0.015
8	Karaganda	46.0±2.7	2004-2023=+4.2	[3.4; 5.2]	< 0.001	9.6±0.7	2004-2023=−2.3	[−4.1; −0.6]	0.007	4.3±0.2	2004-2023=−1.8	[−3.1; −0.6]	0.003
9	Kostanay	42.6±2.5	2004-2023=+3.8	[2.8; 4.9]	< 0.001	10.0±0.5	2004-2023=+0.5	[−1.4; 2.3]	0.615	3.6±0.3	2004-2023=−4.3	[−7.9; −1.5]	0.007
10	Kyzylorda	22.1±1.6	2004-2023=+5.0	[4.0; 6.4]	< 0.001	2.0±0.4	2004-2023=−10.3	[−15.5; −7.3]	< 0.001	1.6±0.2	2004-2023=−2.4	[−6.2; 1.2]	0.172
11	Mangystau	18.4±2.1	2004-2023=+5.8	[2.6; 11.3]	0.002	4.7±0.6	2004-2023=−9.3	[−12.9; −6.6]	< 0.001	1.9±0.2	2004-2023=−2.2	[−5.6; 1.9]	0.291
12	Pavlodar	54.8±3.5	2004-2023=+4.4	[3.2; 5.9]	< 0.001	7.4±1.1	2004-2023=−8.3	[−10.5; −6.8]	< 0.001	2.5±0.3	2004-2023=−5.0	[−8.0; −2.6]	< 0.001
13	North-Kazakhstan	52.7±3.4	2004-2023=+4.5	[3.4; 5.9]	< 0.001	8.6±1.0	2004-2023=−4.9	[−7.2; −3.0]	< 0.001	2.0±0.4	2004-2010=−17.7	[−44.6; −4.4]	0.008
											2010-2023=+12.6	[7.0; 26.7]	< 0.001
14	South-Kazakhstan	19.7±1.1	2004-2023=+3.6	[2.5; 5.1]	< 0.001	2.3±0.2	2004-2023=−4.7	[−7.5; −2.2]	< 0.001	1.3±0.1	2004-2023=−1.9	[−4.7; 1.0]	0.206
15	Almaty city	51.8±2.2	2004-2023=+1.9	[0.8; 3.3]	0.002	7.3±0.9	2004-2023=−7.9	[−9.7; −6.5]	< 0.001	2.8±0.3	2004-2023=−3.1	[−6.2; 0.0]	0.052
16	Astana city	39.4±2.6	2004-2023=+4.3	[3.1; 6.2]	< 0.001	6.3±0.7	2004-2023=−8.4	[−11.4; −5.7]	< 0.001	2.5±0.2	2004-2023=−4.1	[−6.4; −1.7]	< 0.001
17	Kazakhstan	34.8±1.8	2004-2023=+3.8	[3.1; 4.6]	< 0.001	6.1±0.5	2004-2023=−5.6	[−6.3; −4.9]	< 0.001	2.3±0.1	2004-2023=−2.4	[−3.9; −0.9]	< 0.001

*APC, Annual percentage change; **CI, Confidence interval; ***p, level of significance

2023, mean coverage was 95.7%±7.2% (median 98.1%). During the first decade (2010–2018) coverage hovered at or above 98%, culminating in a peak of 103.2% in 2012 – a level attainable only when women outside the nominal target age also attend examinations. In 2018 the eligible cohort was almost doubled by the Ministry of Health (from 0.43 million to 0.76 million women), yet coverage remained robust at 98.6%, testifying to the programme's capacity to absorb a sudden expansion.

The next three years brought a clear inflection: coverage fell to 94.7% in 2019 and was most severely disrupted in the first pandemic year (75.5% in 2020). Recovery was steady but incomplete – 95.7% by 2023, close to pre-pandemic levels but still below the early-period plateau. Over the full period the Joinpoint model identified no joinpoints and a significant negative trend, with APC=−0.8% per year (95% CI −1.5 to −0.6; p<0.001).

