RESEARCH ARTICLE

Editorial Process: Submission:10/21/2021 Acceptance:06/13/2022

Geographic Variability of Gastric Cancer Incidence in Kazakhstan

Rustem Taszhanov[1,2,3], Zhansaya Telmanova[1,2], Yerkezhan Zhadykova[1,2], Lyailya Akhmetova[4], Akmaral Zhantureyeva[1,2], Zhanar Bukeyeva[1,2], Gulshara Aimbetova[5], Dinara Kassenova[1,2], Zhanerke Azhetova[1,2], Zhanar Kozhakhmetova[1,2], Serikbay Orazbayev[1,2], Kairat Adaibayev[1], Kadyr Ospanov[4], Kuanysh Kulayev[4], Yerlan Kuandykov[4], Zarina Bilyalova[2], Gulnur Igissinova[2,5], Saken Kozhakhmetov[1,2], Marcis Leja[6,7,8,9], Nurbek Igissinov[1,2,10]*

Abstract

Objective: The article studies the geographical features of the incidence of gastric cancer (GC) in Kazakhstan. **Methods:** The retrospective study was done for the period 2009-2018. Descriptive and analytical methods of oncoepidemiology were used. Crude (CR), age-specific (ASIR), age-standardized (ASR), equalized incidence rates and approximation were calculated. The dynamics of indicators was investigated using component analysis according to methodological recommendations. The method of drawing up a cartogram based on the determination of the standard deviation (σ) from the mean (x) was applied. **Results:** During the study period, 27,467 new cases of GC were registered. The incidence rate increased from 16.80 (2009) to 15.10 in 2018 and the overall decline was 1.70 per 100,000 population, including due to the age structure – $\sum\Delta_A$=+1.51, due to the risk of acquiring illness – $\sum\Delta_R$=−2.91 and their combined effect – $\sum\Delta_{RA}$=−0.31. The component analysis revealed that the increase in the number of patients with GC was mainly due to the growth of the population (Δ_P=+651.8%), changes in its age structure (Δ_A=+433.9%) and changes associated with the risk of acquiring illness (Δ_R=−832.1%). The cartograms were allocated according to the following criteria: low – up to $14.8^0/_{0000}$, average – from 14.8 to $19.2^0/_{0000}$, high – above $19.2^0/_{0000}$. The results of the spatial assessment showed the highest levels of GC incidence in following regions: Akmola ($22.2^0/_{0000}$), North Kazakhstan ($22.3^0/_{0000}$), and Pavlodar ($23.2^0/_{0000}$). **Conclusion:** Thus, as a result of the epidemiological analysis, the role of the influence of demographic factors and the risk of acquiring illness on the formation of the number of patients and the incidence of GC was evaluated, while sex differences and geographical variability were established.

Keywords: Gastric cancer- incidence- component analysis- Kazakhstan

Asian Pac J Cancer Prev, **23 (6)**, 1935-1944

Introduction

Stomach cancer, despite the global downward trend, remains an important problem in the health system and society. However, it is the most common cancer localization in some countries of the world. According to IARC data, high rates of gastric cancer were found in South Korea 39.6, Mongolia 33.1, and Japan 27.5 (Bray et al., 2018). Mongolia, Bhutan, China, and Kyrgyzstan have high mortality rates (Ferlay et al., 2019).

Gastric cancer is a multifactorial disease (Krejs, 2010; Karimi et al., 2014), the risk factors of which can be divided into genetic (Karimi et al., 2014), environmental (Forman and Burley, 2006) and lifestyle factors (Krejs, 2010). Unmodified risk factors include male gender (Chandanos and Lagergren, 2008), old age, white race (Anderson et al., 2010), and family history (Krejs, 2010; Karimi et al., 2014). Also, there are potentially modifiable factors, such as obesity (Karimi et al., 2014; Forman and Burley, 2006; Yang et al., 2009), smoking (Ladeiras-Lopes et al., 2008; Guggenheim and Shah, 2012; Freedman et al., 2007), H. Pylori infection (Fuccio et al., 2006; Lee et al., 2016; Ma et al., 2012; Epplein et al., 2008), the impact of which can be minimized by correcting the lifestyle. At

*[1]Astana Medical University, Nur-Sultan, Kazakhstan. [2]Central Asian Institute for Medical Research, Nur-Sultan, Kazakhstan. [3]Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan. [4]Khoja Akhmet Yassawi International Kazakh-Turkish University, Shymkent Campus, Kazakhstan. [5]Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan. [6]Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia. [7]Faculty of Medicine, University of Latvia, Riga, Latvia. [8]Riga East University Hospital, Riga, Latvia. [9]Digestive Disease Centre GASTRO, Riga, Latvia. [10]Eurasian Institute for Cancer Research, Bishkek, Kyrgyzstan. *For Correspondence: n.igissinov@gmail.com*

the same time, there are a number of studies that consider peptic ulcer disease (Forman and Burley, 2006), atrophic gastritis (Karimi et al., 2014), intestinal metaplasia (Guggenheim and Shah, 2012), gastroesophageal reflux disease (GERD) (Karimi et al., 2014), pernicious anemia (Vannella et al., 2012), and surgical interventions, in particular, partial gastrectomy (Krejs, 2010; Karimi et al., 2014). In addition, it is necessary to take into account the low socio-economic status (Uthman et al., 2013), radiation (Karimi et al., 2014) and the peculiarities of the diet, namely the low content of fruits and vegetables and the high content of salted and smoked food in the diet (Guggenheim and Shah, 2012; Lee et al., 2016; Zhang et al., 2013), as risk factors.

GC is one of the prognostically unfavorable forms of malignant neoplasms, since the latent (preclinical) period of this disease is from 10 months to 5 years (Mitelman, 2007) and in 75% of the initially identified patients, the disease is registered in stages III and IV (Poddubny et al., 2002). At the age of <40 years, symptoms such as asthenia, adynamia, weight loss and leukocytosis are poor predictors of prognosis in patients with stomach cancer (Trujillo-Rivera et al., 2021).

The high mortality rate of GC is attributed to a long period of asymptomatic course and late manifestation (Sitarz et al., 2018; Miki et al., 2009).

For the early detection and treatment of asymptomatic gastric cancer, mass screenings are conducted in countries with high morbidity and mortality rates. A three-year study conducted in Japan, in the early 2000s, determined that endoscopic examination is an effective research method for screening (Tashiro et al., 2006). It is also recommended to maintain an interval between screenings of less than three years (Nam et al., 2012).

Materials and Methods

Cancer registration and patient recruitment

The cancer registry of the population of Kazakhstan covers considering the administrative-territorial division. New cases of GC were extracted from the reporting forms of the Ministry of Health of the Republic of Kazakhstan (form 7 and form 35) from 2009 to 2018 using the International Disease Code 10, code C16.

Population denominators

Population denominators for calculation of incidence rates were provided by the Bureau of National Statistics. At the same time, data on the number of populations of the republic, taking into account the studied regions, are used, all data are presented on the official website (Bureau of National Statistics, 2018).

