Gaziosmanpaşa Üniversitesi Tıp Fakültesi Dergisi 2022;14(2):61-72 Orijinal Makale

Türkiye'deki Mide Kanseri Trendlerinin Joinpoint Regresyon Analizi
Trends of Stomach Cancer with Joinpoint Regression in Turkey

Özge Pasin[1], Şirin Çetin[2], Hüseyin Evren Eren[3]

[1]Biostatistics Department, Faculty of Medicine, Bezmialem University, Turkey,

[2]Biostatistics Department, Faculty of Medicine, Tokat Gaziosmanpasa University, Turkey

[3]Amasya Şerefeddin Sabuncuoğlu Eğitim Araştırma Hastanesi, Amasya, Turkey

Corresponding author: Ozge Pasin, Biostatistics Department, Faculty of Medicine, Bezmialem University, Turkey,

E-mail: opasin@bezmialem.edu.tr

Özet

Giriş: Kanser, son yılların en önemli sağlık sorunlarından biri olmuştur. Mide kanseri ise, WHO (Dünya Sağlık Örgütü) tarafından yayınlanan verilere göre 2020 yılında 1,09 milyon yeni vaka ile dünya genelinde en sık görülen altıncı kanser türüdür. Mide kanserine yakalanma riskini artırabilecek pek çok besinin belirlenmesinin ardından mide kanseri teşhisi konulan kişi sayısında önemli bir azalma meydana gelmiştir. Bu çalışmada mide kanserine bağlı yeni vaka ve ölüm sayılarının zamana ilişkin eğilimlerin ve değişim noktalarının değerlendirilmesi amaçlanmıştır.

Gereç ve yöntem: Bu çalışmanın amacı, Türkiye'de mide kanserinde azalma eğiliminin zamana bağlı olarak değerlendirilmesidir. Bu amaçla Joinpoint Regresyon yöntemi ile mide kanserinin değişim noktaları belirlenmiştir. Çalışmadaki veriler 1990-2016 yılları arasında elde edilmiştir.

Bulgular: 1990-2016 yılları arasında hem kadınlarda hem de erkeklerde yeni vaka ve ölümlerdeki eğilim değişiklikleri istatistiksel olarak anlamlı bulunmuştur. Kadınlarda yeni vakalarda %2,6, erkeklerde düşüş %2,4 olarak belirlenmiştir. Aynı dönemde kadınlarda ölüm sayısında %3,2'lik anlamlı bir düşüş gözlenirken, erkeklerde %2,4'lük bir düşüş gözlenmiştir (tümü için $p<0,001$).

Sonuçlar: Çalışmada mide kanserine ilişkin eğilimler ortaya konmuştur. Bu yıllık eğilimleri incelemek, mide kanseri ile ilgili önlemlerin alınmasına yardımcı olacaktır. Değişim noktalarında ortaya çıkan azalmalar araştırmacılar tarafından değerlendirilebilir ve hastalık riskinin azaltılmasına yönelik önlemler alınabilir.

Anahtar kelimeler: Mide, kanser, trend, regresyon.

Abstract

Background: Cancer has been one of the most significant health problems in recent years. Stomach cancer is the sixth most common type of cancer worldwide with 1.09 million new cases in 2020, according to data published by the WHO (World Health Organization). A significant decrease has occurred in the number of individuals diagnosed with stomach cancer following the identification of many foods that may increase the risk of developing the disease. In this study, the aim was to evaluate the trends and change points related to new cases and numbers of deaths related to stomach cancer.

Material and methods: The aim of the study was to make a time-dependent evaluation of the decreasing trend for stomach cancer in Turkey. For this purpose, change points of stomach cancer were determined with Joinpoint Regression method. The data in the study were obtained between 1990–2016.

Results: The trend changes for new cases and deaths in both women and men were found to be statistically significant between 1990–2016.For women, a decrease in new cases of 2.6% was determined, while for men the decrease was 2.4%.A significant 3.2% decrease was observed in the number of deaths for women during the same period with a decrease of 2.4% for men (for all $p<0.001$).

Conclusions: The trends relating to stomach cancer were demonstrated in the study. Examining these annual trends will assist in taking relevant precautions regarding stomach cancer. The reductions revealed in the change points can be evaluated by the researchers and precautions can be taken to reduce the risk of the disease.

Key words: Stomach, cancer, trend, regression.

Makalenin başlığı: Türkiye'deki mide kanseri trendlerinin Joinpoint Regresyon analizi.

