RESEARCH COMMUNICATION

Long-term Trends in Cancer Mortality in Korea (1983-2007): A Joinpoint Regression Analysis

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Abstract

Cancer has been the most common cause of death in Korea since 1983 and is a major public concern. The aim of this study was to analyze the secular trend of cancer mortality in Korea from 1983 to 2007. Mortality and population data from 1983 to 2007 were obtained from the Korea Statistical Office. The annual cancer death rates for 18 age groups were estimated, and joinpoint regression was applied to detect significant changes in cancer mortality. The age-standardized mortality rate for all sites combined increased until the mid-1990s and has been decreasing thereafter, this also being the case for cancers of the esophagus, liver, lung and bladder, as well as leukemia. With stomach and uterine cancers a constant reduction was evident throughout the period. The declines in stomach, liver, and uterine cancer mortality have made major contributions to the recent overall favorable trend. Mortality for cancers of the colon and rectum and the prostate increased in the early 2000s and then leveled off, whereas female breast cancer mortality has displayed a constant increasing trend. In conclusion, overall cancer mortality is decreasing in men and women in Korea, and this trend will probably continue and improve further in line with advances in management as well as the expected impact of the national screening program for major five cancers over the next decades.

Keywords: Cancer - mortality - trends - joinpoint regression - Korea

Asian Pacific J Cancer Prev, **11**, 1451-1457

Introduction

Cancer has been the leading cause of death in Korea since 1983, and the annual number of cancer deaths has been increasing steadily as Korea becomes an aged society. In 2007, the number of cancer deaths was 67,561 and comprised 27.6% of total deaths (Korean Statistical Information Sevice, 2009). Because cancer is the major health concern in Korea, an accurate understanding of current trends is important for the evaluation of cancer-control programs.

Initially, mass screening of cancer was introduced in a social insurance program for very limited recipients deprived of a financial support from the government. In 1988, Pap smear was first introduced in a health examination which was serviced to the industrial workers. From 1990, cancer screening for five sites of stomach, liver, colorectal, breast and cervix was provided to applicants among government employees and teachers who willingly pay 50% of the fee for test, as part of the biennial health examination. However, these programs provided benefits to only a small numbers of persons so that target population should have been expanded, especially for medical aid people because it has been known that the lower the social economic status is, the higher the mortality and morbidity of cancer are.

In 1996, the Korean government initiated a comprehensive '10-year Plan for Cancer Control' through 2005. As part of this plan, the National Cancer Screening Program (NCSP) administered by the Ministry of Health and Welfare, was established to provide screening for gastric, breast, and cervix free of charge to medical aid recipients (4% of Korean adults) in 1999. Target population of the NCSP has been expanded to the National Health Insurance (NHI) beneficiaries within the lower 20 percent income bracket from 2002, and it expanded to lower 50% NHI premium (52% of Korean adults) since 2005 (Yoo, 2008). For the lower 50% NHI beneficiaries, 80% of the fund was raised from the NHI finance, 10% from the central government, and 10% from local government for stomach, liver, colorectal and breast screening. For cervix screening, 100% was funded from the NHI finance. The NCSP is managed and monitored by the National Cancer Center cooperating with NHI.

While the cancer screening programs is introduced and expanded during last decade, the impact of the screening program in Korea has not been evaluated intensively. The goal of cancer screening is the reduction of cancer mortality after all, so the assessment of cancer mortality is needed since the introduction of cancer screening

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program in Korea.

Joinpoint analysis has commonly been used to describe changing trends (Wingo et al., 2003; Cayuela et al., 2004; Jemal et al., 2005; Stracci et al., 2007; Aleyamma et al., 2009; Qiu et al., 2009). However, similar analyses of cancer trends have not yet been performed in Korea. We analyzed the long-term trends in cancer mortality for 12 cancer sites in men and 14 sites in women in Korea during 1983-2007. Age-truncated mortality rates for stomach, breast, uterine cervix, and colorectal and liver cancer were evaluated separately.

