RESEARCH ARTICLE

Colorectal Cancer Mortality in Kazakhstan: Spatio-Temporal Epidemiological Assessment

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Abstract

Objective: The aim is to study the trends in colorectal cancer (CRC) mortality in Kazakhstan. **Methods:** The retrospective study was done using descriptive and analytical methods of oncoepidemiology. The extensive, crude and age-specific mortality rates are determined according to the generally accepted methodology used in sanitary statistics. **Results:** CRC mortality in Kazakhstan is considered to be increasing. Therefore, this study (for the period 2009-2018) was undertaken to retrospectively evaluate data across the country available from the central registration bureau. Age standardized data for mortality was generated and compared across age groups. It was determined that during the studied period 15,200 died of this pathology. During the studied years an average age of the dead made 69.8 years (95%CI=69.5-70.0). The average annual standardized mortality rate was 10.2 per 100,000, and in dynamics tended to decrease. Peak of mortality was noted in aged 60-84 years. Trends in age-related mortality rates had a pronounced tendency to increase in 30-34 years (T=+11.7%, R^2=0.7980) and to decrease in 75-79 years (T=−16.4%, R^2=0.8881). In many regions, there is a decrease in the number of deaths. During the compilation of cartograms, mortality rates were determined on the basis of standardized indicators: low – up to 8.9, average – from 8.9 to 11.5, high – above 11.5 per 100,000 for the entire population. In addition, all calculations were made taking into account age-sex differences. **Conclusion:** Trends in mortality from CRC in recent years have decreased from 11.2 to 7.7 per 100,000 of the total population, while the trend is stable (T=−3.6%, R^2=0.8745). The study of regional mortality has theoretical and practical significance: monitoring and evaluation of the effectiveness of early detection and treatment of detected pathology. Health authorities should take into account the results obtained when organizing anti-cancer measures.

Keywords: Colorectal cancer - mortality - trends - age dependence - geographical variation – Kazakhstan

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second leading cause of cancer death in the world (accounting for about 1.9 million new cases and almost 935,173 deaths in 2020), although with some global geographic differences in both incidence and mortality rates, with Asia contributing the highest, 992,755 (53.7%) of incident cases and 498,329 (55.5%) of deaths (all genders and ages) in the world (Ferlay et al., 2020A).

Ongoing demographic changes will lead to a rise in the number of deaths from CRC per year in the vast majority of countries, and according to the International Agency for Research on Cancer, in 2035 it is expected that about 1.4 million people will die from this pathology in the world, including in Kazakhstan, this number will be about 2,950 people (Ferlay et al., 2020B). The number of deaths from both colon and rectal cancer are set to double by 2035 for most countries, suggesting an alarming increase in the future burden of CRC and the need for stronger prevention programmes intended to promote healthier

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lifestyles (Araghi et al., 2019). Predicting future mortality trends is an important aspect of cancer surveillance, as it often points to the need for specific interventions and aids the prioritization of resources and future research (Bray and Moller, 2006).

In recent years, CRC incidence and mortality rates have declined for men and women of all races/ ethnicities (United States Cancer Statistics Working Group. 1999–2013 Incidence and Mortality Web-Based Report, 2017), the extent to which the decrease varies annually by age, race, gender, site and stage is largely unknown. Screening reduces the incidence and mortality of cancer, but it has not been implemented in most countries (Siegel et al., 2012) and only 1.59% of women and men older than 50 years get screened because there is no recommendation for screening in the world (Ferlay et al., 2015). In most Asian countries, screening for early detection of CRC should be considered as a major health priority (Ghoncheh et al., 2016). Studies about the barriers to screening reported that societal education, family physician's increased cooperation, and increased access of the general population to services are important strategies in promoting CRC screening. Screening of CRC remains the most important and cost-effective strategy in reducing the incidence and mortality of this disease, though with a lesser contribution from both risk factor reductions and improved therapies (Edwards et al., 2010).

Improvements in treatment options and accessibility, including tertiary care, are vital in low-income and middle-income countries that face an increasing burden of CRC (Bray et al., 2015). In some of these Asian regions, there is still inadequate clinical capacity in terms of infrastructures (endoscopy units, cancer registries, etc.), oncologists, gastroenterologists, and surgeons (especially females in some Muslim countries) to manage screening-detected lesions (Hyodo et al., 2010; Ahmed, 2013; Sankaranarayanan, 2014; Sankaranarayanan et al., 2014; Gelband et al., 2015; Hasan et al., 2017).