Screen-detected findings and programme performance

Across all rounds the programme screened 8,177,992 women and recorded 1,557,292 abnormal mammograms, equivalent to one referral for every five examinations. Benign breast lesions dominated the caseload (99.1%), while 14,460 cancers were confirmed histologically (benign:malignant ≈ 107:1). Five widely used quality indicators are summarised in Table 6; their long-term movements are briefed below.

• Cancer detection rate. CDR almost doubled – from 0.95 per 1,000 in 2011 to 2.35 per 1,000 in 2023 – with a significant upward slope (APC +3.97% yr^{-1}; 95% CI +1.1 to +7.0; p=0.011).

• Positive predictive value. Despite rising CDR, PPV remained low, fluctuating around 1% and showing no material trend (APC −2.29% yr^{-1}; 95% CI −6.0 to +1.5; p=0.212).

• Benign biopsy rate. BBR climbed steeply in 2010–2017 (APC +15.86% yr^{-1}; 95% CI +4.9 to +28.0; p=0.009), reaching 256 per 1,000 in 2016, then receded (APC −4.22% yr^{-1}; 95% CI −15.6 to +8.7; p=0.046), but still averaged 189 per 1,000 over the study period.

• Number needed to screen. NNS decreased significantly (APC −3.81% yr^{-1}; 95% CI −6.5 to −1.0; p=0.012), improving efficiency but still remaining relatively high (425 in 2023).

• Programme share of national incidence. Screen detection contributed a mean 44% of all breast-cancer diagnoses, but the share oscillated widely, bottoming at 32.9% in 2020 and peaking at 63.4% in 2010; the temporal slope was non-significant (APC −1.14% yr^{-1}; 95% CI −3.8 to +1.6; p=0.378).

Regional heterogeneity (cumulative 2010 – 2023)

Figures 4-7 dissect the same performance metrics across Kazakhstan's 16 regions.

As shown in Figure 4, regional coverage rates ranged from 78.8% in Kostanay to 98.9% in South Kazakhstan, with a national mean of 93.7%. The proportion of women referred for further assessment varied six fold, from 5.8% in Akmola to 34.7% in Almaty City, despite comparable coverage levels in most regions.

This heterogeneity translated into equally wide gaps in outcomes. Cancer detection (Figure 5A) exceeded 2.0 per 1,000 in North Kazakhstan, Karaganda, West Kazakhstan, Atyrau, and Akmola, whereas Zhambyl and Almaty Region achieved <1.2 per 1,000. The diagnostic burden differed even more: Almaty City and South Kazakhstan undertook > 300 benign biopsies per 1,000 screens (Figure 5B), versus <100 per 1,000 in Zhambyl, Aktobe and Akmola.

Across regions, positive predictive value (Figure 6A) ranged five fold, from 0.54% (South Kazakhstan) to 2.57% (Akmola), with most regions falling below 1.5%, indicating substantial variability in the efficiency

Table 6. Key Screening Performance Metrics for the Kazakh National Breast Cancer Programme (2010–2023)

Year	Positive predictive value (PPV) (%)	Cancer detection rate (CDR) (per 1,000)	Benign biopsy rate (BBR) (per 1,000)	Number needed to screen (NNS)	Programme share of national incidence (%)
2010	1.37	1.62	117.01	616	63.38
2011	1.06	0.95	87.98	1056	37.19
2012	1.05	1.13	106.51	884	40.15
2013	1.16	1.4	118.91	716	42.37
2014	1.41	1.65	115.1	605	48.26
2015	0.71	1.67	234.93	599	49.14
2016	0.82	2.13	256.48	469	50.3
2017	0.77	1.94	250.01	515	57.38
2018	0.88	2.01	226.87	498	42.77
2019	1.06	2.01	187.49	497	46.01
2020	0.71	1.44	200.58	695	32.89
2021	0.74	1.76	234.82	569	36.31
2022	0.71	1.83	256.33	547	38.22
2023	1.51	2.35	153.2	425	53.11
Over the period	0.93	1.77	188.66	566	44.01