Materials and Methods

Mortality and population data were abstracted by sex, year, and age at death during 1983-2007 from the Korea National Statistics Office (Korean Statistical Information Sevice, 2009). Cause of death was classified according to the International Classification of Diseases 10th edition (ICD-10) (World Health Organization, 1992). Cancer sites for analysis included all cancers combined and the most common cancers: esophagus (C15), stomach (C16), colon and rectum (C18-C21), liver and intrahepatic bile duct (liver) (C22), gallbladder and other parts of billiary tract (gallbladder, etc.) (C23-C24), lung and bronchus (lung) (C33-C34), breast (C50), uterine cervix (C53-C55), ovary (C56), prostate (C61), non-Hodgkin's lymphoma (C82-C85), and leukemia (C90-C95). The cause of death between cervix and corpus uteri cancers is considered not to reach reasonable accuracy in Korea, so we combined cancer of the uterus and uterine cervix for analysis. For valid mortality data for cervical cancer, we calculated the corrected mortality for cervical cancer using the method suggested by Shin et al. (Shin et al., 2008).

Age-standardized rates (ASRs) were calculated using the WHO world standard population (Segi, 1960). Long-term trends in ASRs of cancer mortality in Korea were analyzed using the joinpoint regression model (Kim et al., 2000). Joinpoint regression was applied to detect significant changes in cancer rates. Changes in the annual age-standardized cancer rates were examined by calculating the average annual percent change (APC) and the corresponding 95% confidence interval. This method describes changes in data trends by connecting several different line segments on a log scale at 'joinpoints.' The analysis starts with the minimum number of joinpoints (i.e., 0 joinpoint, representing a straight line) and tests for model fit with a maximum of four joinpoints. Tests of significance use a Monte Carlo permutation method. The trends in cancer mortality for men and women who were of target age for screening (over 30 years for cervix, over 40 years for stomach, liver, and breast, and over 50 years for colon and rectum), were analyzed separately in order to evaluate the national screening program. The analysis was performed using Joinpoint software (version 3.3, http://srab.cancer.gov/joinpoint) from the Surveillance Research Program of the National Cancer Institute in the USA (National Cancer Institute, 2009).

We also calculated the contribution of individual cancer sites to the change in the overall cancer mortality rates based on the method presented in the annual report from the American Cancer Society (Jemal et al., 2008). The notation is as follows:

$$\frac{r_k(t_0)-r_k(t_1)}{\sum\{r_k(t_0)-r_k(t_1)\}} \times 100,$$

where $r_k(t)$ represents the mortality rate for site k in year t, t0 is the peak year, and t1 is the last year available. We used the peak year identified by the joinpoint regression model. The peak year was 1995, and last available year was 2007.

Results

The crude cancer mortality rate and ASR in males and females are presented in Figure 1. The crude rate for all cancers combined increased during the study period, but age-standardized rates turned to decreasing trends since the early 2000s and mid-1990s for men and women, respectively.

Tables 1 and 2 list the results of the joinpoint analyses by sex and cancer site, applied to mortality rates from 1983 to 2007. In males, the ASRs for all sites combined showed significant increases of 2.8% per year up to 1995, leveled off from 1998 to 2002, and decreased significantly thereafter by 3.0% per year. Among females, the rates increased significantly by 1.5% per year until 1994 and then decreased significantly thereafter.

In males, the leading cause of death was lung cancer (ASR of 39.5 per 100,000 in 2007). In males, the ASRs for lung cancer increased from 1983 to 1994, leveled off from 1994 to 2001, and then decreased significantly by 1.8%

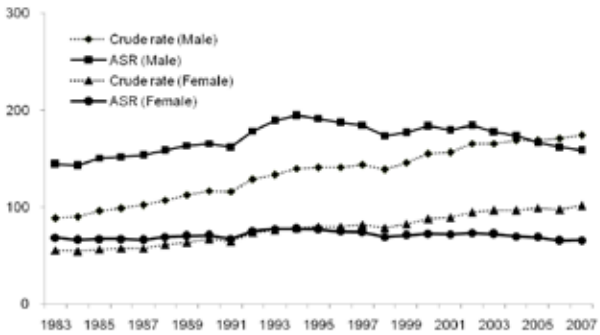

Figure 1. Trend of Crude and Age-Standardized Cancer Mortality Rates in Males and Females in Korea for 1983-2007