Statistical analysis

The main method used in the study of incidence was a retrospective study using descriptive and analytical methods of oncoepidemiology. ASRs were calculated for eighteen different age groups (0-4, 5-9, …, 80-84, and 85+) using the world standard population proposed by WHO (Ahmad et al., 2001) with recommendations from the National Cancer Institute (2013).

The extensive, crude (CR) and age-specific incidence rates (ASIR) 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 paper, since they are detailed in the textbooks on statistics (Merkov and Polyakov, 1974; Glanc, 1999; dos Santos Silva, 1999). Trends were determined using the least squares method, and the average annual growth rates were calculated using the geometric mean.

The dynamics of indicators was investigated using component analysis according to methodological recommendations (Dvoyrin and Aksel, 1987; Chissov et al., 2007).

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, where Student criterion was calculated when comparing the average values.

The GC incidence rates were calculated per 100,000 population. A retrospective study using descriptive and analytical methods of modern epidemiology were used.

The extensive, crude (CR) and age-specific (ASIR) incidence rates were calculated using the generally accepted methods of medical and biological statistics. Age-standardized incidence rates (ASR, World Standard, WHO, 2001) (Ahmad et al., 2001) were calculated as recommended (http://seer.cancer.gov/stdpopulations/world.who.html). The incidence over time was assessed for 10 years; the trends were determined by the least square method, to calculate the average annual growth/decline rates of the dynamic series.

Incidence rate were used in the preparation of cartograms. The method of mapping is applied, based on the determination of the standard deviation (σ) from the average (x) (Igissinov, 1974). The annual averages (M, P), mean error (m), Student criterion, 95% confidence interval (95% CI), and average annual upward/downward rates (T%) were calculated (Merkov and Polyakov, 1974; Glanc, 1999; dos Santos Silva, 1999).

The following symbols and abbreviations were used in this article: AN – absolute number; ASIR – age specific incidence rate; ASP (Δ_A) − the age structure of the population; ASR – age-standardized rate; END − the expected number of diseases; NGC − the number of GC cases; PN (Δ_P) − population number; RAI (Δ_R) − risk of acquiring illness; R_2 – the value of the approximation confidence; SI − structural indexes; P − the incidence; $^0/_{0000}$ – prosantimille, designation per 100,000.

Ethics approval

Because this study involved the analysis of publicly available administrative data and did not involve contacting individuals, consideration and approval by an ethics review board was not required.

Results

During the study period, 27,467 new cases of GC were

Table 1. Gastric cancer in Kazakhstan, 2009-2018

Age	All					Male					Female				
	Number		Incidence			Number		Incidence			Number		Incidence		
		%	per 100,000	T, %	R^2		%	per 100,000	T, %	R^2		%	per 100,000	T, %	R^2
<30	182	0.7	0.2±0.0	−4.4	0.1886	71	0.4	0.2±0.0	−4.8	0.1641	111	1.1	0.3±0.0	−4.1	0.154
30-34	268	1	2.0±0.1	−3.4	0.3466	138	0.8	2.1±0.2	−4.0	0.2964	130	1.3	1.9±0.2	−2.7	0.1045
35-39	454	1.7	3.8±0.3	−5.3	0.6016	262	1.5	4.5±0.4	−5.7	0.5508	192	1.9	3.2±0.3	−4.8	0.2989
40-44	794	2.9	7.2±0.4	−4.1	0.6098	523	3	9.8±0.6	−4.6	0.66	271	2.7	4.8±0.4	−2.9	0.1263
45-49	1538	5.6	14.4±0.6	−3.4	0.5936	1003	5.8	19.7±0.9	−3.2	0.5332	535	5.3	9.5±0.6	−3.7	0.3861
50-54	2611	9.5	26.1±1.3	−4.2	0.6843	1832	10.6	39.5±2.3	−4.6	0.6403	779	7.7	14.5±0.7	−3.5	0.4966
55-59	3770	13.7	46.4±14	−2.6	0.7727	2637	15.2	72.6±2.3	−2.5	0.6589	1133	11.2	25.3±1.1	−3.4	0.6863
60-64	4336	15.8	73.4±2.5	−3.1	0.8507	3000	17.3	119.8±3.4	−2.2	0.6276	1336	13.2	39.5±2.4	−5.1	0.7287
65-69	4142	15.1	105.9±2.7	−0.04	0.0003	2629	15.2	170.4±5.7	−0.2	0.0032	1513	14.9	63.4±2.1	0.2	0.0045
70-74	4264	15.5	128.6±1.9	−0.9	0.3925	2482	14.3	203.8±4.2	−0.1	0.0051	1782	17.6	84.7±2.3	−1.8	0.4594
75-79	3318	12.1	135.6±4.4	−0.8	0.0637	1844	10.6	222.9±10.3	0.2	0.0029	1474	14.5	91.2±2.7	−1.8	0.3939
80-84	1349	4.9	104.3±3.7	1	0.0876	698	4	184.2±8.1	0.3	0.0057	651	6.4	71.3±2.8	1	0.0669
85+	441	1.6	60.8±3.9	−3.7	0.343	212	1.2	119.0±9.0	−3.2	0.1881	229	2.3	42.1±3.9	−5.6	0.374
Total	27467	100	16.1±0.2	−1.0	0.6417	17331	100	21.1±0.2	−0.7	0.3326	10136	100	11.5±0.2	−1.6	0.7849

T, average annual upward/downward rates; R^2, the value of the approximation confidence; CR, crude rate

registered in the country (17,331 (63.1%) – in men, and 10,136 (36.9%) – in women). The greatest proportion of patients (both sexes) falls on the age of 60-74 years (60-64 years – 15.8%, 65-69 years – 15.1% and 70-74 years – 15.5%), a similar pattern in men and women (Table 1).

Age-related indicators of the incidence of GC had a peak in 75-79 years in both sexes ($135.6\pm4.4^{0}/_{0000}$), male ($222.9\pm10.3^{0}/_{0000}$) and female ($91.2\pm2.7^{0}/_{0000}$) population (Table 1).

Trends in the ASIR of GC in the entire population tended to decrease in almost all age groups, except for 80-84 years (T=+1.0%).

Trends of ASIR in the male population increased in 75-79 years (T=+0.2%) and 80-84 years (T=+0.3%). In the female population, the age indicators grown in 65-69 years (T=+0.2%), 80-84 years (T=+1.0%). It should be noted that the value of the accuracy of the approximation of the listed increases is not significant (Table 1).

Trends in age indicators generally affected the overall incidence rates, so the crude rate of GC incidence in the total population of the country lessened from $16.80^{0}/_{0000}$ (2009) to $15.10^{0}/_{0000}$ in 2018 (p=0.000), the total decline was $-1.70^{0}/_{0000}$ (Table 2) and depended on changes in the age structure of the population ($\sum\Delta A=+1.51^{0}/_{0000}$), the risk of acquiring illness ($\sum\Delta_R=-2.91^{0}/_{0000}$) and the combined influence of the age structure and the risk of acquiring illness ($\sum\Delta_{AR}=-0.31^{0}/_{0000}$). At the same time, the average annual growth rate of the aligned indicator was T=−1.0%, and the approximation confidence value was close to 1 (R^2=0.6417).

