

Cancer Statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2011

Kyu-Won Jung, MS^{1,2}
Young-Joo Won, PhD^{1,2}
Hyun-Joo Kong, MS^{1,2}
Chang-Mo Oh, MD, PhD^{1,2}
Duk Hyoung Lee, MD, PhD²
Jin Soo Lee, MD, PhD¹

¹The Korea Central Cancer Registry,
²National Cancer Control Institute,
 National Cancer Center, Goyang, Korea

Correspondence: Young-Joo Won, PhD
 The Korea Central Cancer Registry,
 National Cancer Center, 323 Ilsan-ro,
 Ilsandong-gu, Goyang 410-769, Korea
 Tel: 82-31-920-2015
 Fax: 82-31-920-2179
 E-mail: astra67@ncc.re.kr

Received March 9, 2014
 Accepted March 18, 2014

Purpose

This study aimed to report nationwide cancer statistics in Korea, including incidence, mortality, survival, and prevalence, and their trends.

Materials and Methods

Incidence data from 1993 to 2011 were obtained from the Korea National Cancer Incidence Database, and vital status was followed through December 31, 2012. Mortality data from 1983 to 2011 were obtained from Statistics Korea. Crude and age-standardized rates for incidence, mortality, and prevalence, and relative survival were calculated.

Results

A total of 218,017 cancer cases and 71,579 cancer deaths were reported to have occurred in 2011, and there were 1,097,253 prevalent cases identified in Korea as of January 1, 2012. Over the past 13 years (1999-2011), overall incidence rates have increased by 3.4% per year. The incidence rates of liver and cervical cancers have decreased, while those of thyroid, breast, prostate, and colorectal cancers have increased. Notably, thyroid cancer increased by 23.3% per year in both sexes, and became the most common cancer since 2009. The mortality for all cancers combined decreased by 2.7% per year from 2002 to 2011. Five-year relative survival rates of patients diagnosed in the last 5 years (2007-2011) have improved by 25.1% compared with those from 1993 to 1995.

Conclusion

Overall cancer mortality rates have declined since 2002 in Korea, while incidence has increased rapidly and survival has improved.

Key words

Incidence, Mortality, Survival, Prevalence, Neoplasms, Korea

Introduction

Cancer has been the leading cause of death in Korea since 1983 [1] and is the most burdensome disease [2]. More than 200,000 new cancer cases are diagnosed in Korea each year, and cancer is responsible for one in four total deaths [3]. This article reports the most recent nationwide cancer statistics in Korea, including incidence, mortality, survival, prevalence, and their trends.

1. Data sources

The Ministry of Health and Welfare, Korea, initiated a nationwide hospital-based cancer registry called the Korea Central Cancer Registry (KCCR) in 1980. The registry collected 80-90% of cancer cases annually from more than 180 training hospitals throughout the country. In 1999, the KCCR expanded cancer registration to cover the entire population under the Population-Based Regional Cancer Registry program. Details of the history, objectives, and activities of

the KCCR have been documented elsewhere [4]. Incidence data for 1999-2011 were obtained from the Korea National Cancer Incidence Database (KNCI DB). The completeness of incidence data for 2011 was 97.1%, as determined by the Ajiki method [5].

Cancer cases were classified according to the International Classification of Diseases for Oncology, 3rd edition [6] and converted according to the International Classification of Diseases, 10th edition (ICD-10) [7]. The survival analysis used 2,197,413 cancer cases first diagnosed between 1993 and 2011 from the KNCI DB, and followed vital status until December 31, 2012.

Mortality data from 1983 to 2011 were obtained from Statistics Korea [1]. Cause of death was coded and classified according to ICD-10 [7]. Population data were also obtained from Statistics Korea using the resident registration population on July 1 of specified years.

2. Analysis

Crude rates (CRs) and age-specific rates of cancer incidence and mortality were calculated. Age-standardized rates (ASRs) were calculated using Segi's world standard population [8]. Cumulative risks of cancer, which represent the probability of developing cancer during one's lifetime, were also calculated. Changes in the annual ASRs of cancer incidence were examined by calculating the annual percentage change over a time period as $(\exp(b)-1) \times 100$, where b is the slope of the regression of log ASR for a given calendar year [9].