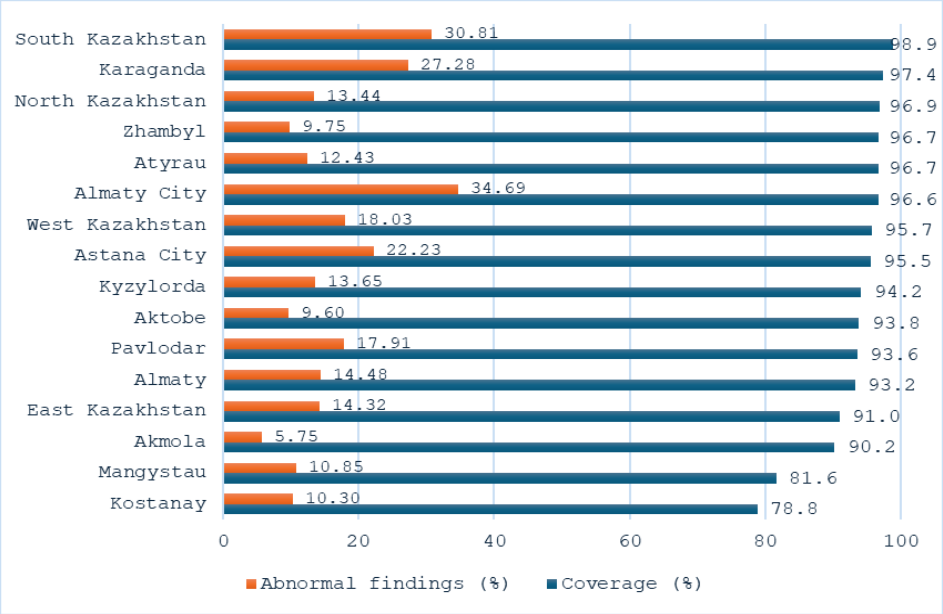

Figure 4. Screening Coverage and Abnormal Finding Rate by Region, Cumulative 2010–2023.

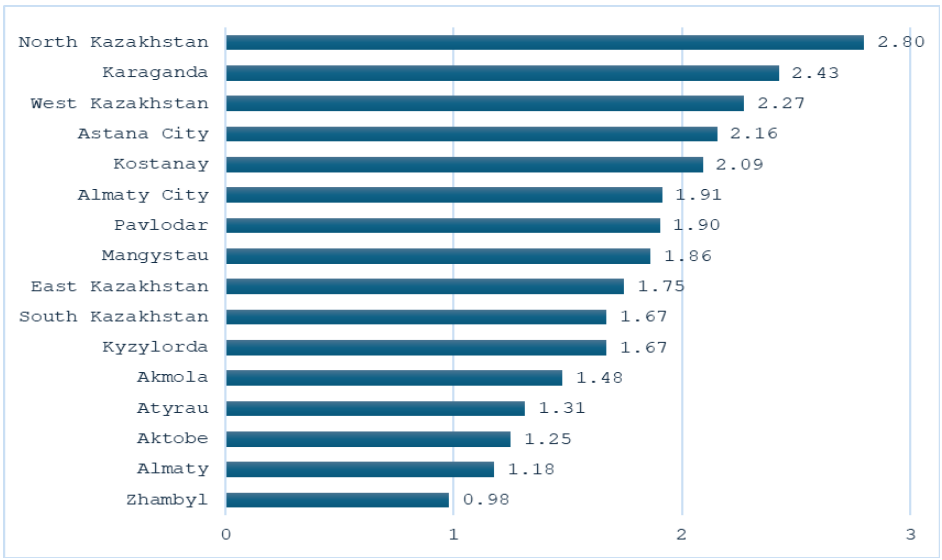

Figure 5A. Breast Cancer Detection Rate (per 1,000 Women Screened) by Region in Kazakhstan, Cumulative 2010-2023.