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

Materials and Methods

Cancer registration and patient recruitment

The population of the Republic of Kazakhstan according to the 2018 census was 18.27 million people, of which 9.42 million were women and 8.85 million were men (Bureau of National Statistics, 2018), while the dynamics of the female population increased by 13.0%, and the male population increased by 14.2% compared to 2009. The cancer registry of the population of Kazakhstan covers 14 regions and cities of national significance-Almaty and Astana (now the city of Nur-Sultan). New cases of CRC were extracted from the accounting and reporting forms of the Ministry of Health of the Republic of Kazakhstan – form 7 and form 35, which were formed from the register of oncological diseases based on the administrative-territorial division of the republic from 2009 to 2018 using the International Disease Code 10, code C18-21.

Statistical analysis

The main method used in the study of mortality was a retrospective study using descriptive and analytical methods of oncoepidemiology. Age-standardized mortality rates (ASRs) 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). ASRs standardized to the world population proposed by World Health Organization (Ahmad et al., 2001) with recommendations from the National Cancer Institute (1976) were estimated for each studied year.

The extensive, crude rate (CR) and age-specific mortality rates (ASMR) are determined according to the generally accepted methodology used in sanitary statistics. The annual averages (M, P), mean error (m), Student criterion, 95% confidence interval (95% CI), and average annual upward/downward rates (T%) were calculated. We did not justify the main calculation formulas in this paper, since they are detailed in the methodological recommendations and textbooks on medical and biological statistics (Merkov and Polyakov, 1974; Glanc, 1999; dos Santos Silva, 1999). The dynamics of mortality rates was studied for 10 years, while the trends of mortality were determined by the least squares method.

The average annual growth/decline rate (T%) was calculated using a geometric mean.

When compiling cartograms, crude rates and ASRs were used for 10 years (2009-2018). The method of compiling a cartogram proposed in 1974 by S.I. Igisinov was used, based on the determination of the standard deviation (σ) from the average (x). The scale of steps was calculated as follows: taking σ as an interval, the maximum and minimum levels of mortality were determined according to the formula: $x \pm 1.5\ \sigma$, with the minimum indicator equal to $x - 1.5\ \sigma$ and the maximum equal to $x + 1.5\ \sigma$.

Viewing and processing of the received materials was carried out using the Microsoft 365 software package (Excel, Word, PowerPoint), in addition, online statistical calculators were used (https://medstatistic.ru/calculators/averagestudent.html), where Student criterion was calculated when comparing the average values.

Ethics approval

Because this study involved the analysis of publicly available administrative data and did not involve contacting individuals, consideration and approval by an ethics review board was not required. At the same time, the submitted data is in accordance with the Law of the Republic of Kazakhstan No. 257-IV of March 19, 2010 "About State statistics" (http://adilet.zan.kz/rus/docs/Z100000257), the information in the summary report is confidential and can only be used for statistical purposes in accordance with the Principles of the World Medical Association (WMA, 2013).

Results

During 10 years (2009-2018) 15,200 people died of CRC, of these, there are 7,505 (49.4%) men and 7,695 (50.6%) women. Extensive proportion of deaths
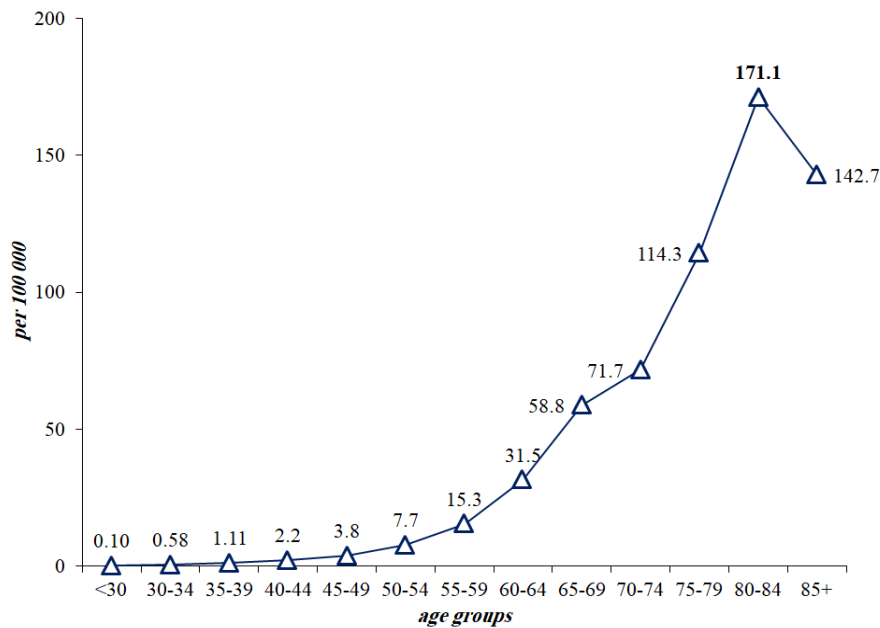
Figure 1. Age Distribution of CRC Mortality in Kazakhstan, 2009-2018

