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Analysis of Cancer Incidence and Mortality in Iran Using Joinpoint Regression Analysis

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Abstract

Background: It is important to be able to predict cancer incidence and mortality rates for planning and managing the risk factors.
Objectives: The present study investigated the changes in the incidence and mortality rates of five most common cancers in Iran.
Methods: The cancer incidence and mortality data were obtained from the national cancer and mortality registries. Five most common cancers in both men and women were selected. Changes in the incidence and mortality rates of the selected cancers in both sexes were estimated by age group, annual percent change (APC), and average APC (AAPC) and then graphically displayed.
Results: The most common cancers (except skin cancer) were breast, colorectal, stomach, esophageal, and thyroid cancers in women and stomach, prostate, bladder, colorectal, and esophageal cancers in men, respectively. The AAPCs of all cancer incidence rates had increased by 11.9% in men and 11.6% in women from 2002 to 2010. Also, the mortality rates had enhanced by 0.4% and 0.1% per year in men and women from 2006 to 2011, respectively. The greatest APC was reported in prostate cancer. The rate had increased by 41.9% from 2002 to 2004, by 13.4% from 2004 to 2008, and slowly augmented by 3.9% from 2008 to 2010. In women, the greatest APC was observed in colorectal cancer; the rate had enhanced by 13.4% per year from 2002 to 2010. The greatest increase for age-standardized mortality and incidence in 2011 was attributed to gastric cancer (12.5% and 17.1% per 100,000 men, respectively). In women, the highest age-standardized mortality rate was related to gastric cancer at 6.9% per 100,000 women. The incidence and mortality patterns of colorectal and esophageal cancers in men and women were similar, although they were slightly higher in men than women.
Conclusions: Overall, cancer incidence rates had increased in both sexes. Many factors were responsible, such as changes in lifestyle, environmental factors, increased life expectancy, improvements in the registration systems, and declining mortality rates due to early detection and treatment. The results of this study provided useful information for the prediction of changes in the incidence and mortality of cancer and subsequent design of cancer control programs in Iran.

Keywords: Neoplasm, Incidence, Mortality, Trends, Joinpoint Regression, Iran

1. Background

Cancer is a major cause of mortality worldwide. As the population advances in age, the increase in risk factors raises the burden of cancer (1). Globocan estimated that 14.1 million new cases and 8.2 million deaths occurred globally in 2012, with the burden shifting towards developing countries (2). Nevertheless, in some developed countries, a noticeable decline has occurred. For instance, in the United States, cancer mortality rate decreased from 215.1 per 100,000 persons in 1991 to 168.7 in 2011 (almost a 22% decline) (3).

The American cancer society predicts that the most common cancers in the United States include prostate, lung and bronchus, and colorectal cancers in males and breast, lung and bronchus, and colorectal cancers in females. The highest mortality rates are attributed to lung and bronchus, prostate, and colorectal cancers in males and lung and bronchus, breast, and colorectal cancers in females (3). In Europe, the most prevalent types of cancer in 2012 were breast, colorectal, prostate, and lung cancers, while the most common causes of cancer-related death were lung, colorectal, breast, and stomach cancer (4).

Cancer is the third leading cause of mortality in Iran (5). A survey in 2010 found that the five most prevalent cancers in both genders except skin cancer were stomach, esophageal, breast, prostate, and colon cancers; also, there were slight differences between genders (6). Overall, as more risk factors develop and spread, the incidence and mortality of cancer is expected to increase (7).

Studies have shown an increasing trend in the global incidence and mortality of cancer (8), especially in developing countries (9). However, some studies have reported a decreasing trend in cancer mortality (10). It is important to be able to predict the incidence and mortality of can-

cer in order to be able to plan and manage the risk factors. Trend analysis is useful for predicting such changes (11).