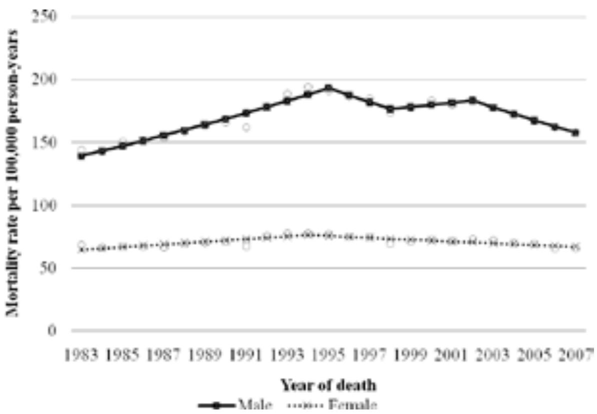

Figure 2. Observed Standardized (Per 100 000 World Standard) Rates and 'Best' Joinpoint Model Estimates for All Sites Combined in Korea, 1983-2007

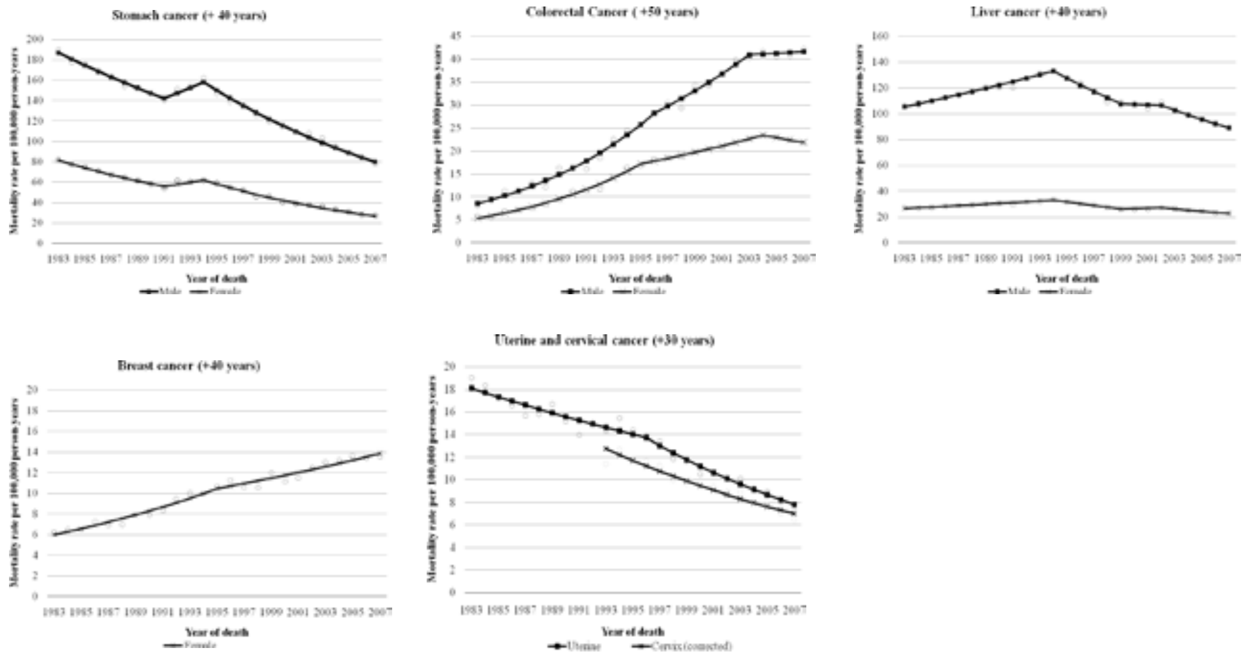

Figure 3. Observed Standardized (Per 100 000 World Standard) Rates and 'Best' Joinpoint Model Estimates for Major Cancer Sites in Korea, 1983-2007

Table 1. Trends in Cancer Mortality Per 100,000 Men by All Cancers Combined and Major Cancers in Korea for 1983-2007