from CRC by age groups (both sexes) of Kazakhstan, characterized by a high proportion of deaths, were identified among people aged 65-69 years (14.9%), 70-74 years (14.7%), 75-79 years (17.2%) and 80-84 years (14.5%). The distribution of age groups by the number of deaths from CRC showed that the groups in the age range from 60 to 84 years were the most numerous 11,236 (73.9%) (Table 1). The proportion of deaths from CRC among the male and female population of Kazakhstan by age groups was similar to that of the general population.

Average age of dead people from CRC in dynamics decreased from 70.3±0.3 years (95%CI=69.7-70.9) in 2009 till 69.5±0.3 years (95%CI=68.9-70.2), and average annual rate of decline made T=–0.1. During the studied years an average age of the dead made 69.8±0.1 years (95%CI=69.5-70.0). The highest mortality rates per 100,000 in the entire population were found in the age groups 75-79 years (114.3±18.2), 80-84 years (171.1±13.1), and 85+ years (142.7±15.9) (Figure 1).

The standardized mortality rate for the country

Table 1. Number and Age-specific Mortality Rate of CRC in Kazakhstan, 2009-2018

Age	All				Male				Female			
	Number (%)	Mortality			Number (%)	Mortality			Number (%)	Mortality		
		per 100,000	T, %	R^2		per 100,000	T, %	R^2		per 100,000	T, %	R^2
<30	50 (0.3)	0.1±0.0	−6.7	0.2009	32 (0.4)	0.1±0.0	−11.9	0.7456	18 (0.2)	0.0±0.0	+2.0	0.0031
30-34	80 (0.5)	0.6±0.1	+11.7	0.798	45 (0.6)	0.7±0.1	+11.8	0.5056	35 (0.5)	0.5±0.1	+11.5	0.658
35-39	132 (0.9)	1.1±0.1	−6.6	0.2744	66 (0.9)	1.1±0.1	−7.6	0.3714	66 (0.9)	1.1±0.2	−5.6	0.1135
40-44	245 (1.6)	2.2±0.1	−1.5	0.0854	119 (1.6)	2.2±0.2	−6.6	0.5049	126 (1.6)	2.2±0.2	+3.5	0.1788
45-49	405 (2.7)	3.8±0.2	+1.1	0.0544	211 (2.8)	4.2±0.3	+5.0	0.4176	194 (2.5)	3.5±0.2	−3.0	0.1862
50-54	772 (5.1)	7.7±0.3	−1.6	0.1463	383 (5.1)	8.2±0.6	−2.0	0.0811	389 (5.1)	7.2±0.2	−1.3	0.2377
55-59	1253 (8.2)	15.3±1.2	−6.3	0.6809	650 (8.7)	17.7±1.3	−5.3	0.5401	603 (7.8)	13.4±1.3	−7.5	0.6359
60-64	1902 (12.5)	31.5±1.7	−4.8	0.7891	979 (13.0)	38.3±2.0	−4.1	0.6226	923 (12.0)	26.6±1.8	−5.8	0.7422
65-69	2266 (14.9)	58.8±4.5	−3.3	0.1908	1168 (15.6)	76.0±5.5	−2.7	0.1493	1098 (14.3)	47.4±3.9	−3.8	0.2196
70-74	2237 (14.7)	71.7±8.0	+7.2	0.3737	1176 (15.7)	102.6±12.0	+8.3	0.4341	1061 (13.8)	53.6±5.8	+6.1	0.2921
75-79	2620 (17.2)	114.3±18.2	−16.4	0.8881	1275 (17.0)	164.6±26.3	−16.4	0.8813	1345 (17.5)	88.5±14.2	−16.2	0.8644
80-84	2211 (14.5)	171.1±13.1	+3.1	0.1593	981 (13.1)	258.1±21.4	+2.7	0.1026	1230 (16.0)	134.9±9.9	+3.1	0.1706
85+	1027 (6.8)	142.7±15.9	−10.5	0.8650	420 (5.6)	241.3±33.8	−13.3	0.8182	607 (7.9)	111.5±11.6	−9.7	0.8614
CR	15200 (100.0)	8.9±0.2	−2.4	0.8128	7505 (100.0)	9.1±0.2	−2.0	0.845	7695 (100.0)	8.7±0.3	−2.8	0.7595
ASR	−	10.2±0.4	−3.6	0.8745	−	13.9±0.54	−3.7	0.9312	−	8.2±0.4	−4.0	0.8272
Average Age	−	69.8±0.1	−0.1	0.5903	−	69.2±0.1	−0.1	0.5069	−	70.3±0.2	−0.1	0.1694