Öz

Giriş: Kanser, son yılların en önemli sağlık sorunlarından biri olmuştur. Mide kanseri ise, WHO (Dünya Sağlık Örgütü) tarafından yayınlanan verilere göre 2020 yılında 1,09 milyon yeni vaka ile dünya genelinde en sık görülen altıncı kanser türüdür. Mide kanserine yakalanma riskini artırabilecek pek çok besinin belirlenmesinin ardından mide kanseri teşhisi konulan kişi sayısında önemli bir azalma meydana gelmiştir. Bu çalışmada mide kanserine bağlı yeni vaka ve ölüm sayılarının zamana ilişkin eğilimlerin ve değişim noktalarının değerlendirilmesi amaçlanmıştır.

Gereç ve yöntem: Bu çalışmanın amacı, Türkiye'de mide kanserinde azalma eğiliminin zamana bağlı olarak değerlendirilmesidir. Bu amaçla Joinpoint Regresyon yöntemi ile mide kanserinin değişim noktaları belirlenmiştir. Çalışmadaki veriler 1990-2016 yılları arasında elde edilmiştir.

Bulgular: 1990-2016 yılları arasında hem kadınlarda hem de erkeklerde yeni vaka ve ölümlerdeki eğilim değişiklikleri istatistiksel olarak anlamlı bulunmuştur. Kadınlarda yeni vakalarda %2,6, erkeklerde düşüş %2,4 olarak belirlenmiştir. Aynı dönemde kadınlarda ölüm sayısında %3,2'lik anlamlı bir düşüş gözlenirken, erkeklerde %2,4'lük bir düşüş gözlenmiştir (tümü için $p<0,001$).

Sonuçlar: Çalışmada mide kanserine ilişkin eğilimler ortaya konmuştur. Bu yıllık

eğilimleri incelemek, mide kanseri ile ilgili önlemlerin alınmasına yardımcı olacaktır. Değişim noktalarında ortaya çıkan azalmalar araştırmacılar tarafından değerlendirilebilir ve hastalık riskinin azaltılmasına yönelik önlemler alınabilir.
Anahtar kelimeler: Mide, kanser, trend, regresyon.

Background: Cancer has been one of the most significant health problems in recent years. Stomach cancer is the sixth most common type of cancer worldwide with 1.09 million new cases in 2020, according to data published by the WHO (World Health Organization). A significant decrease has occurred in the number of individuals diagnosed with stomach cancer following the identification of many foods that may increase the risk of developing the disease. In this study, the aim was to evaluate the trends and change points related to new cases and numbers of deaths related to stomach cancer.
Material and methods: The aim of the study was to make a time-dependent evaluation of the decreasing trend for stomach cancer in Turkey. For this purpose, change points of stomach cancer were determined with Joinpoint Regression method. The data in the study were obtained between 1990–2016.
Results: The trend changes for new cases and deaths in both women and men were found to be statistically significant between 1990–2016. For women, a decrease in new cases of 2.6% was determined, while for men the decrease was 2.4%.A significant 3.2% decrease was observed in the number of deaths for women during the same period with a decrease of 2.4% for men (for all $p<0.001$).
Conclusions: The trends relating to stomach cancer were demonstrated in the study. Examining these annual trends will assist in taking relevant precautions regarding stomach cancer. The reductions revealed in the change points can be evaluated by the researchers and precautions can be taken to reduce the risk of the disease.
Key words: Stomach, cancer, trend, regression.

Introduction

Cancer has long been an important disease human life. Irregular diet, unhealthy living conditions, sedentary lifestyles, and stress all cause incidences of the disease to increase. With advances in cancer-related technologies, highly effective treatments can be applied. In recent years, personalized treatments have become common, and it is known that these methods increase patients' quality of life and reduce death rates. Despite these developments, however, cancer remains one of the most frightening diseases. Stomach cancer is the sixth most common type of cancer, with 1.09 million new cases worldwide in 2020, according to data published by the WHO. With 769.000 deaths from the disease in 2020, it ranked as the fourth most common cause of death [1-5].