Site	Line 1			Line 2			Line 3			Line 4		
	Year	APC	95% CI	Year	APC	95% CI	Year	APC	95% CI	Year	APC	95% CI
All sites	1983-1995	2.8*	2.3, 3.3	1995-1998	-3.0	-9.4, 3.8	1998-2002	1.0	-2.3, 4.3	2002-2007	-3.0*	-4.3, -1.7
Esophagus	1983-1995	3.7*	2.9, 4.6	1995-2007	-3.7*	-4.3, -3.1						
Stomach	1983-1990	-3.9*	-5.1, -2.8	1990-1993	2.3	-6.1, 11.5	1993-2007	-4.6 *	-5.0, -4.2			
Colon & rectum	1983-2002	7.7*	7.1, 8.3	2002-2007	0.9	-1.2, 3.2						
Liver	1983-1994	1.7*	1.4, 2.0	1994-1998	-5.0*	-6.9, -3.1	1998-2002	-0.7	-2.6, 1.2	2002-2007	-3.4*	-4.2, -2.6
Gallbladder, etc.	1983-1996	14.8*	12.9, 16.6	1996-2007	-0.3	-1.3, 0.7						
Pancreas	1983-1985	28.1	-6.2, 74.8	1985-1994	8.7*	6.4, 11.1	1994-2001	1.9	-0.5, 4.3	2001-2007	-1.4	-3.6, 0.6
Lung	1983-1994	9.7*	9.1, 10.2	1994-1998	0.4	-1.9, 2.8	1998-2001	3.1	-1.3, 7.6	2001-2007	-1.8*	-2.5, -1.2
Prostate	1983-2002	13.9*	12.7, 15.0	2002-2007	1.9	-0.9, 4.9						
Bladder	1983-1995	6.7*	4.9, 8.5	1995-1998	-4.2	-21.4, 16.9	1998-2002	10.5*	0.7, 21.2	2002-2007	-5.8*	-9.0, -2.3
Non-Hodgkin's lymphoma	1983-2007	4.2*	2.7, 5.8									
Leukemia	1983-1993	3.8 *	2.3, 5.2	1993-2007	-1.0*	-1.7, -0.2						

*Statistically significant compared to zero. APC, annual percent change; CI, confidence interval

per year since 2001. In females, lung cancer became the second cause of cancer death in 1997, following stomach. ASRs of lung cancer increased from 1983 to 1994, leveled off from 1995 to 2002, and decreased significantly by 1.7% per year since 2002.

In males, stomach cancer was the most common cancer until 1997 and is now the third cause of cancer death, after lung and liver. Among females, stomach cancer was the most common cancer death. ASRs for stomach cancer showed decreasing trends by 3.9 and 5.2% per year from 1983 to 1990, leveled off from 1990 to 1993, and decreased by 4.6 and 5.5% per year since 1993 in males and females, respectively; this decrease was more pronounced in women than in men.

Liver cancer was the second cause of cancer deaths in males and the third in females. For males, ASRs of liver cancer increased by 1.7% per year until 1994, began to decrease by 5.0% per year between 1994 and 1998, leveled off between 1998 and 2002, and decreased by 3.4% per year since 2002. For females, ASRs of liver

Table 2. Trends in Cancer Mortality Per 100,000 Women by All Cancers Combined and Major Cancers in Korea for 1983-2007