T, average annual upward/downward rates; R^2, the value of the approximation confidence; CR, crude rate; ASR, age-standardized rate
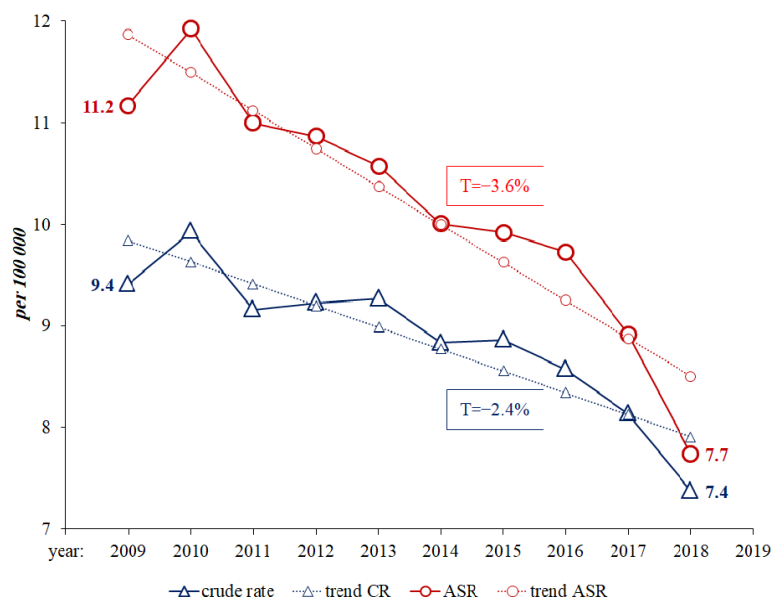
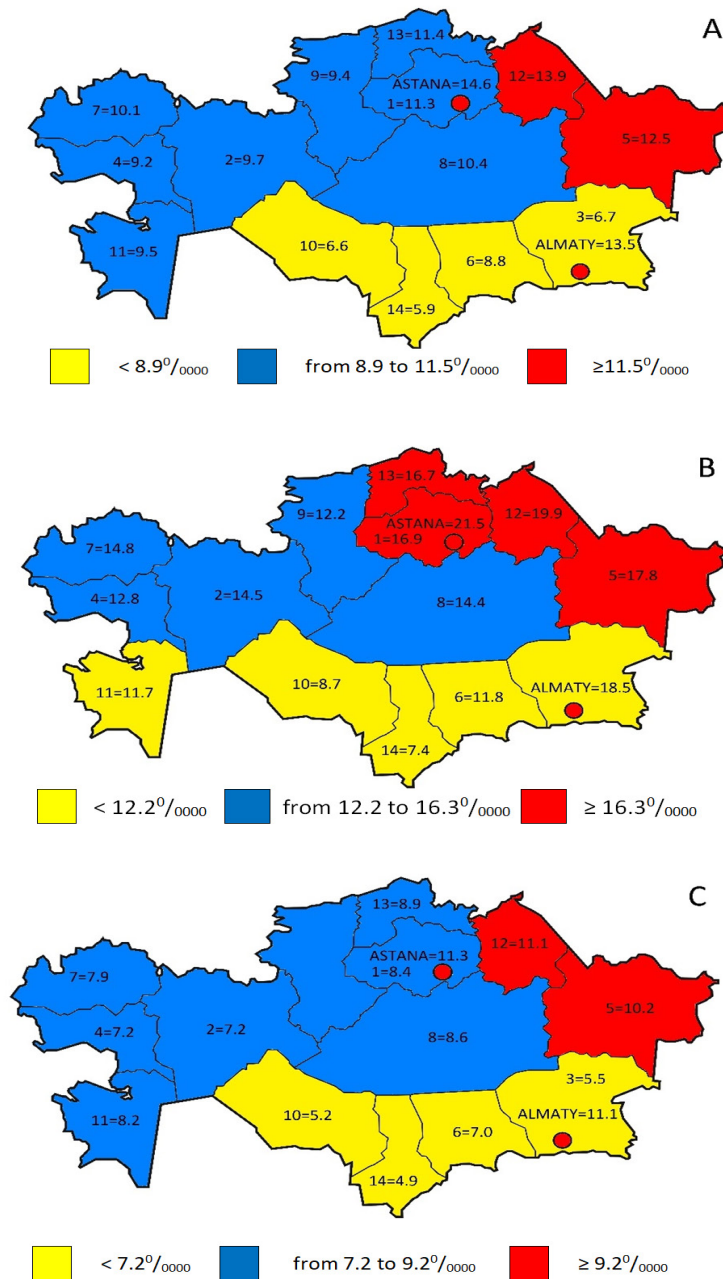Figure 2. Dynamics of CRC Mortality in Kazakhstan, 2009-2018