In the male population of the republic, the crude incidence rates also decreased from $21.65^{0}/_{0000}$ (2009) to $19.69^{0}/_{0000}$ in 2018, the difference is statistically significant (p=0.006). The overall drop ($-1.96^{0}/_{0000}$) depended on changes in the age structure of the population ($\sum\Delta_A=+2.33^{0}/_{0000}$) and the risk of acquiring illness ($\sum\Delta_R=-3.78^{0}/_{0000}$), and their combined effect was not pronounced ($\sum\Delta_{RA}=-0.51^{0}/_{0000}$) (Table 2). The average annual growth rate was T=−0.7% and the approximation value is R^2=0.3326 (Table 1).

In the female population of the country, the overall decrease ($-1.51^{0}/_{0000}$) in crude incidence rates from $12.29^{0}/_{0000}$ (2009) to $10.78^{0}/_{0000}$ (2018) (p=0.004) depended on changes in the age structure of the population ($\sum\Delta_A=+0.92^{0}/_{0000}$), the risk of acquiring illness ($\sum\Delta_R=-2.20^{0}/_{0000}$) and the combined effect of the age structure and the risk of acquiring illness ($\sum\Delta_{RA}=-0.22^{0}/_{0000}$) (T=−1.6; R^2=0.7849) (Tables 1 and 2).

Further, we will consider the results of a component analysis of the dynamics of the number of patients with GC in the whole population, in men and women (Tables 3 and 4). The results of the study show that the reduction in the number of patients with GC in the republic was associated with the influence of the following factors:

1. Growth of population number Δ_P=+651.8% (Male – Δ_P=+370.3%; Female – Δ_P=−1662.5%).

2. Changes in the age structure of the population Δ_A=+433.9% (Male – Δ_A=+281.3%; Female – Δ_A=−950.0%).

Table 2. Component Analysis of the Gastric Cancer Incidence Growth in Kazakhstan, 2009-2018

Age group (i)	ASP ($S_{ij}=N_{ij}/N_j$)		Growth ($S_{i2}-S_{i1}$) (3)−(2)	Incidence		Incidence growth			
						general ($P_{i2}-P_{i1}$)	Including due to changes of		
	2009 (S_{i1})	2018 (S_{i2})		2009 (P_{i1})	2018 (P_{i2})	(6)−(5)	Δ_A (4)×(5)	Δ_R (2)×(7)	Δ_{RA} (4)×(7)
1	2	3	4	5	6	7	8	9	10
Both sexes									
<30	0.5217	0.5011	−0.0206	0.19	0.2	0	−0.004	0.003	0
30-34	0.0761	0.0837	0.0075	2.47	1.38	−1.1	0.019	−0.082	−0.008
35-39	0.0711	0.0699	−0.0012	4.23	2.52	−1.7	−0.005	−0.121	0.002
40-44	0.0669	0.0634	−0.0036	8.6	6.09	−2.5	−0.031	−0.168	0.009
45-49	0.0689	0.0589	−0.0100	16.88	13.55	−3.3	−0.169	−0.229	0.033
50-54	0.0552	0.0559	0.0008	31.99	18.42	−13.6	0.025	−0.749	−0.010
55-59	0.0432	0.0541	0.0109	53.31	39.02	−14.3	0.58	−0.617	−0.155
60-64	0.0256	0.0399	0.0143	81.65	64.28	−17.4	1.17	−0.444	−0.249
65-69	0.0252	0.0295	0.0043	98.26	95.71	−2.6	0.423	−0.064	−0.011
70-74	0.0227	0.0144	−0.0083	140.34	125.63	−14.7	−1.167	−0.334	0.122
75-79	0.0117	0.0159	0.0042	133.96	125.48	−8.5	0.558	−0.099	−0.035
80-84	0.0082	0.0086	0.0004	107.06	108.57	1.5	0.042	0.012	0.001
85+	0.0034	0.0048	0.0013	59.92	54.23	−5.7	0.08	−0.020	−0.008
Total	$\sum S_{i1}$=1.0	$\sum S_{i2}$=1.0		P_1=16.80	P_2=15.10	−1.70	$\sum\Delta_A$=+1.51	$\sum\Delta_R$=−2.91	$\sum\Delta_{RA}$=−0.31
Male*									
Total	$\sum S_{i1}$=1.0	$\sum S_{i2}$=1.0		P_1=21.65	P_2=19.69	−1.96	$\sum\Delta_A$=+2.33	$\sum\Delta_R$=−3.78	$\sum\Delta_{RA}$=−0.51
Female*									
Total	$\sum S_{i1}$=1.0	$\sum S_{i2}$=1.0		P_1=12.29	P_2=10.78	−1.51	$\sum\Delta_A$=+0.92	$\sum\Delta_R$=−2.20	$\sum\Delta_{RA}$=−0.22

Δ_A, the age structure of the population. Δ_R, risk of acquiring illness; Δ_{RA}, risk of acquiring illness and age structure of the population; *The calculations were made in the same way as for the entire population.

3. Combined effect of changes in population number and its age structure Δ_{PA}=+58.9% (Male – Δ_{PA}=+39.1%; Female – Δ_{PA}=−125.0%).

4. Change in the risk of acquiring illness Δ_R=−832.1% (Male – Δ_R=−454.7%; Female – Δ_R=+2287.5%).

5. Combined effect of changes in the risk of acquiring illness and population number Δ_{PR}=−112.5% (Male – Δ_{PR}=−64.1%; Female – Δ_{PR}=+300.0%).

6. Combined effect of changes in the risk of acquiring illness and age structure of the population Δ_{RA}=−87.5% (Male – Δ_{RA}=−62.5%; Female – Δ_{RA}=+225.8%).

7. Combined effect of the changes in the risk of acquiring illness, population number and its age structure Δ_{RAP}=−12.5% (Male – Δ_{RAP}=−9.4%; Female – Δ_{RAP}=+29.3%).

The total increase in the absolute number of patients overall (both sexes) equals the sum of components:

n_2-n_1=365+243+33−466−63−49−7=56 or +2.1% in comparison with the primary number of patients (56÷2685×100=2.1%).

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

$$\underbrace{13.6\%+9.1\%+1.2\%}_{23.9\%}\ \underbrace{-17.4\%}\ \underbrace{-2.3\%-1.8\%-0.3\%}_{-4.4\%}\ =+2.1\%$$

Thus, GC (both sexes) is characterized by an increase in the number of cases because of the changes in the total population size and its structure (23.9% of the total increase of 2.1%). The real increase in the number of cases (risk of acquiring illness) was Δ_R=−17.4%.