Stomach cancer is an insidious disease, progressing quietly but rapidly, and its causes are not clear exactly. For example, it is known that gender affects incidences, with men having a higher risk of developing stomach cancer than women. It is also known that the risk is higher in individuals with gastritis, polyps, and other gastric disorders, and in individuals who have an unhealthy lifestyle, use alcohol and cigarettes, eat fast food, consume few fruit and vegetables, and have sedentary habits. In addition, genetic and environmental

factors also affect the risk of developing the disease. Stomach cancer is described by different names according to its occurrence in various parts of the stomach. It is difficult to diagnose the disease in the initial stages as it is a silently progressive process. In the early stages, there is a mild nausea and fatigue. However, in the advanced stages of the disease, signs include blood in the stool, difficulty in swallowing, fatigue, weight loss, bloating, stomach pain, and constant nausea and vomiting. Stool tests, intestinal x-rays, and endoscopy can all be used in the diagnosis of the disease [2-5].

In the light of recent academic studies identifying many foods that may increase the risk of stomach cancer, a significant decrease has occurred in the number of individuals with the disease. According to the information published by the American Cancer Society in 2018, smoked foods (meat, fish, and cheese), foods containing excessive salt (salted meat, fish, and canned foods), pickles, and frozen foods are on the list of items that increase the risk of stomach cancer. When people become aware of these foods and stay away from them as part of a healthy lifestyle, the risk of developing the disease decreases [5].

The aim of this study was to make a time-dependent evaluation of this decreasing trend in cases ofstomach cancer in Turkey. For this purpose, time-dependent changes and change points of stomach cancer were determined by using the Joinpoint Regression method.

Materials and methods

The study was based on the numbers of new stomach cancer cases and deaths of individuals with the disease in Turkey between 1990–2016, with data obtained using Gapminder [6]. Ethical approval was not taken in this study. Because the data was open for users.Also there is no intervation to human or animals. For death rates, the study considered the annual number of deaths due to stomach cancer per 100.000 residents. This rate is calculated as if each country has the same age composition as the world population. The annual number of new cases is also described per 100.000. The study considered the trends of deaths and new cases in both female and male patients. The Joinpoint Regression method was used in the analysis. This method is used for the analysis of time-dependent trends. In classical time series analysis, trends are usually calculated under the assumption of stable change curves. Joinpoint analysis evaluates changes that occur over time. Generally, the time-dependent trend of the disease does not remain constant because of changes in risk factors for the disease, developing treatment methods, social awareness, and government policies over time. This trend is liable to fracture at some point, and such fractures are not explained in a single model, making time series analysis unsuitable. Joinpoint analysis detects these fractures in the trend curve and creates separate models for the trends consisting of each fracture point. When determining the fractures in the model, analysis is started with the minimum number of joinpoints before the model is updated for each fracture and the significance of the models is tested. Finally, the best model is obtained, depending on the number of fractures. When used to identify trend changes between years, the Joinpoint Regression model defines two parameters: Annual Percentage Change (APC) and Average Annual Percentage Change (AAPC). APC refers to the annual percentage change of rates between trend change points, while AAPC describes the

average annual percentage change achieved over the entire period of the study.
APC is calculated via the following equation [7, 8].

$$APC = \frac{e^{b_0+b_1(x+1)} - e^{b_0+b_1x}}{e^{b_0+b_1x}} * 100$$
$$= (e^{b_1} - 1) * 100$$

To determine the parameters in the model, the natural logarithm of the rate for year x is used. For AAPC, it is obtained by taking the weighted average of the APC values calculated for each segment. If the model has no segments, that is, if the trend is stable, the APC estimation will be equal to AAPC. The Monte Carlo resampling permutation test is used to determine the number of change points, while the Bayesian Information Criterion is used in model comparisons. This study used the Joinpoint Regression Program (version 4.9.0.0,2021, Statistical Research and Applications Branch; National Cancer Institute). The statistical significance level was taken as 0.05.

Results

The numbers of new cases and deaths due to stomach cancer per 100.000 residents during the years under examination were analyzed with the Joinpoint method. For new cases, the results are seen in Table 1. Models were created separately for men and women. Figure 1 shows the trend graph for the number of new cases of stomach cancer in women annually. As seen in the graph, there are two change points for stomach cancer case numbers: 1996 and 2008. Significant decreases in the number of cases were observed for women at these breaking points (Figure 1). When the trends for men were analyzed, it was determined that the breaking point was between 1995 and 2008. It was determined that the number of cases decreased significantly from 1995–2008 and from 2008–2016 (Figure 2). When the number of stomach cancer cases in women was evaluated, it was observed that the trend between 1990 and 2016 was statistically significant (p<0.001). For women, a decrease of 2.6% was determined during this period. When evaluated according to the cut-off points, it was observed that the trend between 1990–1996 was not significant, but that the 4.4% decrease between 1996–2008 and the 1% decrease between 2008-2016 were statistically significant (respectively p<0.001; p=0.025). Considering the number of stomach cancer cases for men, a 2.4% decrease was found to be significant between 1990– 2016 (p<0.001). When the trends were evaluated according to the years 1995 and 2008, which were the breaking points for men, it was determined that there was a 3.9% decrease between 1995–2008 and a 1% decrease between 2008–2016 (p<0.001 for each) (Table 1). Table 2 contains parameter estimates of the models created for each breakpoint for men and women (Table 2).