was 10.2 per 100,000 population. And the average annual growth rate was T=−3.6% (R^2=0.8745). Crude rates of CRC mortality among residents of Kazakhstan (Figure 2) tended to decrease from 9.4±0.2 (95% CI=8.9-9.9) (2009) to 7.4±0.2 (95%CI=7.0-7.8) in 2018 per 100,000, the average was 8.9±0.2 per 100,000 (95%CI=8.4-9.3). The average annual rate of mortality decline by CRC was significant (T=−2.4%), 95%CI of the

indicators do not overlap with each other, which suggests that these indicators are influenced by different factors, and a high degree of reliability of the approximation (R^2=0.8128) which proves a true decrease in mortality from this form of cancer in Kazakhstan. Crude mortality rates are 4.2% higher in men than in women, mortality is not significantly different in men and women younger than age 60 years but is almost 33% and 45% higher in

Table 2. Number and Mortality Rate of CRC in Regional Aspect, 2009-2018

Age	All				Male				Female			
	Number (%)	Mortality			Number (%)	Mortality			Number (%)	Mortality		
		per 100,000*	T, %	R^2		per 100,000	T, %	R^2		per 100,000	T, %	R^2
South Kazakhstan	940 (6.2)	5.9±0.34	−1.0	0.0294	483 (6.4)	7.4±0.58	+0.4	0.0032	457 (5.9)	4.9±0.31	−2.0	0.0937
Kyzylorda	305 (2.0)	6.6±0.71	−2.4	0.0537	168 (2.2)	8.7±1.12	−0.9	0.0050	137 (1.8)	5.2±0.62	−4.7	0.1612
Almaty	1081 (7.1)	6.7±0.40	−3.6	0.3753	566 (7.5)	8.6±0.49	−2.6	0.2207	515 (6.7)	5.5±0.44	−4.9	0.3893
Zhambyl	703 (4.6)	8.8±0.45	−3.2	0.3957	360 (4.8)	11.8±0.89	−4.3	0.3290	343 (4.5)	7.0±0.34	−2.6	0.3032
Atyrau	360 (2.4)	9.2±0.61	−1.4	0.0473	187 (2.5)	12.8±0.65	−3.0	0.3579	173 (2.2)	7.2±0.72	+0.3	0.0007
Kostanay	1009 (6.6)	9.4±0.52	−4.5	0.6644	470 (6.3)	12.2±0.59	−2.6	0.2948	539 (7.0)	8.0±0.61	−6.0	0.6470
Mangistau	286 (1.9)	9.5±0.67	−2.1	0.0858	138 (1.8)	11.7±1.03	−3.6	0.1728	148 (1.9)	8.2±0.62	−0.3	0.0020
Aktobe	605 (4.0)	9.7±0.72	−6.4	0.7524	319 (4.3)	14.5±1.60	−7.4	0.4627	286 (3.7)	7.2±0.77	−6.4	0.3675
West Kazakhstan	628 (4.1)	10.1±0.61	−4.4	0.5558	320 (4.3)	14.8±1.46	−7.6	0.6047	308 (4.0)	7.9±0.53	−2.1	0.1061
Karaganda	1550 (10.2)	10.4±0.87	−7.2	0.7601	725 (9.7)	14.4±1.23	−7.0	0.6873	825 (10.7)	8.6±0.72	−7.4	0.7857
Akmola	919 (6.0)	11.3±0.62	−3.9	0.5343	489 (6.5)	16.9±1.13	−3.4	0.2729	430 (5.6)	8.4±0.53	−4.1	0.4584
North Kazakhstan	853 (5.6)	11.4±0.89	−6.2	0.6507	431 (5.7)	16.7±1.51	−7.7	0.7462	422 (5.5)	8.9±0.86	−5.7	0.3601
East Kazakhstan	2085 (13.7)	12.5±0.50	−2.5	0.4065	1000 (13.3)	17.8±0.73	−2.7	0.4367	1085 (14.1)	10.2±0.58	−3.0	0.2990
Almaty city	2038 (13.4)	13.5±0.78	−4.5	0.6246	950 (12.7)	18.5±1.09	−4.5	0.6022	1088 (14.1)	11.1±0.71	−4.8	0.5776