The dynamics of the incidence of GC had regional characteristics. Thus, the overall increase in the GC incidence was growing only in Kostanay (+$0.03^0/_{0000}$), South Kazakhstan (+$0.39^0/_{0000}$), Mangystau (+$1.36^0/_{0000}$), and Aktobe (+$7.76^0/_{0000}$) regions. In the Aktobe region, the overall increase in the incidence of GC in the entire population was the highest from 13.350/0000 in 2009 to $21.10^0/0_{000}$ in 2018 (p=0.000) (Table 5) and primarily depended on the risk of acquiring illness ($\sum\Delta_R$=+$4.57^0/_{0000}$), secondly on changes in the age structure of the population ($\sum\Delta_A$=+$2.35^0/_{0000}$), and the combined effect of the age structure and the risk of acquiring illness reduced the indicator ($\sum\Delta_{RA}$=+$0.84^0/_{0000}$). At the same time, the average annual growth rate of the aligned indicator was T=+2.8%, and the confidence value of the approximation equaled to R^2=04435. Analyzing the role of various components, it was found (Table 5) that the growth of patients in this region is associated with demographic factors (Δ_P+A+P_A=+42.0%) and the complex influence of the risk of acquiring illness (Δ_R=+43.2%) with the components of the population size, its age structure, and the influence of all the three above-mentioned factors (Δ_R+P_R+R_A+R_{AP}=+58.1%).

Analyzing the average annual growth rate of aligned indicators of GC incidence in the entire population, the most pronounced growing was found in the Mangystau (T=+5.4%; R^2=0.4308), while the growth in 2018 was statistically significant in comparison with 2009, and the values of the accuracy of the approximation were moderate (Table 5).

Analyzing the results of the influence of various components by region for the entire population (Table 5), it was found that there is a pronounced decrease in the Kostanay region (Δ_P=−111.8%) due to changes in the population size, and the largest increase is in Atyrau region (Δ_P=+511.3%). The role of the influence of age structure in the increase in the number of patients was positive in all regions, but most pronounced ones are in the Karaganda (Δ_A=+511.4%) and Kostanay (Δ_A=+1414.3%) regions. The combined effect of changes in the population size and its age structure showed a decline only in Akmola (Δ_{PA}=−0.02%), North Kazakhstan (Δ_{PA}=−9.5%), and Kostanay (Δ_{PA}=−17.1%) regions, while in other regions there was an increase – especially in the Zhambyl (Δ_{PA}=+22.0%) and Atyrau (Δ_{PA}=+36.8%) regions.

There is a significant decrease in the absolute number of patients with GC due to the risk of acquiring illness in the majority of regions, the most pronounced are in Karaganda (Δ_R=−706.6%) and Kostanay (Δ_R=−946.8%) regions. The increase was found only in Mangystau (Δ_R=+6.5%) and Aktobe (Δ_R=+43.2%) regions.

A pronounced increase in the combined impact of the risk of acquiring illness and the population size was found in the North Kazakhstan (Δ_{PR}=+8.5%) and Kostanay (Δ_{PR}=+11.4%) regions. Changes in the risk of acquiring illness and the age structure led to a sharp decrease in the number of patients in the Kostanay region (Δ_{RA}=−455.6%), and the maximum rise was noted in Karaganda region (Δ_{RA}=+161.8%). In Atyrau region, the increase in patients due to the combined influence of the risk of acquiring illness, population size and age structure (Δ_{RAP}=+14.3%) was the highest compared to other regions.

Thus, the component analysis revealed geographical variability in the dynamics of the number of patients and the incidence of GC in Kazakhstan, which were associated with a difference in the influence of demographic factors (changes in population size, its age structure) and the risk of acquiring illness, i.e., a set of reasons that led to an increase, decrease or stabilization of the rates.

Based on the calculated GC indicators, the cartograms were compiled. The levels of CC CR based on the following criteria were determined: low – up to $14.8^{0}/_{0000}$, average – from 14.8 to $19.2^{0}/_{0000}$, high – above $19.2^{0}/_{0000}$. As a result, the following groups of regions were revealed

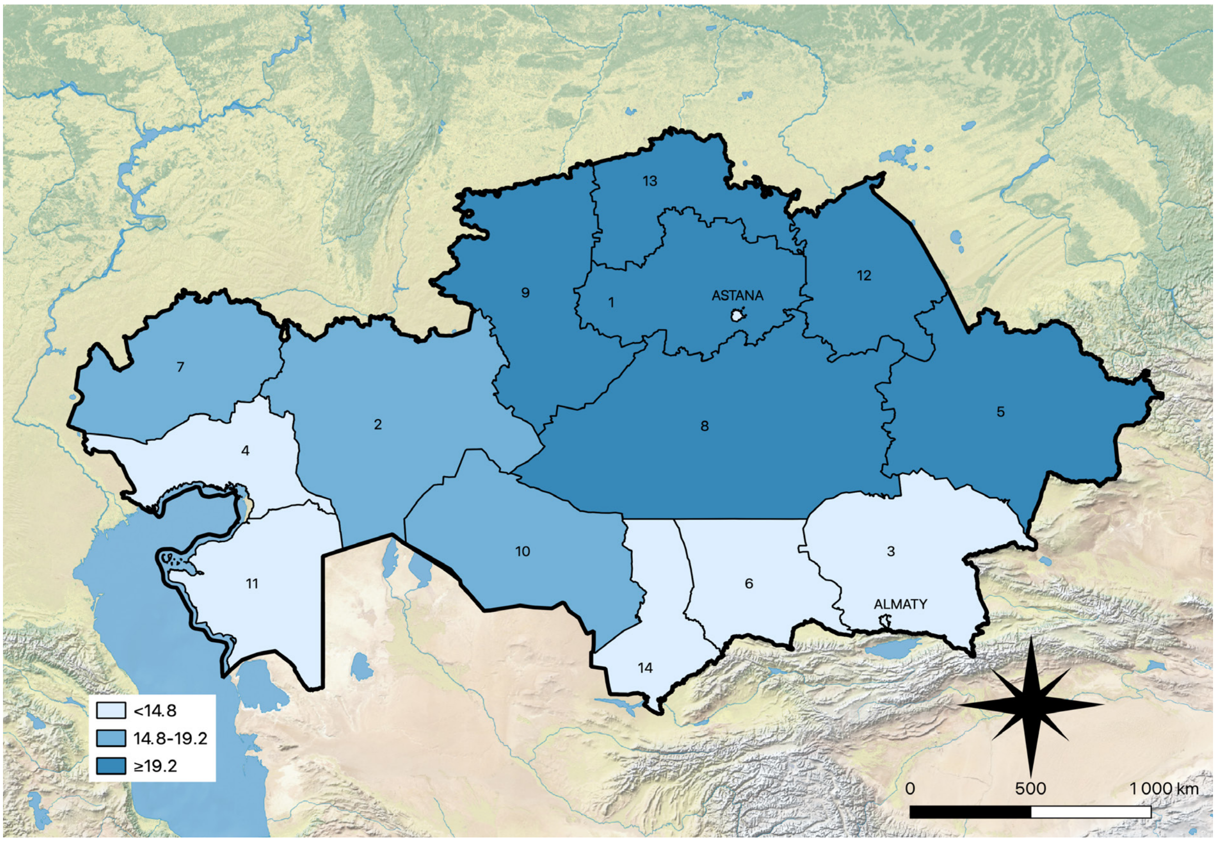

Figure 1. Cartogram of Gastric Cancer Incidence in Kazakhstan. Regions: 1. Akmola, 2. Aktobe, 3. Almaty, 4. Atyrau,5. East-Kazakhstan, 6. Zhambyl, 7. West-Kazakhstan, 8. Karaganda, 9. Kostanay, 10. Kyzylorda, 11. Mangystau, 12. Pavlodar, 13. North-Kazakhstan, 14. South-Kazakhstan