Although the incidence and mortality rates of cancer could be analyzed, using Poisson's regression and negative binomial regression models (12), joinpoint regression analysis allows visualization of these changes and finds the best fit for the incidence and mortality trends (13). Moreover, by using the joinpoint regression analysis, the authors can investigate the changes over distinct periods of time (14) and can measure the average annual percent change (AAPC) instead of the annual percent change (APC) (13).

APC constantly assumes the rate of changes, which could be a main limitation, as changes in some subgroups (sex, age, and race subgroups) may vary. This limitation could be more important, when the study period is lengthened. However, through applying AAPC, we can consider trend transition (13, 15).

2. Objectives

The present study investigated the changes in the incidence and mortality rates of five most prevalent cancers in Iranian males and females.

3. Methods

3.1. Data Sources

In this cross-sectional study, we analyzed the available national cancer data. Information concerning the incidence of cancer (2002 - 2010) was obtained from the national cancer registry, and morality-related data (2006 - 2011) were retrieved from the center for health network management of the ministry of health and medical education. In the national registration system of Iran, the center for disease control collects and analyzes cancer information. This center receives data about cancer patients from health centers in different cities and provinces. Due to the time lag in collecting and recording the cancer data, the latest available national data were used.

Classification and coding of cancer were based on the international classification of diseases for oncology (ICD-O) standards by the world health organization (12). Information on all cancer-related deaths, recorded in all provinces of Iran (except Tehran and Alborz), was collected from medical universities and colleges by the center for health network management and was classified and coded, based on ICD-10. Only the data related to Iranian patients in the defined period of time were examined, and data collection was performed by the first author. The population figures from 2006 and 2011 censuses were used to calculate the trends. For other years, population information by the statistical center of Iran (SCI) was applied for predictions, according to age and gender groups.

3.2. Statistical Analysis

In order to assimilate the data, all the codes were converted to ICD-10. The five most common cancers in men and women were then selected and compared. The samples were divided into 18 age groups of five years. The equal variance choice was assumed, and the maximum number of joinpoints was 2 points for cancer incidence and 1 point for mortality. The network search method (grid search method) was selected to determine the number of joinpoints. A significance level of 0.05 was applied.

The age-standardized incidence rate was calculated, using the direct standardization method and standard world population in 2000 per 100,000 people (WHO report). The incidence and mortality rates, number of new cancer cases, and deaths per year were calculated for the estimated population at risk in the same year.

To plot the graph, the easiest possible joinpoint model for cancer was fitted, using the network search technique (grid search method). Next, the minimum and maximum joinpoints were determined and their statistical significance was tested. For cancer incidence, 0 - 2 joinpoints and for mortality, 0 - 1 joinpoint were used; the results were reported, based on the maximum number of joinpoints.

APC, AAPC, and line slope were then estimated. Changes in the incidence and mortality of selected cancers for both genders and different age groups were determined, and the APC was estimated at a 95% confidence interval (CI). The latest version of joinpoint software 4.2.02 by the national cancer institute (Surveillance, epidemiology, and end results program, June 2015) was used for the analysis.

4. Results

In 2002 - 2010, a total of 514,550 cases of cancer were recorded, 55.8% of whom were men. Also, there were 175,199 cases of death due to cancer in 2006 - 2011 (66.6% were men). Table 1 shows the incidence of five main cancers for each gender. The age-standardized incidence in men and women increased over the study period (Figure 1). The AAPC based on the age-standardized incidence rate for all cancers combined increased by 11.9% for men and by 11.6% for women (Table 1). The AAPC of mortality based on the age-standardized rate increased by 0.4% for men and by 0.1% for women (Table 2). Based on the age-standardized mortality rate in 2011, death from gastric cancer was ranked first (12.5), followed by prostate (6.3),

esophageal (3.3), colorectal (3.2), and bladder (1.7) cancers (Table 3).

The highest age-standardized incidence rates in men were attributed to gastric (17.1) and prostate (13.8) cancers, which was similar to the mortality rates and ranked the highest. These cancers were followed by bladder (11.8), colorectal (11.3), and esophageal (5.6) cancers (Figure 2). In women, the highest mortality was due to gastric cancer (6.9), followed by breast (5.7), esophageal (2.4), colorectal (2.2), and thyroid (0.3) cancers (Table 3).