Pavlodar	1170 (7.7)	13.9±0.46	−2.4	0.5221	565 (7.5)	19.9±0.95	−2.2	0.2254	605 (7.9)	11.1±0.47	−3.1	0.5628
Astana city	668 (4.4)	14.6±0.98	+3.5	0.2541	334 (4.5)	21.5±1.28	+2.2	0.1359	334 (4.3)	11.3±0.98	+3.8	0.1782
Kazakhstan	15200 (100.0)	10.2±0.40	−3.6	0.8745	7505 (100.0)	13.9±0.54	−3.7	0.9312	7695 (100.0)	8.2±0.37	−4.0	0.8272

T, average annual upward/downward rates; R^2, the value of the approximation confidence; ASR, age-standardized rate; *the table is built taking into account the sorting from A to Z of mortality rate

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 3. Cartogram of CRC mortality in Kazakhstan, 2009-2018 (A,both sexes; B, male; C, female)

men than in women ages 60-69 and 70+ years, respectively (51.9 vs 34.6 per 100,000 and 147.5 vs 81.4 per 100,000). Taking standardized mortality rates for each gender, we saw the same situation, but with a larger difference (41%). This indicates a different age structure of the male and female population when compared with the global age structure.

Spatial assessment of mortality from CRC in the entire population (Figure 3A) shows that the southern regions (Almaty, Zhambyl, Kyzylorda, South Kazakhstan) were among the regions with a low mortality rate. A similar pattern was observed in men (Figure 3B), as well as in women (Figure 3C). At the same time, in men, the Mangystau region also belonged to the regions with a low mortality rate (Figure 3B).

The cartogram of mortality from CRC in the entire (Figure 3A) and female (Figure 3C) population indicates that the regions with a high mortality rate include East Kazakhstan, Pavlodar regions, as well as the cities of Almaty and Astana. And in the male population, the regions with a high mortality rate also included the Akmola and North Kazakhstan regions (Figure 3B).

The remaining regions, respectively, in the total (Figure 3A), male (Figure 3B) and female (Figure 3C) populations belonged to regions with an average mortality rate.

Thus, the geographical variability of the number of patients and mortality with CRC in Kazakhstan was revealed (Table 2). Analyzing the average annual growth rates of standardized indicators, it was found that there was a downward trend in all regions (the minimum indicator was in the South Kazakhstan (T=−1.0%; R^2=0.0294), and the maximum in the Karaganda (T=−7.2%; R^2=0.7601)), except for the city of Astana (T=+3.5%; R^2=0.2541). A high level of approximation was found in such regions as Aktobe (R^2=0.7524), Kostanay (R^2=0.6644), North Kazakhstan (R^2=0.6507) and Almaty (R^2=0.6246).