Table 3. Component Analysis of the Gastric Cancer Incidence in Dynamics in Kazakhstan, 2009-2018

Age group (i)	NCRC (n_{ij})		PN (N_{ij})		Crude (P_{ij})		Standardized (P_{ij}^{c})		END in 2018 ($P_{ij}N_{i2}10^{-5}$) (6)×(5)×10^{-5}
	2009 *(j=1)*	2018 *(j=2)*	2009 *(j=1)*	2018 *(j=2)*	2009 *(j=1)*	2018 *(j=2)*	2009 *(j=1)*	2018 *(j=2)*	
1	2	3	4	5	6	7	8	9	10
Both sex									
<30	16	18	8338308	9099474	0.19	0.20		0.103	17.5
30-34	30	21	1216653	1519070	2.47	1.38		0.105	37.5
35-39	48	32	1135971	1268564	4.23	2.52		0.179	53.6
40-44	92	70	1069726	1150288	8.60	6.09		0.407	98.9
45-49	186	145	1101902	1070014	16.88	13.55		0.934	180.6
50-54	282	187	881544	1015469	31.99	18.42		1.016	324.8
55-59	368	383	690245	981581	53.31	39.02		1.685	523.3
60-64	334	466	409084	724939	81.65	64.28		1.645	591.9
65-69	396	513	403032	536021	98.26	95.71		2.413	526.7
70-74	509	328	362684	261088	140.34	125.63		2.851	366.4
75-79	251	362	187376	288503	133.96	125.48		1.471	386.5
80-84	140	169	130769	155662	107.06	108.57		0.888	166.7
85+	33	47	55076	86664	59.92	54.23		0.187	51.9
Total	n_1=2685	n_2=2741	N_1=15982370	N_2=18157337	P_1=16.80	P_2=15.10	P_1^c=16.80	P_2^c=13.89	$E(n_2)$=3326
Growth	(n_1-n_2)/n_1 (100)=2.1		$(N_1-N_2)/N_1$(100)=13.6		$(P_1-P_2)/P_1$ 100=-10.1		$(P_1^c-P_2^c)/(P_1^c)$ 100=-17.3		
Male*									
Total	n_1=1667	n_2=1731	N_1=7698875	N_2=8791298	P_1=21.65	P_2=19.69	P_1^c=21.65	P_2^c=17.87	$E(n_2)$=2109
Growth	(n_1-n_2)/n_1 100=3.8		$(N_1-N_2)/N_1$ (100)=14.19		$(P_1-P_2)/P_1$ (100)=-9.1		$(P_1^c-P_2^c)/(P_1^c)$ (100)=-17.5		
Female*									
Total	n_1=1018	n_2=1010	N_1=8283495	N_2=9366039	P_1=12.29	P_2=10.78	P_1^c=12.29	P_2^c=10.09	$E(n_2)$=1237
Growth	$(n_1-n_2)/n_1$ (100)=-0.8		$(N_1-N_2)/N_1$ (100)=13.07		$(P_1-P_2)/P_1$(100)=-12.3		$(P_1^c-P_2^c)/(P_1^c)$ (100)=-17.9		

END, the expected number of diseases; *The calculations were made in the same way as for the entire population.

(Figure 1):

1. Regions with the lowest indicators (up to $14.8^{0}/_{0000}$): Mangistau ($10.6^{0}/_{0000}$), South Kazakhstan ($10.7^{0}/_{0000}$), Almaty ($12.2^{0}/_{0000}$), Atyrau ($12.9^{0}/_{0000}$), Zhambyl ($13.8^{0}/_{0000}$), Almaty city ($14.3^{0}/_{0000}$) and Astana city ($14.6^{0}/_{0000}$).

2. Regions with average indicators (from 14.8 to $19.2^{0}/_{0000}$): Kyzylorda ($14.8^{0}/_{0000}$), Aktobe ($18.4^{0}/_{0000}$) and West Kazakhstan ($18.4^{0}/_{0000}$).

3. Regions with high indicators ($19.2^{0}/_{0000}$ and above): Karaganda ($20.7^{0}/_{0000}$), East Kazakhstan ($21.0^{0}/_{0000}$), Kostanay ($21.8^{0}/_{0000}$), Akmola ($22.2^{0}/_{0000}$), North Kazakhstan ($22.3^{0}/_{0000}$) and Pavlodar ($23.2^{0}/_{0000}$).

Thus, the incidence cartograms more clearly reflect the spatial distribution of GC in the republic, while the discrepancy between the theoretical and actual distribution incidence by regions and cities is small, the Pearson

Table 4. Influencing Components on the Number of Cases of Gastric Cancer in Kazakhstan

Components of growth in the number of cases due to:	Both sexes			Male			Female		
	AN	%, growth		AN	%, growth		AN	%, growth	
		to (n_2-n_1)	to n_1		to (n_2-n_1)	to n_1		to (n_2-n_1)	to n_1
1. Growth PN. $\Delta_P=\frac{N_1-N_2}{N_1}n_1$	365	651.8	13.6	237	370.3	14.2	133	1662.5	13.1
2. Changes ASP. $\Delta_A=\frac{N_1}{N_2}(E(n_2)-n_2-\Delta_H$	243	433.9	9.1	180	281.3	10.8	76	950	7.5
3. Combined effect of changes in PN+ASP. $\Delta_{PA}=\frac{N_2-N_1}{N_1}\Delta_A$	33	58.9	1.2	25	39.1	1.5	10	125	1
	$\sum_{1-3}$=+1144.6		$\sum_{1-3}$=+23.9	$\sum_{1-3}$=+690.6		$\sum_{1-3}$=+26.5	$\sum_{1-3}$=+2737.5		$\sum_{1-3}$=+21.5
4. Change of RAI. $\Delta_R=N_1(P_2^c-P_1^c)\times 10^{-5}$	−466	−832.1	−17.4	−291	−454.7	−17.4	−183	−2287.5	−17.9
5. Combined effect of changes of RAI+PN. $\Delta_{RP}=\frac{N_2-N_1}{N_1}\Delta_R$	−63	−112.5	−2.3	−41	−64.1	−2.5	−24	−300	−2.4
6. Combined effect of changes of RAI+ASP. $\Delta_{RA}=\frac{N_2-N_1}{N_1}\Delta_R$	−49	−87.5	−1.8	−40	−62.5	−2.4	−18	−225.8	−1.8
7. Combined effect of the changes RAI+PN+ASP. $\Delta_{RAP}=\frac{N_1}{N_2}\left(n_2-n_1-\sum_{x=1}^{5}\right)$	−7	−12.5	−0.3	−6	−9.4	−0.4	−2	−29.3	−0.2
	$\sum_{4-7}$=−1044.6		$\sum_{4-7}$=−21.8	$\sum_{4-7}$=−590.6		$\sum_{4-7}$=−22.7	$\sum_{4-7}$=−2837.5		$\sum_{4-7}$=−22.3
Total ∑1-7	56	100	2.1	64	100	3.8	−8	100	−0.8

AN, absolute number; PN, population number; ASP, age structure of the population; RAI, risk of acquiring illness.