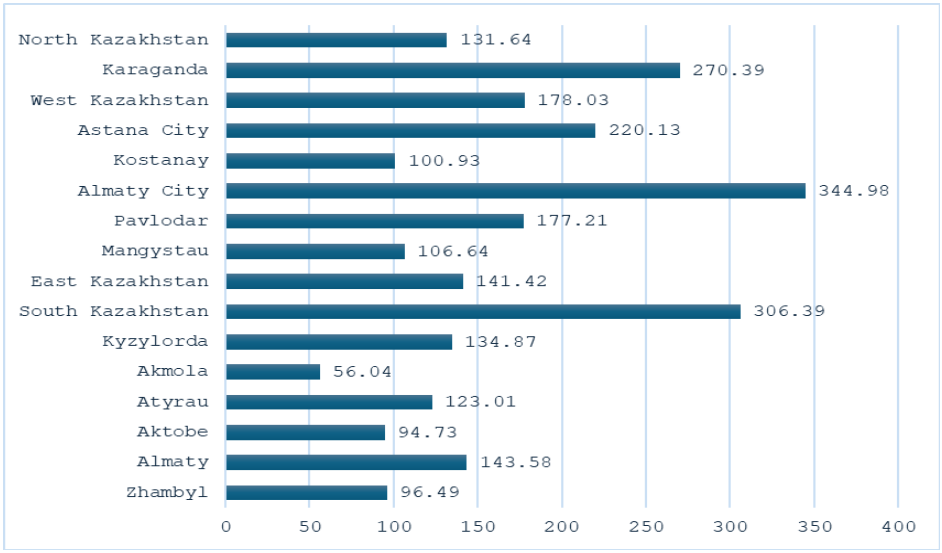

Figure 5B. Benign Biopsy Rate (per 1,000 Women Screened) by Region in Kazakhstan, Cumulative 2010-2023.

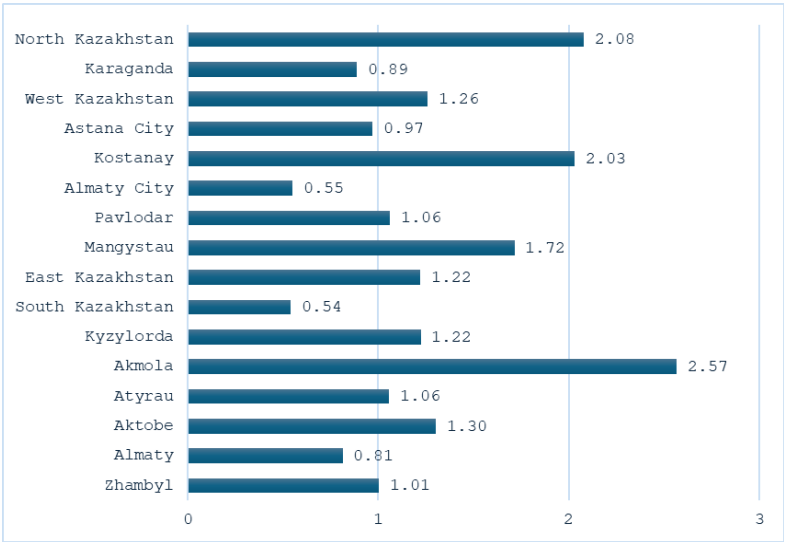

Figure 6A. Regional Variation in Positive Predictive Value for Screen-Detected Breast Cancer, 2010–2023. *Regions are ordered by CDR (as in Figure 3) to facilitate cross-metric comparison