Analyzing the average annual growth rate of the standardized indicator in the male population by region, a decrease in the indicator was also found, except for the South Kazakhstan region (T=+0.4%; R^2=0.0032) and the city of Astana (T=+2.2%; R^2=0.1359). The same decrease in this indicator was found in the female population, and an increase was established in the Atyrau region (T=+0.3%; R^2=0.0007) and in the city of Astana (T=+3.8%; R^2=0.1782).

Discussion

Mortality rates in Kazakhstan reflect the global trend. The results of the study show that despite the fact that in Kazakhstan there is a decrease in mortality from CRC, our republic belongs to the region with high mortality rates, the standardized mortality rate was 10.2 per 100,000 population and difference between men (13.9) and women (8.2) is statistically significant. According to IARC (Farley et al., 2020), the standardized mortality rate is highest in Slovakia (21.00/0000), Hungary (20.20/0000) and Croatia (19.60/0000). And the smallest are set in Bangladesh (2.30/0000), Bhutan (2.50/0000) and Nepal (2.50/0000). Men die more often than women, according to the results of a Minnesota study on the fight against colon cancer (Shaukat et al., 2013). Reasons for higher rates in men are not completely understood but to some extent likely reflect differences in exposures to risk factors and sex hormones, as well as complex interactions between these influences (Siegel et al., 2017).

As in the whole world, mortality in Kazakhstan is low at the age of less than 50 years (up to 50 years – 1.30/0000), but increases greatly with age (from 50 years and older – 52.10/0000). For example, we see the same trend in the USA (up to 50 years – 1.50/0000, from 50 years and older – 34.00/0000), in the UK (up to 50 years – 1.30/0000, from 50 years and older – 52.00/0000), and in Turkey (up to 50 years – 1.20/0000, from 50 years and older – 45.50/0000). Several studies have shown that CRC mortality rates have been steadily decreasing for at least two decades in many high-income countries in Northern America, Oceania and Northern and Western Europe (Arnold et al., 2017; Siegel et al., 2017). On the other hand, significant increases are seen in CRC mortality rates in less developed countries in Asia, Africa and Latin America, where rates have been historically low (Bosetti et al., 2005; Center et al., 2009; Souza et al., 2014). The distribution of CRC burden varies widely, with more than two-thirds of all cases and about 60% of all deaths occurring in countries with a high or very high human development index (HDI)

(CRC Collaborators, 2019). In several high-income countries and countries of east Asia and eastern Europe, mortality has been decreasing since the 1980s, probably because of improved early detection and treatment, but rates have continued to increase in countries or areas with poor health-care resources, including countries in Central and South America and rural areas in China (Bosetti et al., 2011; Guo et al., 2012; CRC Collaborators, 2019) However, CRC screening has been found to be the most important aspect in reducing morbidity and mortality from this disease, but the screening strategy is offered only to a smaller proportion of people worldwide (Schreuders et al., 2015). In Asia, a considerable number of countries including Japan, South Korea, Singapore, and Taiwan where CRC is highly prevalent, have developed population-based screening programs (Schreuders et al., 2015). CRC screening in Asia as well as in other countries has been shown to be cost-effective or even cost-saving compared with no screening at all (Tsoi et al., 2008; Lansdorp-Vogelaar et al., 2011; Levin et al., 2018). Kazakhstan is the only country in the post-Soviet space where there is a screening program at the national level, introduced in 2011. There is no such program in any of the Central Asian countries. The implementation of screening has been shown to lead to short-term increases in CRC incidence as a result of increased detection of prevalent cases, typically followed by a long-term reduction in incidence and mortality from CRC due to the removal of precancerous polyps (Araghi et al., 2019; Brown et al., 2021). This may for example explain the decrease in observed CRC mortality rates in Israel and Japan, countries with longstanding CRC screening programs in place since the early-1990s (Minami et al., 2006). As stated in the results of a cross-sectional study carried in the northern part of Iran, it's expected that CRC will have an increasing trend, which may be related to the level of detection of CRC, as well with early diagnosis, treatment and its cost (Janbabaee et al., 2021). Taking into account the results of recent studies on the incidence of CRC in Kazakhstan (Mauyenova et al., 2021), where there is an increase in the incidence, we can also expect that in the future the incidence and mortality rates will decrease.