The highest age-standardized incidence rate in women was related to breast cancer (30.2), followed by colorectal (10.3) and gastric (8.9) cancers; esophageal and thyroid cancers ranked below gastric cancer (Figure 3). The pattern of the incidence and mortality of colorectal cancer in men and women was similar and increasing, although it was slightly higher in men than women (11.3 versus 10.3 for incidence and 3.2 versus 2.2 for mortality, respectively; Figures 1 and 4). The patterns of the incidence and mortality of esophageal cancer were similar in men and women, although they were slightly higher in men than women (Figures 1 and 4).

4.1. APC Analysis

Tables 2 and 3 show the increase or decline in the incidence and mortality rates, based on the changes in APC.

4.2. Increasing Incidence

The AAPC for the incidence of the selected cancers for men and women increased during the study period, based on the age-standardized incidence; this trend was significant at $P < 0.05$. During 2002 - 2004, the APC in women was 34.8% for gastric cancer, 27.4% for colorectal cancer, and 37.1% for esophageal cancer. The rate for all cancers increased by 27.3%, although it was not statistically significant (Table 1).

4.3. Increasing Mortality

The age-standardized rate of mortality for colorectal and prostate cancers increased in men, although the trend was not statistically significant.

4.4. Decreasing Incidence

From 2008 to 2010 (trend 3), the incidence of all cancers (except thyroid cancer in women and prostate cancer in men) was negative, and none of the APC values for cancer incidence during this period were statistically significant.

4.5. Decreasing Mortality

Despite the rise in the age-standardized incidence of esophageal and bladder cancers in men (Figures 1 and 2), the AAPC for these cancers in men showed a decreasing trend (4.9% and 3.8%, respectively), and the decline was statistically significant. The decrease in age-standardized mortality of esophageal (5.4%) and colorectal (1.2%) cancers was statistically significant in women.

5. Discussion

All cancers showed an increasing trend for the age-standardized incidence rates until 2008; these figures were significant for women and insignificant for men. After 2008, a decreasing trend was observed in both genders. A roughly steady age-standardized mortality rate was observed for all cancer sites. More precisely, there was a fairly decreasing trend from 2006 to 2009 and a slight increasing trend from 2009 to 2011, all of which were statistically significant.

The present study is the first research in Iran using the joinpoint regression model on a national scale to analyze both the incidence and mortality of cancer in Iran. In this regard, a previous study only included three provinces of Iran, namely, Gilan, Golestan, and Mazandaran. The aforementioned study in northern Iran indicated that the age-standardized incidence rate increased significantly from 2004 to 2009, with estimated AAPC values of 10.3% for Gilan, 8.5% for Mazandaran, and 5.2% for Golestan (9). In 2008, the population-based cancer registry was established in Iran by 17 universities and reported an average 16% increase in cancer incidence (16).

The high incidence rates in 2008 could be to some extent attributed to the population-based cancer registry. Moreover, recently, efforts have been made to collect as much data as possible from pathology centers; hence, higher incidence rates should be expected. Age is considered as the most important risk factor for cancer incidence (17). According to two latest censuses in Iran, the proportion of people over the age of 60 years increased from 6.6% in 1996 to 8.2% in 2011 (18). The aging population is another probable reason for the increase in cancer incidence in recent years.