Table 5. Component Analysis of Gastric Cancer Incidence by Regions of Kazakhstan, 2009-2018 (both sexes)

Regions	Incidence, 0/0000		Incidence growth. $^{0}/_{0000}$				T. %	p	R^2	AN	Change/Combined. %							Total
			general*	Including due to changes of							Δ_P	Δ_A	Δ_{PA}	Δ_R	Δ_{RP}	Δ_{RA}	Δ_{RAP}	
	2009	2018		ΔA	ΔR	ΔRA												
Pavlodar	27.21	20.67	−6.55	1.95	−9.17	0.67	−1.5	0.112	0.2648	−46	7.4	31.4	0.5	−147.9	−2.5	10.9	0.2	100
Almaty city	18.72	12.32	−6.40	0.37	−7.01	0.24	−5.5	0	0.8463	−33	249.7	15.2	4.9	−289.5	−93.6	10	3.2	100
Almaty	12.8	9.91	−2.89	1.32	−3.66	−0.55	−1.5	0.007	0.1958	−31	88.1	76.8	9.1	−213.1	−25.2	−31.9	−3.8	100
Kyzylorda	17.12	14.81	−2.30	2.98	−4.79	−0.49	−2.1	0.28	0.4508	−9	181.4	191.4	26.9	−375.4	−52.9	−62.7	−8.8	100
Zhambyl	14.89	12.71	−2.18	2.28	−3.64	−0.82	−1.0	0.178	0.1128	−10	143.6	232.8	22	−371.8	−35.1	−83.6	−7.9	100
West Kazakhstan	20.22	18.09	−2.14	0.83	−2.52	−0.45	−0.3	0.397	0.0052	−4	245.6	123.5	10	−376.3	−30.6	−66.8	−5.4	100
Akmola	22.2	20.16	−2.03	2.92	−3.66	−1.29	−0.4	0.406	0.0427	−15	0.2	143.7	−0.02	−180.4	0.03	−63.4	0.01	100
Atyrau	13.75	11.76	−1.99	0.99	−3.36	0.39	−0.5	0.373	0.0092	3	511.3	167.8	36.8	−570.6	−125.0	65.4	14.3	100
North Kazakhstan	21.76	20.23	−1.53	4.13	−3.72	−1.94	−0.6	0.552	0.068	−17	−49.8	145.2	−9.5	−130.6	8.5	−68.3	4.5	100
Astana city	16.36	15.04	−1.32	2.34	−2.32	−1.34	−0.4	0.485	0.018	56	124.2	25.3	17.8	−25.0	−17.6	−14.5	−10.2	100
East Kazakhstan	20.76	19.95	−0.81	2.75	−2.68	−0.88	−0.4	0.596	0.0644	−14	−19.5	274.2	−2.6	−267.6	2.5	−87.9	0.8	100
Karaganda	20.5	20.35	−0.15	2.29	−3.16	0.72	0.2	0.953	0.0184	6	134.4	511.4	15	−706.6	−20.7	161.8	4.7	100
Kostanay	20.87	20.9	0.03	3.19	−2.14	−1.03	−0.2	1	0.0082	−2	−111.8	1414.3	−17.1	−946.8	11.4	−455.6	5.5	100
South Kazakhstan	10.39	10.79	0.39	1.54	−0.82	−0.32	−0.7	0.638	0.0684	60	80.8	63.2	12	−33.9	−6.4	−13.2	−2.5	100
Mangistau	7.87	9.24	1.36	0.9	0.31	0.15	5.4	0.464	0.4308	23	60.8	18.9	7	6.5	2.4	3.2	1.2	100
Aktobe	13.35	21.1	7.76	2.35	4.57	0.84	2.8	0	0.4435	80	16.8	22.2	3	43.2	5.8	8	1.1	100

*The table is built taking into account the sorting from A to Z of the general growth; T, average annual upward/downward rates; p, significance level. R^2, the value of the approximation confidence; AN, absolute number; Δ_P, population number; Δ_A, the age structure of the population; Δ_{PA}, population number and its age structure; Δ_R, risk of acquiring illness; Δ_{RP}, risk of acquiring illness and population number; Δ_{RA}, risk of acquiring illness and age structure of the population; Δ_{RAP}, risk of acquiring illness, population number and its age structure.

criterion (χ^2) equals 16.8.

Discussion

The results of our study show that in Kazakhstan there is a global trend of reducing the incidence of gastric cancer (Rugge et al., 2015; Siegel et al., 2014), which is certainly related to the diagnosis and successful treatment of Helicobacter pylori (Siegel et al., 2014; Fuccio et al., 2006; Lee et al., 2016). The trends of incidence reduction in the female population were characterized as more pronounced (R^2=0.7849) than in men (R^2=0.3326). It should be noted that the crude incidence rate in men ($21.1^{0}/_{0000}$) was almost 2 times higher than in women ($11.5^{0}/_{0000}$). While the standardized incidence rate in women ($10.7^{0}/_{0000}$) was three times less than in men ($31.1^{0}/_{0000}$). In our previous studies, the same pattern was revealed (Igissinov et al., 2018). Especially pronounced decrease was in men aged 55-59 (R^2=0.6589), and in women aged 60-64 (R^2=0.7287). Forman and Burley (2006), having studied the incidence rates obtained from population cancer registries around the world, found that the incidence rates in men are about twice as high as in women, and in both sexes they are closely related to age. According to GLOBOCAN 2020 similar difference in morbidity by sex was found in South Korea, China, and Iran. At the same time, there are studies explaining these sexual differences in incidence. Hormonal influences were put forward as an explanation. So, longer years of fertility and the use of hormone replacement therapy reduce the risk of stomach cancer by about 25%, while the use of tamoxifen increases the risk by about 80%, which indicates the protective effect of estrogens in the risk of gastric cancer (Camargo et al., 2012).