In Kazakhstan, with the introduction of screening, mortality rates decreased by 25% (from 9.9 in 2010 to 7.4 in 2018 per 100,000). The temporal changes in CRC outcomes following the implementation of organized screening are consistent with shorter duration community-based CRC mortality studies which have evaluated programmatic fecal immunochemical test, as well as modeling studies of the ≥80% screening target. Such studies proving the effectiveness of screening programs in reducing mortality have been conducted in many countries (Chiu et al., 2015; SEER Stat Fact Sheets: Colon and Rectum Cancer, 2017; Meester et al., 2018). Although the observational design precludes confirming a direct causal link between the increases in screening and the decreases in CRC outcomes, temporal changes in cancer risk factors or treatment are unlikely sole alternative explanations for several reasons. First, CRC incidence is stable or increasing in many comparable developed countries without substantial screening programs, including Finland,

Norway, France and Australia. Substantial declines are reported almost exclusively in countries with at least moderate use of cancer screening tests (Siegel et al., 2012). Second, a sophisticated modeling study suggested that changes in risk factors and treatment have relatively small influences on population-level CRC mortality statistics (Schreuders et al., 2015). With recent advances in treatment, mortality rates remain high despite an increase in survival time (Moghimi-Dehkordi and Safaee, 2012).

Despite the introduction by our state of a screening program for the detection of CRC, mortality rates are at a high level. Which in turn implies insufficient coverage of screening and untimely treatment. Advances in treatment options and regimens differ extensively among countries, which may also explain lower CRC mortality rates in some countries. Major advances in the treatment of CRC are the result of improved surgical techniques, often in combination preoperative chemo-radiation therapy or radiation alone (Sauer et al., 2004; van Gijn et al., 2011). In many less developed countries, the lack of access to adjuvant therapy has been previously reported (Kingham et al., 2013). Moreover, lack of awareness, higher diagnostic costs and delays in treatment may explain part of the higher mortality that was observed and projected in the Latin America and Caribbean region (Sierra and Forman, 2016).

Mortality rates in our country also had geographical variability. The lowest indicators were found in the southern regions, and the highest in the eastern region. This is due to the ethnic composition of the population, changes in the age structure and nutritional and behavioral characteristics. Ethnicity has been found to be an important etiological factor for CRC in Asia (Pourhoseingholi, 2014). Some ethnic groups such as Chinese, Korean, and Japanese have higher CRC incidence. In certain countries with multi-ethnic populations such as Singapore and Malaysia, the Chinese population, in particular, have a substantially greater incidence of CRC compared to Malays and Indians though living in the same environment with similar lifestyle and dietary habits (Sung et al., 2007; Pourhoseingholi, 2014; Chiu et al., 2017). Even among the same ethnic groups, for example in China, higher incidence and mortality rates have been shown in those living in coastal areas compared with those in the hinterlands (Chiu et al., 2017; Zhu et al., 2017). A similar pattern is observed in Nepal, where in recent years there has been an increase in the incidence rate, which is presumably associated with an increase in life expectancy and risk factors that are ubiquitous in the world - alcohol consumption, irregular physical activity, obesity, intake of spicy and fatty foods, as well as food with low fiber levels (Shrestha et al., 2020).

Our research has limitations. The accounting and registration of mortality in the Republic of Kazakhstan is observed very strictly and our study covered secondary information obtained from administrative data. However, mortality in CRC can be due to other causes, for example, acute coronary syndrome, concomitant chronic diseases, therefore it is important to differentiate mortality from other causes and from CRC during patient's life. On the other hand, we conducted a comprehensive standardized mortality assessment to determine geographic and age characteristics.

Assessment and study of incidence and mortality by stages, by the level of morphological verification is a priority for our future research.

The study of mortality trends from CRC 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

DM, AA, ZhT, AB, ZhB, AZ, ZK – Collection and preparation of data, primary processing of the material and their verification. DM, AA, AB, ZB, GI, YK, AA, GN – Statistical processing and analysis of the material, writing the text of the article (material and methods, results). DM, AA, ZB, GI, SO, SK, AMJ – Writing the text of the article (introduction, discussion). NI, AMJ, IK, DM, AA – 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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