The results showed an increasing trend for the age-standardized incidence of esophageal cancer from 2002 to 2008; however, this became a decreasing trend from 2008 to 2010. The increasing trends in both genders could be attributed to unknown risk factors, unhealthy dietary patterns, drinking hot beverages, and low intake of fruits and vegetables (19). Stomach cancer, e.g., esophageal cancer, has a high incidence rate in Eastern Asia, while the rates

Table 1. Trends in Age-Standardized Incidence Rates for All and Major Cancers in Iran Among Men and Women According to the Joinpoint Analysis in 2002 - 2010

	AAPC in 2002 - 2010				Trend 1		Trend 2		Trend 3	
	AAPC[a]	95% Confidence Interval		P Value	Years	APC[b]	Years	APC	Years	APC
		Lower	Upper							
Males										
All sites	11.9	9.5	14.4	0	2002 - 2004	35.1	2004 - 2008	9.5	2008 - 2010	-3
Esophagus	6.5	1.2	12.1	0	2002 - 2004	25.8	2004 - 2008	8.1	2008 - 2010	-12.6
Stomach	10.0	8.8	17.5	0	2002 - 2004	34.8[c]	2004 - 2008	6	2008 - 2010	-3.3
Colorectal	15.2	12.4	18.0	0	2002 - 2004	39.2	2004 - 2008	14.2	2008 - 2010	-2.9
Bladder	9.6	5.4	13.9	0	2002 - 2004	35.4	2004 - 2008	8.1	2008 - 2010	-8.9
Prostate	17.4	12.1	22.9	0	2002 - 2004	41.9	2004 - 2008	13.4	2008 - 2010	3.9
Female										
All sites	11.6	11.4	11.8	0	2002 - 2004	27.3[c]	2004 - 2008	10.9[c]	2008 - 2010	-0.8
Esophagus	5.9	4.9	6.9	0	2002 - 2004	27.4[c]	2004 - 2008	5.8	2008 - 2010	-11.9
Stomach	10.0	3.9	16.6	0	2002 - 2004	25.4	2004 - 2008	8.7	2008 - 2010	-1.1
Colorectal	14.4	13.4	15.5	0	2002 - 2004	37.1[c]	2004 - 2008	12.0[c]	2008 - 2010	-0.3
Breast	10.9	4.9	17.2	0	2002 - 2005	21	2005 - 2008	11.4	2008 - 2010	-3.4
Thyroid	12.9	3.0	23.7	0	2002 - 2005	26.7	2005 - 2008	6.3	2008 - 2010	3.9

[a] Average annual percent change.
[b] Annual percent change.
[c] APC is significantly different from 0 ($P < 0.05$).

Table 2. Trends in Age-Standardized Mortality Rates for All and Major Cancers in Iran Among Men and Women According to the Joinpoint Analysis in 2006 - 2011

	AAPC in 2006 - 2011				Trend 1		Trend 2	
	AAPC	95% Confidence Interval		P Value	Years	APC[a]	Years	APC
		Lower	Upper					
Males								
All sites	0.4	-5.8	7.0	0.9	2006 - 2009	-0.6	2009 - 2011	1.9
Esophagus	-4.9	-6.6	-3.2	0.0	2006 - 2008	-6.7	2008 - 2011	-3.8
Stomach	-5.5	-11.3	0.6	0.1	2006 - 2009	-2.0	2009 - 2011	-10.5
Colorectal	4.6	3.3	5.8	0.0	2006 - 2008	14.4	2008- 2011	-1.6
Bladder	-3.8	-4.5	-3.2	0.0	2006 - 2009	-3.6	2009 - 2011	-4.2
Prostate	1.6	-11.9	17.1	0.8	2006 - 2009	-2.0	2009 - 2011	-10.5
Female								
All sites	0.1	-7.7	8.6	1.0	2006 - 2009	-2.0	2009 - 2011	3.4
Esophagus	-5.4	-8.3	-2.5	0.0	2006 - 2008	-2.3	2008 - 2011	-7.4
Stomach	-5.4	-13.3	3.3	0.2	2006 - 2009	-5.1*	2009 - 2011	-5.9
Colorectal	-1.2	-1.2	-1.2	0.0	2006 - 2008	0.7*	2008 - 2011	-2.5*
Breast	3.7	-5.5	13.8	0.4	2006 - 2009	1.0	2009 - 2011	7.8
Thyroid	-1.2	-6.7	4.5	0.7	2006 - 2008	2.2	2008 - 2011	-3.5

[a] APC is significantly different from 0 ($P < 0.05$).

are low in Europe and Northern America (7). In the present study, the trend for stomach cancer showed an increasing of incidence, while mortality decreased form 2006-2011.