Early detection of GC requires financial and demographic support, as well as affordable medical services. The Updated Japanese Guidelines (2018) recommend the use of radiographic screening as population-based screening (Hamashima, 2018). The peak incidence of stomach cancer occurs in the 6th decade of human life (Uchendu and Akpo, 2021). The current guideline offers upper endoscopy for men and women aged 50 years or older (Hamashima, 2018), but the endoscopic screening coverage remains low and participation is predominantly in urban areas (Hamashima and Goto, 2017). Endoscopic examination of gastric cancer has a higher sensitivity than the radiographic method (Tsubono and Hisamichi, 2000). Endoscopy of the upper gastrointestinal tract has been recognized as the gold standard for the diagnosis of gastric cancer (Choi and Suh, 2014; Karimi et al., 2014). Both radiographic and endoscopic examinations of patients as a screening method can help to avoid the development of stomach cancer (Matsumoto et al., 2013). The endoscopic screening method reduces mortality from GC by 30% compared to the population where screening is not carried out at all (Hamashima et al., 2013). East Asian countries account for about half of stomach cancer diagnoses worldwide, and with such high incidence rates, aggressive screening programs have allowed for frequent early diagnosis and improved results. However, in Western countries, where the incidence is relatively low, screening is expensive, and stomach cancer is usually diagnosed at a relatively late stage (Johnston and Beckman, 2019). However, under various assumptions about both efficiency and cost, it has been shown that population screening for *H. pylori* and eradication of infection are cost-effective (Liou et al., 2020). Population-based programs of screening and treatment for *H. pylori* currently appear to hold the greatest promise for reducing the burden of gastric cancer (Thrift and El-Serag, 2020).

Kazakhstan is one of the regions with high incidence rates (the country maintains its leading position in terms of incidence). In this regard, endoscopic screening for early detection of esophageal and stomach cancer was introduced in Kazakhstan from 2013 to 2018 as part of a pilot project. In 2013, in such regions as: East Kazakhstan, West Kazakhstan, Kyzylorda, Pavlodar regions, the cities of Astana and Almaty. Since 2014, it has been expanded in the following regions: Aktobe, Atyrau, Karaganda, Kostanay and North Kazakhstan regions and by 2016, screening was implemented throughout the republic. Subsequently, taking into account WHO recommendations, gastric cancer was excluded from screening programs.

Higher consumption of fresh fruits and vegetables and limited intake of salt and canned foods, as well as lifestyle changes, including higher levels of physical activity and smoking restriction, can also reduce the risk of contracting this disease (IARC, 2003; Elingarami et al., 2014). Another approach is to prevent the development of GC by eradicating *H.pylori*. Studies have shown that *H. pylori* treatment can reduce the incidence of GC (Graham and Shiotani, 2005; Ford et al., 2014; Ma et al., 2012; Fukase et al., 2008).

According to a study conducted as part of the GISTAR regional pilot study, the prevalence of gastric mucosal atrophy among asymptomatic individuals in Kazakhstan was very low, although the incidence of gastric cancer and the prevalence of *H. pylori* in this area are high. This finding suggests that factors other than atrophy play a role in gastric carcinogenesis (Mezmale et al., 2019). Also, more than half of the study participants were infected with H. pylori, and the prevalence of H. pylori infection was independently associated with old age and regular high salt intake (Mezmale et al., 2021).

According to the results of the component analysis, the reduction in morbidity occurs due to a sharp decrease in the influence of risk factors, especially in men, than in women. Perhaps the male population has become less likely to drink alcohol, smoke cigarettes and eat junk food, further investigations required.

Although the incidence of GC is predicted to continue declining in a growing number of countries in the future, on a global scale the number of newly diagnosed GC cases will remain high, or increase even further, due to changes in population size and increasing risks observed in younger generations.

Cancer remains a problem with noticeable local and international differences in incidence. There is also a need for a targeted cancer screening program among the population, cancer literacy, access to basic cancer diagnostic tools and treatment facilities to ensure a reduction in morbidity and mortality from it (Uchendu 2020).

Thus, the study of GC incidence trends is of both theoretical and practical interest and plays an essential role in monitoring and assessment of screening programs implemented in the country and secondary prevention. Health authorities should consider the obtained results in the arrangement of anti-cancer activities.

Author Contribution Statement

RT, ZhT, ZhB, AZh, ZhK, SO, YK – Collection and preparation of data in the whole republic and regions (14 regions and 2 cities), primary processing of the material and their verification.

RT, ZB, GA, YK, LA, DK, KK, ZhT – Statistical processing and analysis of the material, writing the text of the article (material and methods, results).

RT, ZB, GI, KA, KO, SK, ZhA – Writing the text of the article (introduction, discussion).

NI, ML, RT, 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.

Acknowledgments

The authors greatly appreciate the contribution of the Ministry of Healthcare of the Republic of Kazakhstan to the current research by providing the data.

This study was not funded, it was performed within the framework of the Rustem Taszhanov dissertation.

Conflict of interest

The authors declare that there is no conflict of interest.

References

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

Anderson WF, Camargo MC, Fraumeni JF Jr, et al (2010). Age-specific trends in incidence of noncardia gastric cancer in US adults. *JAMA*, **303**, 1723-8.

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.

Camargo MC, Goto Y, Zabaleta J, et al (2012). Sex hormones, hormonal interventions, and gastric cancer risk: a meta-analysis. *Cancer Epidemiol Biomarkers Prev*, **21**, 20-38.

Chandanos E, Lagergren J (2008). Oestrogen and the enigmatic male predominance of gastric cancer. *Eur J Cancer*, **44**, 2397–2403.

Chissov V, Starinskiy V, Kovalev B (2007). The organization of oncological service in Russia (methodical recommendations, manuals for doctors). Moscow, 663 p. (Russian)

Choi KS, Suh M (2014). Screening for Gastric Cancer: The Usefulness of Endoscopy. *Clin Endosc*, **47**, 490–6.

Demographic Yearbook of Kazakhstan (2018). Statistical compendium. Astana.

Dvoyrin VV, Aksel EM (1987). Component analysis of the dynamics of malignant neoplasms: guidelines. Moscow, 130 p. (Russian)

Elingarami S, Liu M, Fan J, He N (2014). Applications of nanotechnology in gastric cancer: Detection and prevention by nutrition. *J Nanosci Nanotechnol*, **14**, 932–45.

Epplein M, Nomura AM, Hankin JH, et al (2008). Association of Helicobacter pylori infection and diet on the risk of gastric cancer: a case-control study in Hawaii. *Cancer Causes Control*, **19**, 869-77.

Ferlay J, Colombet M, Soerjomataram I, et al (2019). Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer*, **144**, 1941-53.

Ford AC, Forman D, Hunt RH, Yuan CY, Moayyedi P (2014). Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals: Systematic review and meta-analysis of randomised controlled trials. *BMJ*, **348**, g3174.

Forman D, Burley VJ (2006). Gastric cancer: global pattern of the disease and an overview of environmental risk factors. *Best Pract Res Clin Gastroenterol*, **20**, 633-49.

Freedman ND, Abnet CC, Leitzmann MF, et al (2007). A prospective study of tobacco, alcohol, and the risk of esophageal and gastric cancer subtypes. *Am J Epidemiol*, **165**, 1424-33.

Fuccio L, Zagari RM, Minardi ME, Bazzoli F (2007). Systematic review: Helicobacter pylori eradication for the prevention of gastric cancer. *Aliment Pharmacol Ther*, **25**, 133-41.

Fukase K, Kato M, Kikuchi S, et al (2008). Effect of eradication of Helicobacter pylori on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: An open-label, randomised controlled trial. *Lancet*, **372**, 392–7.

Glanc S (1999). Biomedical statistics. Moscow, Practice, 460.

Graham DY, Shiotani A (2005). The time to eradicate gastric cancer is now. *Gut*, **54**, 735–8.