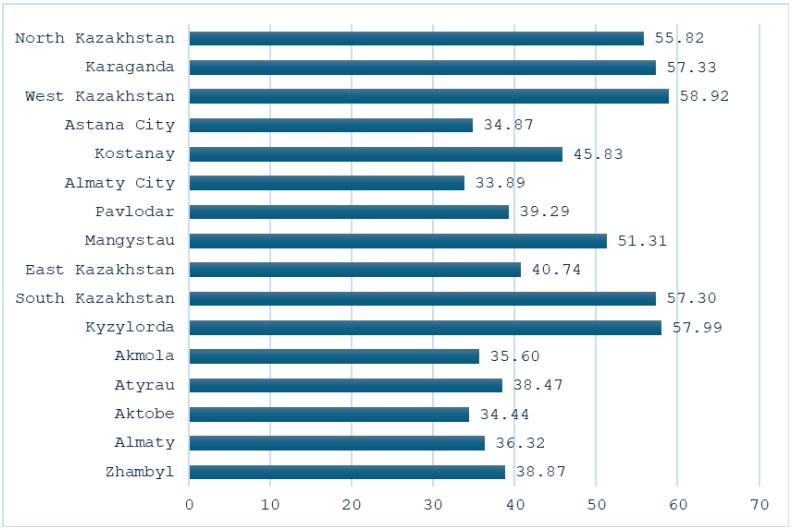

Figure 6B. Regional Contribution of Screening to National Breast Cancer Incidence, 2010-2023. *Regions are ordered by CDR (as in Figure 4) to facilitate cross-metric comparison

of referral pathways.

The proportion of all breast cancer cases nationally identified through screening (Figure 6B) varied between 33.9% (Almaty City) and 58.9% (West Kazakhstan), reflecting both programme penetration and underlying regional incidence.

The number needed to screen to detect one cancer (Figure 7) ranged from 357 (North Kazakhstan) to 1,021 (Zhambyl), with a national median of 523. Regions with low NNS (<500), such as North Kazakhstan, Karaganda, and West Kazakhstan, combined high CDR with moderate BBR, suggesting more balanced performance.

Discussion

Across 2004-2023, Kazakhstan shows the characteristic "incidence-up/mortality-down" trajectory seen when early detection and treatment expand. Age-standardised incidence rose steadily (APC +1.9%/year), while mortality declined significantly after 2010 (APC −3.6%/year), with corresponding reductions in the case-fatality ratio and mortality-to-incidence. These divergent slopes imply earlier diagnosis and improved survivorship rather than a true fall in disease occurrence – consistent with global experience in organised programmes [19, 20]. The burden in YPLL also contracted meaningfully: among women ≤75 years and among those aged 20-59, YPLL fell by 46% and 41%, respectively, underscoring gains in survival at working ages. Together, the population indicators point to real outcome improvement despite rising case ascertainment.

Age-specific incidence was negligible before 25 years, rose sharply from the early 40s, and peaked at 65-69 years (162 per 100,000); mortality increased monotonically with a maximum at 80-84 years. By counts, the modal burden clustered in 50–59 years, with ≥50 years accounting for most incident cases and deaths. These distributions support the logic of the 2018 expansion to ages 40-70: the policy now spans the steeply rising risk segment and captures most of the population burden while still permitting