A previous study reported an increasing trend for the incidence of stomach cancer in both males and females (20). Explanations for the increase in incidence include higher exposure to *Helicobacter pylori* (21), unhealthy diets, consumption of salty foods, and lower rates of consumption of fruits and fresh vegetables (22). Despite the gradual decline in the global mortality rates, stomach cancer was a major cause of death in the present study for both males and females. Overall, age-standardized mortality rates in both developing and developed countries (23) show a steady decrease which could be attributed to healthier diets (24).

In the present study, the results showed that bladder cancer was the third most common cancer in males, but not among the top five most prevalent cancers in females. A previous study noted a slight decline (from 1.12 to 1.09 per 100,000) in Iran from 2006 to 2010 (25). Numerous stud-

Table 3. Crude and Age-Standardized Mortality Rates for Major Cancers in Iran Among Men and Women in 2006 - 2011

	Male				Female			
	2006		2011		2006		2011	
	CDR	ASMR	CDR	ASMR	CDR	ASMR	CDR	ASMR
All sites	56.4	70.5	65.4	75.0	35.1	45.4	43.6	48.8
Esophagus	3.3	4.3	2.8	3.3	2.3	3.0	2.0	2.4
Stomach	13.1	16.7	11.3	12.5	6.7	9.0	6.1	6.9
Colorectal	2.0	2.5	2.8	3.2	1.6	2.2	2.0	2.2
Bladder	1.6	2.0	1.4	1.7	-	-	-	-
Prostate	4.6	5.5	6.1	6.3	-	-	-	-
Thyroid	-	-	-	-	0.2	0.30	0.3	0.31
Breast	-	-	-	-	3.5	4.5	5.1	5.7

Abbreviations: CDR, crude death rate; ASMR, age-standardized mortality rate per 100,000.