Table 1. Joinpoint analysis result for the number of new cases of stomach cancer per 100.000 residents during the years under examination for women and men

Sex		Segment	Lower endpoint	Upper endpoint	Value	Lower CI	Upper CI	*p*
Women	APC	1	1990	1996	-1.1	-2.4	0.3	0.118
		2	1996	2008	-4.4	-4.9	-3.9	<0.001
		3	2008	2016	-1	-1.9	-0.1	0.025
	AAPC		1990	2016	-2.6	-3.1	-2.2	<0.001
Men	APC	1	1990	1995	-0.5	-1.4	0.4	0.266
		2	1995	2008	-3.9	-4.1	-3.6	<0.001
		3	2008	2016	-1	-1.4	-0.6	<0.001
	AAPC		1990	2016	-2.4	-2.6	-2.1	<0.001

Table 2. The number of new cases of stomach cancer per 100.000 residents during the years under

Sex	Parameter	Parameter Estimates	Standard Error	*P*
Women	Intercept	23.63	12.89	0.08
	Slope 1	-0.010	0.006	0.11
	Slope 2-Slope 1	-0.034	0.007	<0.001
	Slope 3-Slope 2	0.035	0.005	<0.001
Men	Intercept	12.89	8.38	0.14
	Slope 1	-0.004	0.004	0.26
	Slope 2-Slope 1	-0.034	0.004	<0.001
	Slope 3-Slope 2	0.029	0.002	<0.001

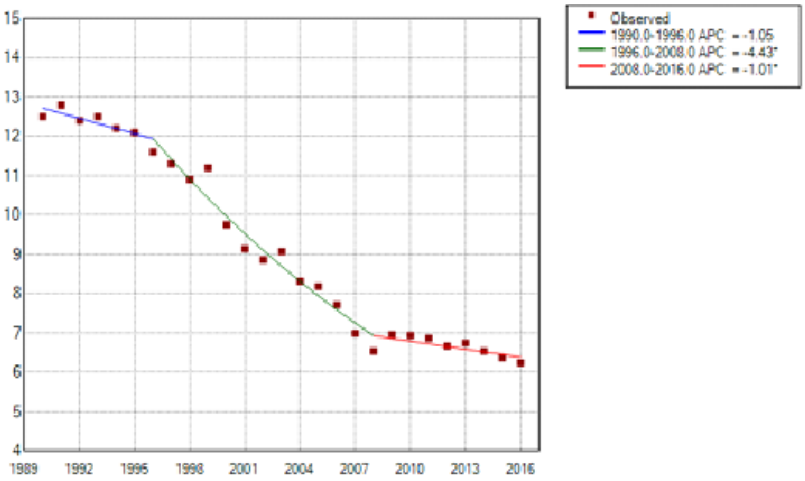

Figure 1. Trend graph for the number of new cases of stomach cancer per 100.000 residents during the years under examination for women

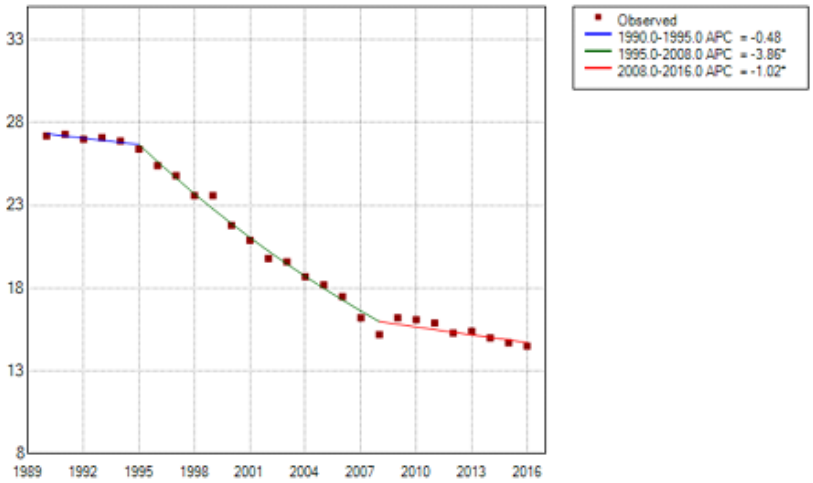

Figure 2. Trend graph for the number of new cases of stomach cancer per 100.000 residents during the years under examination for men