Prevalence was also calculated to assess cancer burden, which includes new and pre-existing cancer patients diagnosed during a given time period still alive on an index date. Using cancer incidence database data from 1999 to 2011, we defined prevalent cases as patients who were diagnosed

Table 1. 2011 Cancer incidence, prevalence, and deaths by sex in Korea

Site/Type	New cases			Deaths			Prevalent cases ^{a)}		
	Both	Male	Female	Both	Male	Female	Both	Male	Female
All sites	218,017	110,151	107,866	71,579	44,860	26,719	1,097,253	491,505	605,748
Lip, oral cavity, and pharynx	2,876	2,102	774	940	727	213	15,525	10,517	5,008
Esophagus	2,245	2,053	192	1,507	1,368	139	6,813	6,157	656
Stomach	31,637	21,344	10,293	9,719	6,321	3,398	188,995	125,526	63,469
Colon and rectum	28,112	17,157	10,955	7,660	4,351	3,309	154,816	92,236	62,580
Liver	16,463	12,189	4,274	10,946	8,226	2,720	47,698	35,689	12,009
Gallbladder ^{b)}	4,993	2,479	2,514	3,701	1,825	1,876	13,531	6,895	6,636
Pancreas	5,080	2,807	2,273	4,379	2,394	1,985	6,379	3,504	2,875
Larynx	1,108	1,042	66	387	354	33	8,143	7,651	492
Lung	21,753	15,167	6,586	15,867	11,503	4,364	48,795	31,857	16,938
Breast	16,015	73	15,942	2,018	19	1,999	117,652	523	117,129
Cervix uteri	3,728	-	3,728	989	-	989	41,077	-	41,077
Corpus uteri	1,921	-	1,921	217	-	217	13,563	-	13,563
Ovary	2,010	-	2,010	901	-	901	12,918	-	12,918
Prostate	8,952	8,952	-	1,403	1,403	0	42,157	42,157	-
Testis	226	226	-	20	20	0	1,979	1,979	-
Kidney	3,989	2,722	1,267	834	583	251	23,076	15,549	7,527
Bladder	3,549	2,847	702	1,169	853	316	23,779	19,358	4,421
Brain and CNS	1,592	847	745	1,214	663	551	8,013	4,160	3,853
Thyroid	40,568	7,006	33,562	389	116	273	215,178	33,112	182,066
Hodgkin lymphoma	259	163	96	49	36	13	1,812	1,154	658
Non-Hodgkin lymphoma	4,367	2,396	1,971	1,389	809	580	23,627	12,837	10,790
Multiple myeloma	1,050	589	461	661	357	304	3,431	1,842	1,589
Leukemia	2,862	1,598	1,264	1,557	904	653	13,672	7,527	6,145
Other and ill-defined	12,662	6,392	6,270	3,663	2,028	1,635	64,624	31,275	33,349

CNS, central nervous system. ^{a)}Limited-duration prevalent cases on January 1, 2012. These are patients who were diagnosed between January 1, 1999 and December 31, 2011 and who were alive on January 1, 2012. Multiple primary cancer cases were counted multiple times, ^{b)}Includes the gallbladder and other/unspecified parts of the biliary tract.

between January 1, 1999 and December 31, 2011, and still alive on January 1, 2012. We calculated limited-duration prevalences, namely, 1- and 5-year prevalences. For example, the 5-year prevalence was calculated as the number of people alive on January 1, 2012 who had been diagnosed with cancer within the previous 5 years. We applied this counting method using the SEER*Stat software [10] to calculate the number of cases while adjusting for patients lost to follow-up.

The survival duration for each case was determined as the interval between the date of initial diagnosis and the date of death, date of loss to follow-up, or closing date for follow-up. Observed survival rates were calculated using the life-table method and relative survival rates with the Ederer II method [11] were based on an algorithm written in SAS by Paul Dickman [12], with some minor modifications.

Selected Findings

1. Incidence

The overall number of incident cancer cases, deaths, and prevalent cases by sex and cancer site for 2011 in Korea are shown in Table 1. A total of 218,017 incident cancer cases and 71,579 deaths were reported to occur in 2011. As of January 1, 2012, 1,097,253 prevalent cancer cases diagnosed between 1999 and 2011 were identified. The cumulative risk of developing cancer during one's lifetime in 2011 was 38.1% for males and 33.8% for females.