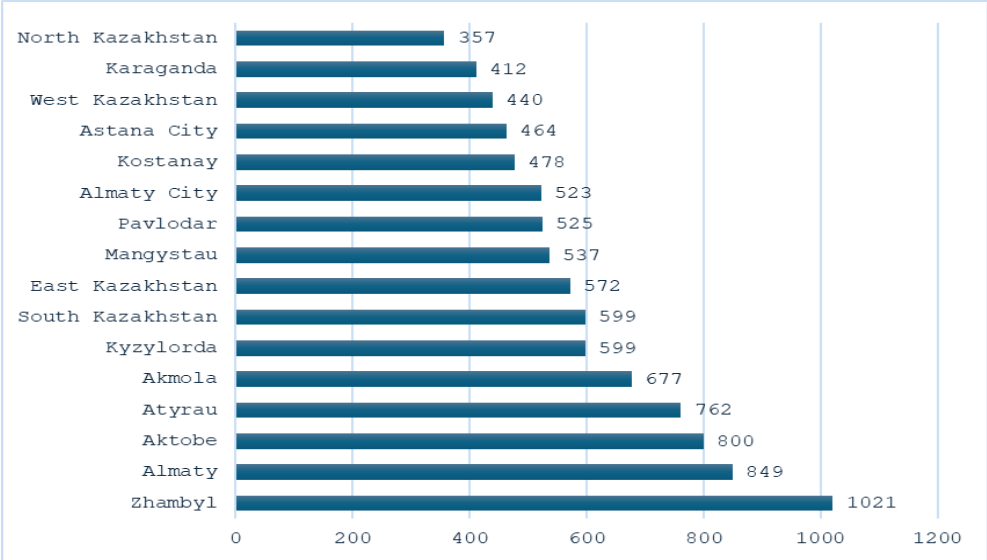

Figure 7. Regional Variation in Number Needed to Screen, 2010-2023

biennial intervals aligned with international guidance [21].

Regional heterogeneity: who does well, who lags, and why?

Between-region contrasts were large and informative across levels and trends:

• Early-stage (I-II) ASIR was highest in Pavlodar, North Kazakhstan, Almaty City and lowest in Mangystau, South Kazakhstan, Kyzylorda – a 3-fold spread. By contrast, stage III remained comparatively high in Akmola, Kostanay, and stage IV in Karaganda, Kostanay, signalling differing diagnostic pathways and case-mix.

• Incidence trends rose in most regions (steepest in Atyrau), while mortality trends broadly fell, often with post-joinpoint accelerations (e.g., Atyrau, Zhambyl, Akmola, Astana). M/I clustered near 0.3–0.4 in most areas but stayed 0.5 in Zhambyl, indicating scope to improve survival conditional on incidence.

• On programme metrics, regions combining high coverage with moderate abnormal finding rates (≈13-18%) tended to achieve higher CDR and lower NNS – signatures of better targeting and pre-biopsy triage. Akmola (abnormal finding rate 5.8%) and Kostanay exemplify high-specificity profiles with high PPV and low BBR. In contrast, Almaty City and South Kazakhstan show exceptionally high abnormal finding rate (~30–35%) and very high BBR (>300 per 1,000) but only middling CDR (~1.9–2.0 per 1,000), indicating heavy benign workload without commensurate malignant yield.

These patterns are mutually coherent: where referral quality is tighter (moderate abnormal finding rates), PPV is higher, BBR lower, and NNS shorter; where thresholds are looser, benign work-ups inflate without proportional gains in CDR, and downstream survival (as proxied by M/I) improves more slowly.

Screening performance in international context

Programme coverage in Kazakhstan was high through the 2010s, absorbed a large 2018 denominator expansion, dipped sharply in 2019–2020, and then partially recovered by 2023 (APC −0.8%/year overall). Yield efficiency improved (CDR up; NNS down), yet PPV remained ≈1% and BBR stayed high – evidence that sensitivity has been prioritised over specificity.

Benchmarking against high-income programmes highlights both progress and headroom:

• Cancer detection rate: NHS England reported ~8.1 per 1,000 in the core 50-70 group in 2023-24 [22]; Breast Cancer Surveillance Consortium (BCSC) benchmarks in the US typically show ~4-5 per 1,000 [23]. Kazakhstan's long-run CDR (~1–2 per 1 000, reaching 2.35 in 2023) is lower, compatible with lower underlying prevalence in screened ages and/or residual under-capture.

• Abnormal finding rate: US screening abnormal finding rates are commonly 8-12%; our national abnormal finding rate averages 19% - considerably higher. High abnormal rates with low PPV (~1%) indicate over-referral relative to international norms (PPV around 4% in BCSC) [23].