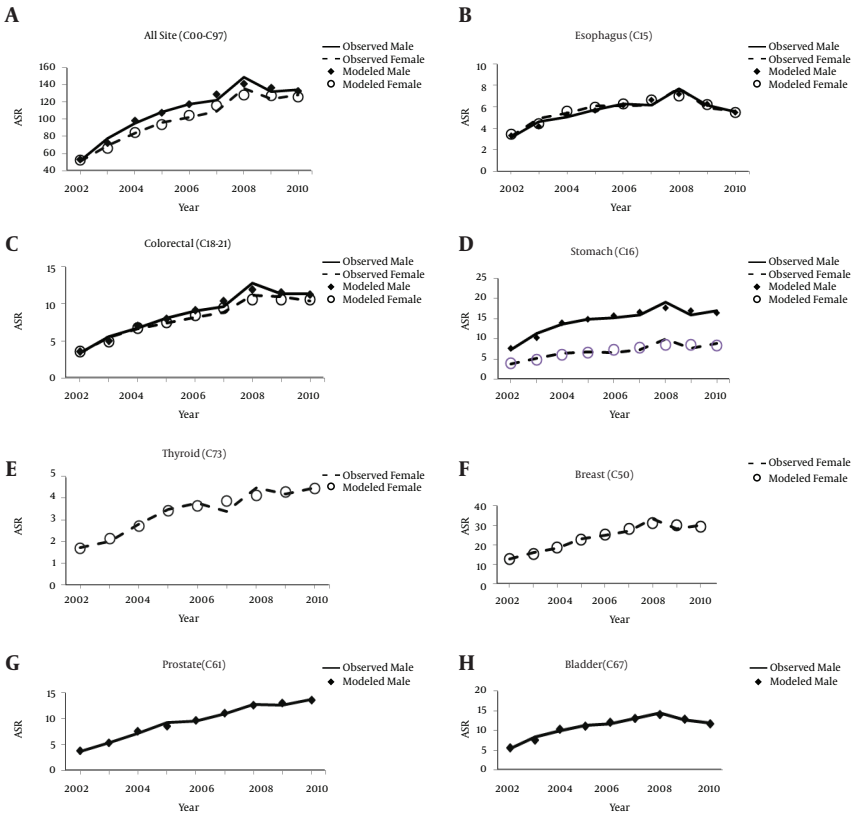

Figure 1. Observed and Modeled Age-Standardized Incidence Rates Per 100,000 Population (Males; Solid Line, Females; Dashed Line) and the 'Best' Joinpoint Model Estimates for the Selected Cancer Sites by Gender

ies have listed tobacco as a leading risk factor for bladder cancer (26, 27). Some studies have shown a decline in both bladder cancer mortality and incidence with reducing tobacco use rates (28, 29); however, there is no evidence for changes in the trend of tobacco use in Iran (30).

Globally, the incidence of thyroid cancer has increased and the mortality rate has decreased in recent decades (31, 32). Apparently, in Iran, the increase in the number of radiologists and other skilled medical specialists is the reason for the rise in the incidence rates (33), while social determinants have affected the mortality rate, as well (34). In females, breast cancer was the most common and the main cause of death from cancer globally (1). In the present study, the incidence rate increased up to 2008 and de-

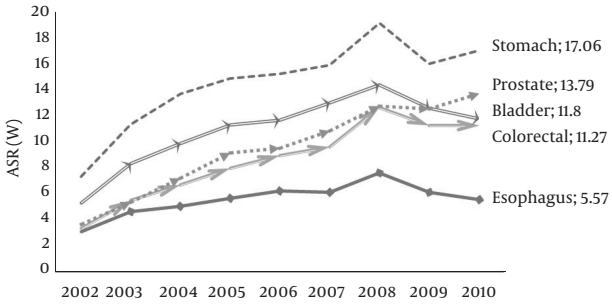

Figure 2. Trends in Age-Standardized Incidence Rates (Per 100,000 Population) of Common Cancers in Males in 2002 - 2010

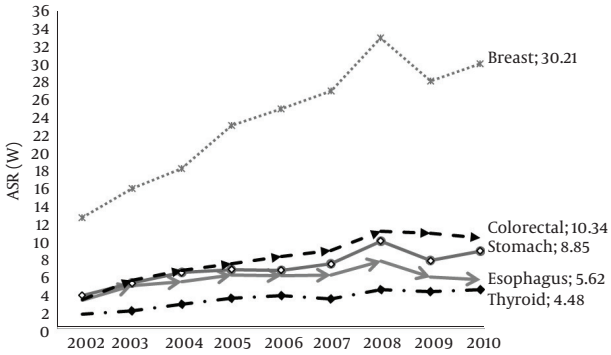

Figure 3. Trends in age-Standardized Incidence Rates (Per 100,000 Population) of Common Cancers in Females in 2002 - 2010

creased slightly afterwards. Nevertheless, another study noticed a decreasing trend in the incidence of breast cancer (35).

The increased risk of developing cancer is related to female reproductive history, such as sex-related endogenous hormones, advanced age at first live birth, and lifestyle factors such as a westernized diet and anthropometric indices, including body mass index (35). The decrease in the global incidence could be attributed to improved screening programs and mammography, as well as the decrease in hormone therapy in some countries (3, 36).

In the present study, both the incidence and mortality of prostate cancer showed increasing trends which were not significant; changes in lifestyle and aging of the population could be also held accountable (37). Despite the rise, the incidence rate of prostate cancer in Iran is lower than some developed countries, which can partly be explained by the lack of national screening programs in Iran (38).