The cancer incidence rates in 2011 by sex and cancer site are shown in Table 2. The 2011 CRs per 100,000 of all sites combined were 439.2 and 431.0 for males and females, respectively. The ASRs per 100,000 of all sites combined were 332.9 and 286.2 for males and females, respectively. In males,

Table 2. Crude and age-standardized cancer incidence rates by sex in Korea, 2011

Site/Type	Crude incidence rate per 100,000			Age-standardized incidence rate per 100,000 ^{a)}		
	Both	Male	Female	Both	Male	Female
All sites	435.1	439.2	431.0	299.8	332.9	286.2
Lip, oral cavity, and pharynx	5.7	8.4	3.1	4.0	6.3	2.1
Esophagus	4.5	8.2	0.8	3.0	6.2	0.4
Stomach	63.1	85.1	41.1	42.5	63.3	25.1
Colon and rectum	56.1	68.4	43.8	37.8	51.4	26.4
Liver	32.9	48.6	17.1	22.2	35.6	10.3
Gallbladder ^{b)}	10.0	9.9	10.0	6.4	7.6	5.5
Pancreas	10.1	11.2	9.1	6.6	8.5	5.1
Larynx	2.2	4.2	0.3	1.5	3.1	0.2
Lung	43.4	60.5	26.3	28.3	46.0	15.1
Breast	32.0	0.3	63.7	22.2	0.2	43.8
Cervix uteri	7.4	-	14.9	5.2	-	10.1
Corpus uteri	3.8	-	7.7	2.7	-	5.3
Ovary	4.0	-	8.0	2.9	-	5.7
Prostate	17.9	35.7	-	11.8	27.4	-
Testis	0.5	0.9	-	0.5	0.9	-
Kidney	8.0	10.9	5.1	5.6	8.1	3.4
Bladder	7.1	11.4	2.8	4.6	8.7	1.5
Brain and CNS	3.2	3.4	3.0	2.7	3.0	2.4
Thyroid	81.0	27.9	134.1	58.3	20.2	96.8
Hodgkin lymphoma	0.5	0.6	0.4	0.5	0.6	0.4
Non-Hodgkin lymphoma	8.7	9.6	7.9	6.5	7.7	5.5
Multiple myeloma	2.1	2.3	1.8	1.4	1.8	1.1
Leukemia	5.7	6.4	5.1	5.2	6.1	4.5
Other and ill-defined	25.3	25.5	25.1	17.8	20.3	15.7

CNS, central nervous system. ^{a)}Age-adjusted using the world standard population, ^{b)}Includes the gallbladder and other/unspecified parts of the biliary tract.

Table 3. The top 10 leading causes of death in Korea for 2011

Rank	Cause of death	No. of deaths	Percentage of all deaths	Age-standardized death rate per 100,000 ^{a)}
	All causes	257,396	100.0	331.9
1	Cancer	71,579	27.8	91.8
2	Cerebrovascular disease	25,404	9.9	30.3
3	Heart disease	24,944	9.7	30.5
4	Intentional self-harm (suicide)	15,906	6.2	23.4
5	Diabetes mellitus	10,775	4.2	13.0
6	Pneumonia	8,606	3.3	10.2
7	Chronic lower respiratory diseases	6,959	2.7	8.0
8	Disease of liver	6,751	2.6	9.0
9	Transport accidents	6,316	2.5	9.7
10	Hypertensive diseases	5,038	2.0	5.9
	Others	75,118	29.2	99.9

Source: Mortality data, 2011, Statistics Korea [1]. ^{a)}Age-adjusted using the world standard population.

the five leading primary cancer sites were stomach (CR, 85.1; ASR, 63.3), colon and rectum (CR, 68.4; ASR, 51.4), lung (CR, 60.5; ASR, 46.0), liver (CR, 48.6; ASR, 35.6), and prostate (CR, 35.7; ASR, 27.4), which together accounted for 67.9% of all newly diagnosed cancers in 2011. In females, the most common cancer site was thyroid (CR, 134.1; ASR, 96.8), followed by breast (CR, 63.7; ASR, 43.8), colon and rectum (CR, 43.8; ASR, 26.4), stomach (CR, 41.1; ASR, 25.1), and lung (CR, 26.3; ASR, 15.1), which together accounted for 71.7% of all newly diagnosed cancers. Thyroid cancer alone accounted for 31.1% of incident cases (n=33,562) among females in 2011.

2. Mortality

A total of 71,579 cancer deaths were reported in Korea for 2011, accounting for 27.8% of all deaths (Table 3). In 2011, the CRs per 100,000 for all sites combined were 178.9 and 106.7 in males and females, respectively. The ASRs per 100,000 for all sites combined were 137.3 and 59.1 for males and females, respectively. Cancers of the lung, liver, stomach, and colon/rectum were the main leading causes of cancer death, together accounting for approximately 61.7% of all cancer deaths in 2011 (Table 4).