The WHO Global Breast Cancer Initiative sets a population goal of reducing breast cancer mortality by 2.5% per year for 20 years [20]. Kazakhstan's post-2010 mortality decline is directionally consistent with this aim. To sustain and potentially accelerate these gains, quality-assurance guidance from European Commission Initiative on Breast Cancer and performance benchmarks from BCSC and National Mammography Database Study indicate that organised programmes should maintain high participation, keep recall rates within target ranges, maximise cancer detection per 1 000 screens, and improve positive predictive value while reducing unnecessary benign biopsies [20, 24, 25].

Mechanistic synthesis

Three mechanisms plausibly connect the observed data streams:

1. Stage shift as the proximal driver of mortality decline. The sustained rise in stage I-II and contraction of stage III-IV – together with increasing CDR and falling NNS – Indicates that more cancers are captured earlier, which should translate to improved survival provided

treatment quality is adequate.

2. Specificity gap in parts of the system. High abnormal finding rates coupled with low PPV and very high BBR point to permissive recall/biopsy thresholds and variable adherence to BI-RADS assessment principles (e.g., management of BI-RADS3). This dilutes PPV, burdens patients and services, and may not proportionally raise CDR - explaining why some high-workload regions show only modest CDR and slower improvements in M/I.

3. Regional implementation effects. Regions that combine stable coverage, moderate abnormal rates, and declining advanced-stage incidence also show steeper mortality declines. Conversely, areas with flat stage III or recent upturns in stage IV (e.g., Kostanay, in part Akmola) require pathway review; however, both Akmola and Kostanay exhibit high PPV and low BBR – a high-specificity profile. The priority there is to improve case capture (sensitivity) without eroding specificity (e.g., targeted reader feedback and diagnostic-access audits). By contrast, Almaty City and South Kazakhstan illustrate very high recall and BBR with only modest CDR, consistent with lower specificity.

Implications for practice and policy

• Tighten referral quality while maintaining sensitivity. Set target bands for abnormal-assessment (≈10–15%), PPV ≥4%, and biopsy recommendation ~1-2% (tailored to local risk) with quarterly feedback at facility/oblast level. Use double-reading/consensus in outlier centres; standardise management of BI-RADS 3 to reduce unnecessary immediate biopsy.

• Protect coverage and diagnostic throughput during system shocks; recovery of early-stage share lagged coverage dips in 2020–2021.

• Focus on stage and M/I in high-priority regions (e.g., Zhambyl, Kostanay, Akmola): implement targeted packages blending reader retraining, triage ultrasound/tomosynthesis, fast-track image-guided biopsy, and treatment-access audits.

Strengths and limitations

National scope, long horizon, unified metrics, and formal trend modelling are strengths. Limitations include the ecological design, absence of interval-cancer auditing and stage-specific survival, and potential heterogeneity in BI-RADS use and biopsy pathways that may inflate benign workload in some settings. These caveats favour cautious causal language while still permitting a coherent interpretation of stage shift → improved survival. In addition, potential BI-RADS misclassification (e.g., upward drift from 3→4A or inter-reader/site variability) and a high benign biopsy rate can inflate recall and biopsy volumes, depress PPV, and simulate apparent improvements (e.g., stage shift) without corresponding gains in outcome. Therefore, interpretation should be anchored to outcome-proximal indicators – advanced-stage incidence, interval-cancer rates, and stage-specific survival – and supported by BI-RADS-stratified PPV and site-adjusted analyses to mitigate these biases.

Author Contribution Statement

AT, ZhT, RM – Collection and preparation of data, primary processing of the material and their verification. AJ, DB, SD – Statistical processing and analysis of the material, writing the text of the article (material and methods, results). AT, GI, DT, DK – Writing the text of the article (introduction, discussion). NI, ZB, IK– 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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Conflict of interest

The authors declare that there is no conflict of interest.

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