Site	Line 1			Line 2			Line 3			Line 4		
	Year	APC	95% CI	Year	APC	95% CI	Year	APC	95% CI	Year	APC	95% CI
All sites	1983-1994	1.5*	0.8, 2.2	1994-2007	-1.0*	-1.4, -0.5						
Esophagus	1983-1995	-0.8	-2.1, 0.5	1995-2007	-7.1*	-8.3, -5.8						
Stomach	1983-1990	-5.2*	-6.1, -4.3	1990-1993	1.2	-5.7, 8.6	1993-2007	-5.5*	-5.8, -5.2			
Colon & rectum	1983-1994	9.1*	8.1, 10.2	1994-2004	4.2*	3.5, 5.0	2004-2007	-1.6	-4.8, 1.7			
Liver	1983-1994	1.0*	0.5, 1.5	1994-1999	-5.2*	-7.2, -3.2	1999-2002	2.6	-3.8, 9.5	2002-2007	-3.7*	-5.0, -2.3
Gallbladder, etc.	1983-1992	18.7*	15.6, 21.8	1992-2001	6.1*	4.6, 7.7	2001-2007	-1.4	-3.1, 0.3			
Pancreas	1983-1994	11.2*	9.8, 12.6	1994-2007	1.3*	0.7, 1.8						
Lung	1983-1994	7.8*	6.7, 8.9	1994-2002	1.6*	0.2, 2.9	2002-2007	-1.7	-3.6, 0.2			
Breast	1983-1994	4.3*	3.2, 5.5	1994-2007	2.4*	1.8, 3.0						
Uteri	1983-1995	-2.4*	-3.2, -1.7	1995-2007	-4.6*	-5.3, -3.9						
Cervix (corrected)	1993-2007	-4.5*	-5.1, -3.9									
Ovary	1983-1993	16.5*	12.8, 20.4	1993-2007	3.2*	2.3, 4.2						
Bladder	1983-1992	7.9*	3.3, 12.7	1992-2003	2.8*	0.6, 5.2	2003-2007	-4.1	-11.2, 3.5			
Non-Hodgkin's lymphoma	1983-2007	4.6*	3.0, 6.2									
Leukemia	1983-1993	2.0*	0.8, 3.3	1993-2007	-2.0*	-2.6, -1.3						

* Statistically significant compared with zero. APC, annual percent change; CI, confidence interval

cancer increased by 1.0% per year until 1994, began to decrease by 5.2% per year between 1994 and 1999, leveled off between 1999 and 2002, and decreased by 3.7% per year since 2002.

Colorectal cancer was the fourth leading cause of cancer death in males and females. Recent trends (since 2002 in males, 2004 in females) show a leveling off of the mortality rates, following the steady increase observed previously.

The ASR of uterine cancer decreased 2.4% per year from 1983 to 1995 and 4.6% per year from 1995 to 2007.

Along with the significant increase in the incidence of prostate and female breast cancer, the mortality rates of these cancers have also increased. Mortality from prostate cancer increased significantly by 13.9% per year until 2002, and then leveled off. The mortality rate of breast cancer increased by 4.3% per year from 1983 to 1994 and by 2.4% per year from 1994 to 2007. Some cancers, such as ovarian cancer and non-Hodgkin's lymphoma, also continued to increase during the study period.

Age-standardized mortality rates of esophagus and bladder cancer and leukemia increased and then changed to decreasing trends in the mid-1990s. Similar patterns were observed in males and females.

The trend for stomach, liver, colon and rectum, female breast, uterine, and corrected cervical cancers for the screening ages in the national screening program are depicted in Figure 3. When truncated rates for the screening ages were considered, the trends were similar to those observed at all ages, and the degrees were greater than those of the all-ages group.

Table 3 shows the contribution of individual cancer sites to the total changes in mortality of all cancers combined. Overall cancer mortality rates peaked in 1995 in men and in 1994 in women. We therefore calculated the contribution using the change between 1995 and 2007 for men and for women. The overall cancer mortality rates decreased by 32.9% for men and by 14.6% for women. Stomach and liver cancer contributed 78.2% to the total decrease in cancer mortality for men. For women, stomach, cervical, and liver cancer contributed 85.4% to the total decrease in cancer mortality.

Discussion

Understanding cancer trends is important in the monitoring of cancer control and to evaluate changes in cancer risks, cancer screening modalities, and the effectiveness of health care (Wingo et al., 2003). This is the first analysis of cancer mortality trends using a joinpoint regression analysis of all cancers combined and major cancers in Korea during 1983-2007. This analysis revealed declining trends of cancer mortality in Korea since the mid 1990s. Such declines were also observed in Japan, the European Union, and the United States since 1988 (Levi et al., 2002; Levi et al., 2003; Wingo et al.,

Table 3. Age-standardized (World Population) Mortality Rates (per 100,000) from All Cancers Combined and Major Cancers in 1995 and 2007