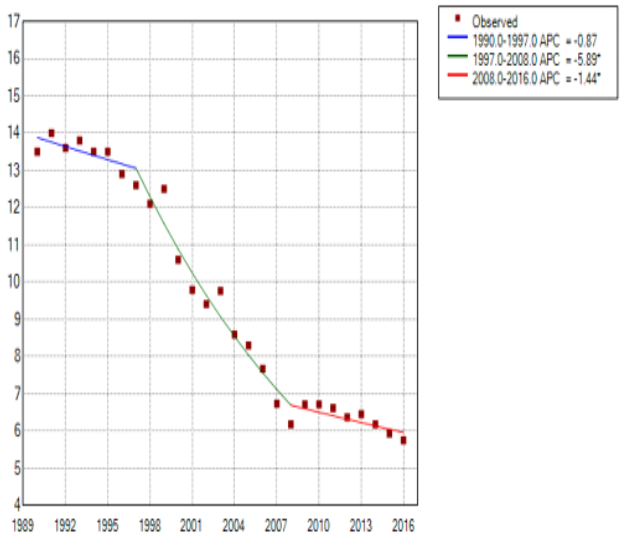

Figure 3. Trend graph for the number of death cases of stomach cancer per 100.000 residents during the years under examination for women

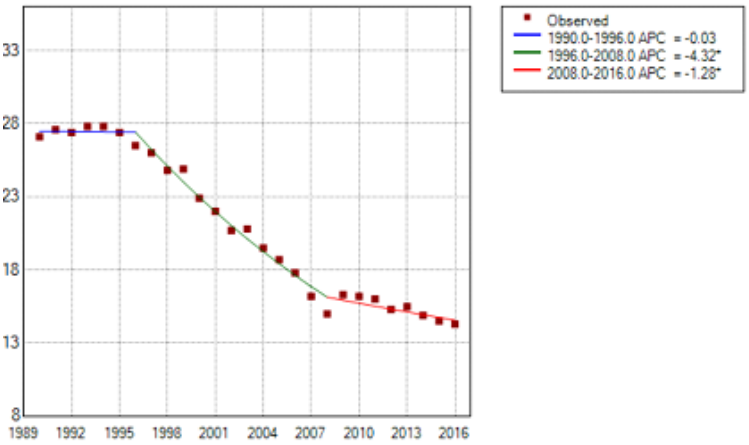

Figure 4. Trend graph for the number of death cases of stomach cancer per 100.000 residents during the years under examination for men

In the second stage of the study, the number of deaths due to stomach cancer was investigated. Trends were analyzed with the Joinpoint method and predictive values were obtained for men and women. Figures 1 and 2 show trend graphs of the number of deaths from stomach cancer for men and women. In line with the number of new cases, it was determined that there were fractures at two different points. A significant 3.2% decrease was observed in the number of deaths for women between 1990–2016 (p<0.001). Similarly, a significant decrease of 2.4% was observed

for men (p<0.001). There are two joinpoints for women, the breakpoints being 1995 and 2008. For men, these points were also identified as 1995 and 2008. In women, a decrease of 5.9% was observed between 1997–2008 and 1.4% between 2008–2016 (p<0.001, p=0.015, respectively). While a statistically significant decrease of 4.3% was observed for men between 1996–2008, and the rate of decline was 1.3% in the same period (p<0.001 for each) (Table 3). Table 4 contains parameter estimates of the models created for each breakpoint for men and women.