Guggenheim DE, Shah MA (2013). Gastric cancer epidemiology and risk factors. *J Surg Oncol*, **107**, 230–6.

Hamashima C (2018). Systematic Review Group and Guideline Development Group for Gastric Cancer Screening Guidelines. Update version of the Japanese Guidelines for Gastric Cancer Screening. *Jpn J Clin Oncol*, **48**, 673-83.

Hamashima C, Goto R (2017). Potential capacity of endoscopic screening for gastric cancer in Japan. *Cancer Sci*, **108**, 101-7.

Hamashima C, Ogoshi K, Okamoto M, et al (2013). A community-based, case-control study evaluating mortality reduction from gastric cancer by endoscopic screening in Japan. *PLoS One*, **8**, e79088.

Igissinov NS, Kozhakhmetov SK, Malayev NB, et al (2018). Evaluation gastric cancer incidence in Kazakhstan. *Medicine*, **9**, 30–6.

Igissinov SI (1974). Preparation and application method of cartograms in oncology. *Healthcare Kazakhstan*, **2**, 69-71.

International Agency for Research on Cancer. IARC Handbooks of Cancer Prevention. Volume 8 IARC; Lyon, France: 2003. Fruit and vegetables.

Isabel dos Santos Silva (1999). Cancer epidemiology: principles and methods. Lyon, France, IARC, 442.

Johnston FM, Beckman M (2019). Updates on Management of Gastric Cancer. *Curr Oncol Rep*, **21**, 67.

Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F (2014). Gastric Cancer: Descriptive Epidemiology, Risk Factors, Screening, and Prevention. *Cancer Epidemiol Biomarkers Prev*, **23**, 700–13.

Krejs GJ (2010). Gastric Cancer: Epidemiology and Risk Factors. *Dig Dis*, **28**, 600–3.

Ladeiras-Lopes R, Pereira AK, Nogueira A, et al (2008). Smoking and gastric cancer: systematic review and meta-analysis of cohort studies. *Cancer Causes Control*, **19**, 689–701.

Lee YC, Chiang TH, Chou CK, et al (2016). Association Between Helicobacter pylori Eradication and Gastric Cancer Incidence: A Systematic Review and Meta-analysis. *Gastroenterology*, **150**, 1113–24.

Liou JM, Malfertheiner P, Lee YC, et al (2020). Screening and eradication of Helicobacter pylori for gastric cancer prevention: the Taipei global consensus. *Gut*, **69**, 2093-2112.

Ma JL, Zhang L, Brown LM, et al (2012). Fifteen-Year Effects of Helicobacter pylori, Garlic, and Vitamin Treatments on Gastric Cancer Incidence and Mortality. *J Natl Cancer Inst*, **104**, 488–92.

Matsumoto S, Ishikawa S, Yoshida Y (2013). Reduction of gastric cancer mortality by endoscopic and radiographic screening in an isolated island: A retrospective cohort study. *Aust J Rural Health*, **21**, 319–24.

Merkov AM, Polyakov LE (1974). Sanitary statistics. Leningrad, Medicine, 384.

Mezmale L, Isajevs S, Bogdanova I, et al (2019). Prevalence of Atrophic Gastritis in Kazakhstan and the Accuracy of Pepsinogen Tests to Detect Gastric Mucosal Atrophy. *Asian Pac J Cancer Prev*, **20**, 3825-9.

Mezmale L, Polaka I, Rudzite D, et al (2021). Prevalence and Potential Risk Factors of Helicobacter pylori Infection among Asymptomatic Individuals in Kazakhstan. *Asian Pac J Cancer Prev*, **22**, 597-602.

Miki K, Fujishiro M, Kodashima S, Yahagi N (2009). Long-term results of gastric cancer screening using the serum pepsinogen test method among an asymptomatic middle-aged japanese population. *Dig Endosc*, **21**, 78–81.

Mitelman LY (2007). Adjuvant radiation therapy of gastric cancer. Tomsk, p 17.

Nam JH, Choi IJ, Cho SJ, et al (2012). Association of the interval between endoscopies with gastric cancer stage at diagnosis in a region of high prevalence. *Cancer*, **118**, 4953–60.

Poddubny BK, Kuvshinov YP, Kashin SV, et al (2002). Modern endoscopic methods of diagnosis and treatment of precancerous pathology and early gastric cancer. *Russian J Gastroenterol*, **3**, 52-6.

Recommendations of the National Cancer Institute (USA) on the use of the World Standard (WHO 2000-2025). http://seer.cancer.gov/stdpopulations/world.who.html.

Rugge M, Fassan M, Graham DY (2015). Epidemiology of gastric cancer. In Gastric Cancer: Principles and Practice (pp. 23–34). Springer International Publishing. https://doi.org/10.1007/978-3-319-15826-6_2.

Siegel R, Ma J, Zou Z, Jemal A (2014). Cancer statistics. *CA Cancer J Clin*, **64**, 9-29.

Sitarz R, Skierucha M, Mielko J, et al (2018). Gastric cancer: epidemiology, prevention, classification, and treatment. *Cancer Manag Res*, **10**, 239–48.

Tashiro A, Sano M, Kinameri K, Fujita K, Takeuchi Y (2006). Comparing mass screening techniques for gastric cancer in Japan. *World J Gastroenterol*, **12**, 4873-4.

Trujillo-Rivera A, Sampieri CL, Morales L, Montoya A, Lamadrid-Figueroa H (2021). Prognostic Factors for Survival in Patients with Gastric Cancer Treated at Two Public Health Institutions in Mexico. *Asian Pac J Cancer Care*, 6, 429-40.

Thrift AP, El-Serag HB (2020). Burden of Gastric Cancer. *Clin Gastroenterol Hepatol*, **18**, 534-42.

Tsubono Y, Hisamichi S (2000). Screening for gastric cancer in Japan. *Gastric Cancer*, **3**, 9–18.

Uthman OA, Jadidi E, Moradi T (2013). Socioeconomic position and incidence of gastric cancer: a systematic review and meta-analysis. *J Epidemiol Community Health*, **67**, 854–60.

Uchendu O (2020). Cancer Incidence in Nigeria: A Tertiary Hospital Experience. *Asian Pac J Cancer Care*, **5**, 27-32.

Uchendu O, Akpo E (2021). Primary Gastrointestinal Tract Cancers in Nigeria, Epidemiological and Histopathological Study. *Asian Pac J Cancer Care*, **6**, 3-7.

Vannella L, Lahner E, Osborn J, Annibale B (2013). Systematic review: gastric cancer incidence in pernicious anaemia. *Aliment Pharmacol Ther*, **37**, 375–82.

Yang P, Zhou Y, Chen B, et al (2009). Overweight, obesity and gastric cancer risk: Results from a meta-analysis of cohort studies. *Eur J Cancer*, **45**, 2867–73.

Zhang Z, Xu G, Ma M, Yang J, Liu X (2013). Dietary Fiber Intake Reduces Risk for Gastric Cancer: A Meta-analysis. *Gastroenterology*, **145**, 113–20.