Sites	ASM 1995	ASM 2007	Change Absolute	Change Relative	C (%)
Men					
All sites	191.1	158.2	-32.9	-17.2	
Decreasing					
Stomach	46.1	25.3	-20.7	-45.0	48.9
Liver	41.7	29.3	-12.4	-29.8	29.3
Esophagus	7.9	4.9	-3.0	-38.1	7.1
Lung	40.2	39.5	-0.7	-1.8	1.7
Leukemia	3.5	3.2	-0.3	-9.3	0.8
Bladder	2.8	2.8	0.0	0.0	0.0
Others	23.5	18.3	-5.2	-22.3	12.3
Total			-42.5		100.0
Increasing					
Colon & rectum	8.2	14.1	5.9	72.1	60.9
Prostate	1.9	4.6	2.8	147.8	28.4
Pancreas	6.7	7.1	0.4	5.7	3.9
NHL	2.5	2.9	0.4	13.9	3.6
Gallbladder, etc.	6.0	6.3	0.3	5.2	3.2
Total			9.7		100.0
Women					
All sites	76.8	65.6	-11.2	-14.6	
Decreasing					
Stomach	18.6	9.3	-9.3	-50.0	55.8
Cervix (corrected)	5.1	2.8	-2.3	-45.6	13.9
Liver	10.1	7.5	-2.6	-25.9	15.7
Leukemia	2.7	2.1	-0.6	-22.1	3.6
Esophagus	0.8	0.3	-0.5	-59.2	2.7
Others	9.9	8.6	-1.4	-13.9	8.3
Total			-17.1		100.0
Increasing					
Colon & rectum	5.3	7.4	2.1	38.5	34.6
Gallbladder, etc.	3.3	4.4	1.1	33.8	18.5
Breast	3.8	4.9	1.1	27.6	17.9
Ovary	1.6	2.3	0.7	43.4	11.6
Pancreas	3.6	4.2	0.6	16.3	9.9
NHL	1.1	1.3	0.2	21.1	3.9
Lung	9.2	9.4	0.1	1.3	2.0
Bladder	0.5	0.6	0.1	19.1	1.5
Total			5.9		100.0

ASM, Age standardized mortality; C, Contribution; NHL, Non-Hodgkin's lymphoma

2003; Qiu et al., 2009). The fall in stomach, liver and uterine cancer mortality has contributed to the overall recent favorable trend.

The stomach was the most common cancer site in Korea during 1983-2001 and is now the third most common site, after lung and colorectal cancers, in mortality rates. Northeastern asia, including Korea and Japan, has the highest stomach cancer incidence and mortality in the world (Ferlay et al., 2004), but this has been reduced markedly. The trend in stomach cancer mortality rates has been attributed to the effects of substantial improvements in food conservation, a more affluent diet with increased consumption of fresh fruit and vegetables, and the control of Helicobacter pylori infection (Howson et al., 1986; Lee et al., 2002; Levi et al., 2004; Crew and Neugut, 2006; Bertuccio et al., 2009). The 5-year survival rates of stomach cancer have increased from 43.0 to 57.0 (1993-1995 and 2001-2005) in men and from 42.6 to 55.1 in women (Ministry for Health, Welfare and Family Affairs, 2008). This relative improvement in survival is likely associated with treatment modification and early diagnosis. The national screening program for stomach cancer began in 1999 as a part of NCSP. Opportunistic screening was also relatively common, and lifetime gastric cancer screening rates were 53.5% in the 2006 Korean National Cancer Screening Survey (Kwak et al., 2008).

The reduction of liver cancer mortality since 1996 was interpreted as largely an effect of the decreasing prevalence of hepatitis B virus (HBV). HBV infection plays the major role in the etiology of liver cancer in Korea. About 70% of hepatocellular carcinoma is caused by HBV, and approximately 20% by hepatitis C virus infection in Korea (Han and Kim, 2007; Kim et al., 2008). The national HBV vaccination program since 1985 and the introduction of treatment of chronic hepatitis B might also have attributed to reducing the incidence and mortality of liver cancer. Over twenty years after the initiation of the national HBV vaccination program, the number of children testing positive for HBsAg has fallen substantially from 7-8% to 0.6% (Han and Kim, 2007). Along with this decrease in the HBsAg carrier state, the incidence of liver cancer also decreased by 2.0% annually in men and by 1.7% in women from 1999 to 2005 (Jung et al., 2009).