Table 3. Joinpoint analysis results for the number of death cases of stomach cancer per 100.000 residents during the years under examination for women and men

Sex		Segment	Lower endpoint	Upper endpoint	Value	Lower CI	Upper CI	*p*
Women	APC	1	1990	1997	-0.9	-2.2	0.5	0.201
		2	1997	2008	-5.9	-6.6	-5.1	<0.001
		3	2008	2016	-1.4	-2.5	-0.3	0.015
	AAPC		1990	2016	-3.2	-3.7	-2.6	<0.10
Men	APC	1	1990	1996	-0.0	-0.9	0.9	0.937
		2	1996	2008	-4.3	-4.7	-4	<0.001
		3	2008	2016	-1.3	-1.8	-0.7	<0.001
	AAPC		1990	2016	-2.4	-2.7	-2.1	<0.10

Table 4. The number of death cases of stomach cancer per 100.000 residents during the years under examination—trend model parameter estimate results for women and men

Sex	Parameter	Parameter Estimates	Standard Error	p
Women	Intercept	20.005	13.133	0.144
	Slope 1	-0.008	0.006	0.200
	Slope 2-Slope 1	-0.051	0.007	p<0.001
	Slope 3-Slope 2	0.046	0.006	p<0.001
Men	Intercept	3.995	8.538	0.645
	Slope 1	-0.003	0.004	0.937
	Slope 2-Slope 1	-0.043	0.005	<0.001
	Slope 3-Slope 2	0.031	0.003	<0.001

Discussion

Stomach cancer is one of the most common types of cancer and the most common cause of death in Turkey. However, with advancing treatment methods, determination of the risk factors of the disease, and the application of preventive measures, it is seen that there has been a significant decrease in the number of stomach cancer cases and deaths in recent years. With this study, an evaluation was made in relation to the number of new cases and deaths for stomach cancer over a 26-year period. Since the trends are not fixed for the time intervals, change points were determined within the period. New cases and death rates were not directly evaluated in the analysis, standardizations were made for these calculations. In terms of new cases, it was determined that the trend change in men and women according to years was similar. However, in the number of deaths, the rate of decrease in women was more rapid than in men. In general, the number of new cases and deaths from stomach cancer in men is higher than in women. The study determined that the change points for new cases of stomach cancer in Turkey were 1996 and 2008 for women, and 1995 and 2008 for men. In terms of deaths, the dates were 1997 and 2008 for women and 1996 and 2008 for men. When the trends are evaluated, a rapid decrease in the number of cases and deaths was observed from 1995–2007, while this decrease continued at lower rates in 2007 and beyond. The reason for this decrease can be shown to be rising awareness about the risk factors that may cause the disease. Studies in recent years have shown significant decreases in the number of

individuals with the determination of the risks affecting stomach cancer.

Main points

In this study, the trends relating to stomach cancer were demonstrated.

Examining these annual trends will assist in taking relevant precautions regarding stomach cancer.

The reductions revealed in the change points can be evaluated by the researchers and precautions taken to reduce the risk of the disease.

An advanced method named as joinpoint analysis was used for the calculations.

Conflict of interest: The authors declare that there is no other conflict of interest to disclose.

References

1. WHO. World Health Statistics Available from:https://www.who.int/data/gho/publications/world-health-statistics. Accessed June 02, 2021
2. Sessiz ve derinden ilerleyen bir hastalık mide kanseri. İşte Sağlık Dergisi. Erişim adresi: http://www.istesaglikdergisi.com.tr/index.php/2014/10/30/sessiz-ve-derinden-ilerleyen-bir-hastalik-mide-kanseri/. Erişim tarihi 02 Haziran 2021
3. Şendir M. Mide kanserinde beslenme. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi 2006;9:76-84.
4. Brenner H, Rothenbacher D, Arndt V. Epidemiology of stomach cancer. Methods Mol Biol 2009;472:467-477. https://doi.org/10.1007/978-1-60327-492-0_23
5. World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR). Continuous update project report: diet, nutrition, physical activity and stomach cancer 2016. London: World Cancer Research Fund International, 2018. Available at: https://www.wcrf.org/wp-content/uploads/2021/02/stomach-cancer-report.pdf. Accessed November 23, 2021
6. Animating data. Available from: http://www.gapminder.org. Accessed June 02, 2021
7. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000;19:335-351. https://doi.org/10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z
8. Dragomirescu I, Llorca J, Gómez Acebo I, Dierssen Sotos T. A join point regression analysis of trends in mortality due to osteoporosis in Spain. Sci Rep 2009;9:4264. https://doi.org/10.1038/s41598-019-40806-0

Ethics committee approval: Ethical approval was not taken in this study. Because the data was open for users.

Contributions of the authors to the article

Ö.P. constructed/constructed the main idea and hypothesis of the study. Ö.P. developed the theory and arranged/edited the material and method section. Ö. P. and Ş.Ç. and H.E. evaluated the data in the Results section. The discussion part of the article was written by Ö.P., Ş.Ç. and Ş.Ç., H.E. reviewed, made the necessary corrections and approved. In addition, all authors discussed the entire study and approved the final version.