The increasing trend in the incidence of colorectal cancer in the present study, as shown by two systematic reviews in Iran, has been reported for both genders (39, 40). The main reasons are lifestyle changes (to a western lifestyle) and increased consumption of fast foods (41). The incidence of colorectal cancer increased in conjunction with improvements in the detection of (glandular) polyps, which have been shown to be effective in developed countries (42). Overall, there is a need to implement screening and treatment programs in Iran. In a previous study, the mortality rate of colorectal cancer showed a decreasing trend (43). Early detection and cancer registry are probable reasons for the declining trend in mortality; however, one should not forget the variation in cancer incidence, obtained from cancer registries.

This study presented a comprehensive image of common cancer trends in Iran for one decade. The data analysis was based on the most developed method of time-trend analysis in the world. The results can help future studies on the accuracy of cancer registry in Iran, although completeness of the cancer registry in some parts of the country is questionable.

5.1. Limitations

The mortality data was unavailable for the period before 2006; as a result, proper comparisons could not be made between the nine-year incidence and mortality rates. Another shortcoming of the present study was the time period of the study. It should be noted that the overall change in the incidence and mortality rates of cancer is a long process.

5.2. Conclusion

Despite limitations, the results of this study could provide comprehensive information on the patterns of the incidence and mortality of cancer in Iran and could be useful for policymakers and health administrators in the development of more precise cancer control programs. Many factors are known responsible for the increasing trends in cancer incidence rates. In Iran, these include rapid changes in lifestyle and increasing exposure to risk factors. However, improved registry systems and declining mortality rates can result in early detection and treatment.

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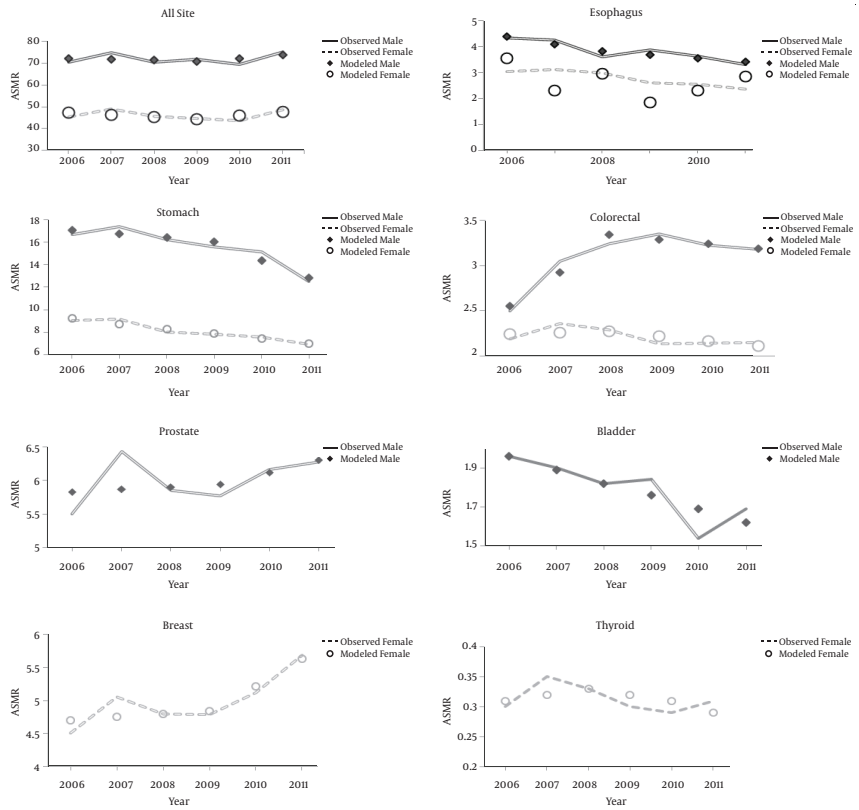
Figure 4. Observed and Modeled Age-Standardized Mortality Rates Per 100,000 Population (Males; Solid Line, Females; Dashed Line) and the 'Best' Joinpoint Model for the Selected Cancer Sites by Gender



ASMR, age-standardized mortality rate per 100,000 standard population (WHO).

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