Mortality due to uterine cancer has been declining. Joinpoint analyses demonstrated that uterine cancer mortality rates declined significantly, by 2.4% per year from 1983 through 1995 and by 4.6% per year from 1995 through 2007. The decreasing trend in uterine cancer mortality may be due to the introduction of NPCR for cervical cancer in 1999.

Lung cancer is the third most common cancer in incidence and the most common cancer resulting in death. Our results indicate that lung cancer mortality peaked in the years 2001-2002 and began to decrease in all ages after that time. The smoking rate in Korean adult males (over 20 years) was 67.6% in 2000; however, the smoking rate in females was quite low at 3.0% (Jee, 2003). Although the smoking rate in Korean adult males was among the highest in the world, the smoking rate has decreased by 18.8% compared to 1980 (Jee, 2003). The development of treatment may also influence the reduction of mortality due to lung cancer, especially non-small-cell lung cancer (Kim et al., 2009).

Meanwhile, some cancers such as colon and rectum, prostate, and female breast cancers have increased in incidence, similar to trends observed in Japan (Qiu et al., 2009). Colorectal cancer was the second most common cancer in 2005, and the incidence increased by 7.4% annually in men and by 5.4% in women from 1999 to 2005 (Jung et al., 2009). The incidence of prostate and female breast cancer increased annually from 1999 to 2005 by 12.9% in women and by 7.1% in men and women (Jung et al., 2009). Prostate cancer remains less frequent in Korea than in Western populations (Bouchardy et al., 2008), although the mortality rate has increased rapidly recent years. Breast cancer has been the second most common cancer since 2005 after thyroid cancer; breast cancer was the fifth highest cause of cancer mortality in Korean women in 2007. Women in Korea still have relatively low incidence and mortality rates for breast cancer compared to western countries. A possible explanation for these increases is the change to a Westernized lifestyle, such as the high consumption of fat and less physical activity, as well as more early and more complete detection. Increases in breast cancer mortality could be interpreted as a result of increasing lifetime exposure to estrogen, related to earlier menarche, later menopause, later pregnancies, and lower parity (Yoo et al., 2002; Bray et al., 2004; Lee et al., 2007; McCracken et al., 2007).

Regarding the sources of bias in dealing with mortality trends, we must take into account the errors in death certification, incidence registration, and cure rates (Doll and Peto, 1981). First, errors in death certification are likely to have been reduced over the past decades with the establishment of national healthcare systems in Korea (Kwon, 2009). Especially, it is not possible to distinguish between cervix and corpus uteri cancers, though the causes of these two cancers are largely different, because a large proportion of deaths are registered as 'uterus, unspecified' in Korea (Shin et al., 2008). For this reason, we analyzed data on uterine cancer without distinguishing among cervix, corpus, and unspecified uterine cancer deaths, and analyzed cervical cancer data using a corrected method. The KNSO used the data of the Korea Central Cancer Registry in order to improve the validity of cancer death reporting since 2000, so the validity and completeness of cancer mortality data have increased since then. As a result, statistics for cancer mortality increased artificially, affecting the observed trend in cancer mortality. Some cancers, including all sites and lung cancer for men and liver cancer for women, turned to an increasing (but not significant) trend near the 2000s and decreased thereafter.

Second, errors of incidence registration have decreased due to improvements in cancer registration in Korea (Shin et al., 2005). The recent increases of the incidence rates in Korea may be partly attributable to the expanded coverage provided by the improved registration system (Won et al., 2009). Third, errors in the estimation of cure rates have changed as cancer prognosis has improved, with advances in management and early detection, improvements in cancer survival being reported (Jung et al., 2007).

In this study, joinpoint analysis demonstrated declines in all cancers combined and in the majority of observed cancers in Korea in recent years. However, the aging population and overall increases in risk of cancer have still increased the crude death rate and the absolute total number of cancer deaths in Korea. The trend in cancer mortality can be used as an important resource to plan and evaluate the cancer-control program in Korea. An effective cancer-control program including primary prevention, early detection, and treatment should thus be implemented to further reduce cancer mortality.

Acknowledgements

The authors declare no conflict of interest.

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