In males, the five most common sites of cancer death in 2011 were lung (CR, 45.9; ASR, 35.0), liver (CR, 32.8; ASR, 24.3), stomach (CR, 25.2; ASR, 19.3), colon and rectum (CR, 17.3; ASR, 13.4), and pancreas (CR, 9.5; ASR, 7.3). In women, lung cancer (CR, 17.4; ASR, 9.1) was the leading cause of cancer death in 2011, followed by stomach (CR, 13.6; ASR, 7.1), colon and rectum (CR, 13.2; ASR, 6.9), liver (CR, 10.9; ASR, 6.1), and breast (CR, 8.0; ASR, 5.2).

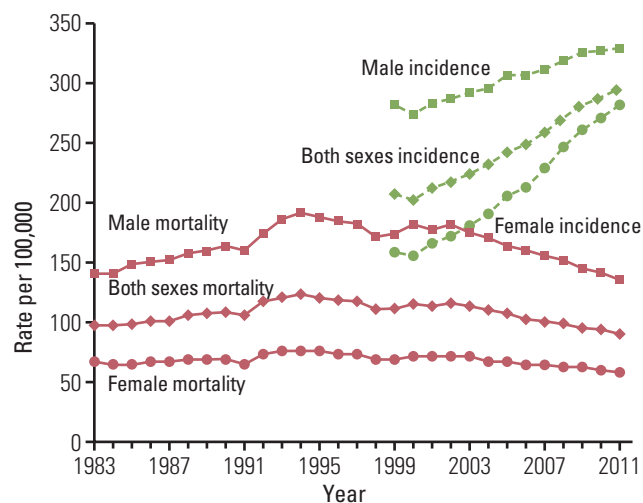


Fig. 1. Annual age-standardized cancer incidence and death rates by sex for all sites from 1983 to 2011 in Korea. Age standardization was based on the world standard population.

3. Trends in cancer incidence

The cancer incidence rates from 1999 to 2011 in Korea for all sites combined and for selected sites are shown in Tables 5-7. The incidence for all sites combined increased by 3.4% per year (1.6% in males, 5.4% in females) from 1999 to 2011. The rapid increase in cancer incidence is also illustrated in Fig. 1.

The incidence rates for colorectal and thyroid cancers have continued to increase in both sexes, as have those for prostate cancer in males and breast cancer in females (Fig. 2).

Table 4. Crude and age-standardized cancer mortality rates by sex in Korea, 2011

Site/Type	Crude mortality rate per 100,000			Age-standardized mortality rate per 100,000 ^{a)}		
	Both	Male	Female	Both	Male	Female
All sites	142.8	178.9	106.7	91.8	137.3	59.1
Lip, oral cavity, and pharynx	1.9	2.9	0.9	1.2	2.2	0.5
Esophagus	3.0	5.5	0.6	1.9	4.1	0.3
Stomach	19.4	25.2	13.6	12.3	19.3	7.1
Colon and rectum	15.3	17.3	13.2	9.6	13.4	6.9
Liver	21.8	32.8	10.9	14.5	24.3	6.1
Gallbladder ^{b)}	7.4	7.3	7.5	4.6	5.7	3.8
Pancreas	8.7	9.5	7.9	5.6	7.3	4.2
Larynx	0.8	1.4	0.1	0.5	1.1	0.1
Lung	31.7	45.9	17.4	19.8	35.0	9.1
Breast	4.0	0.1	8.0	2.7	0.1	5.2
Cervix uteri	2.0	-	4.0	1.3	-	2.3
Corpus uteri	0.4	-	0.9	0.3	-	0.6
Ovary	1.8	-	3.6	1.2	-	2.2
Prostate	2.8	5.6	-	1.6	4.6	-
Testis	0.0	0.1	-	0.0	0.1	-
Kidney	1.7	2.3	1.0	1.1	1.8	0.5
Bladder	2.3	3.4	1.3	1.4	2.7	0.6
Brain and CNS	2.4	2.6	2.2	1.8	2.2	1.5
Thyroid	0.8	0.5	1.1	0.5	0.4	0.5
Hodgkin lymphoma	0.1	0.1	0.1	0.1	0.1	0.0
Non-Hodgkin lymphoma	2.8	3.2	2.3	1.8	2.5	1.3
Multiple myeloma	1.3	1.4	1.2	0.9	1.1	0.7
Leukemia	3.1	3.6	2.6	2.4	3.0	1.8
Other and ill-defined	7.3	8.1	6.5	4.8	6.3	3.7

CNS, central nervous system. ^{a)}Age-adjusted using the world standard population, ^{b)}Includes the gallbladder and other/unspecified parts of the biliary tract.

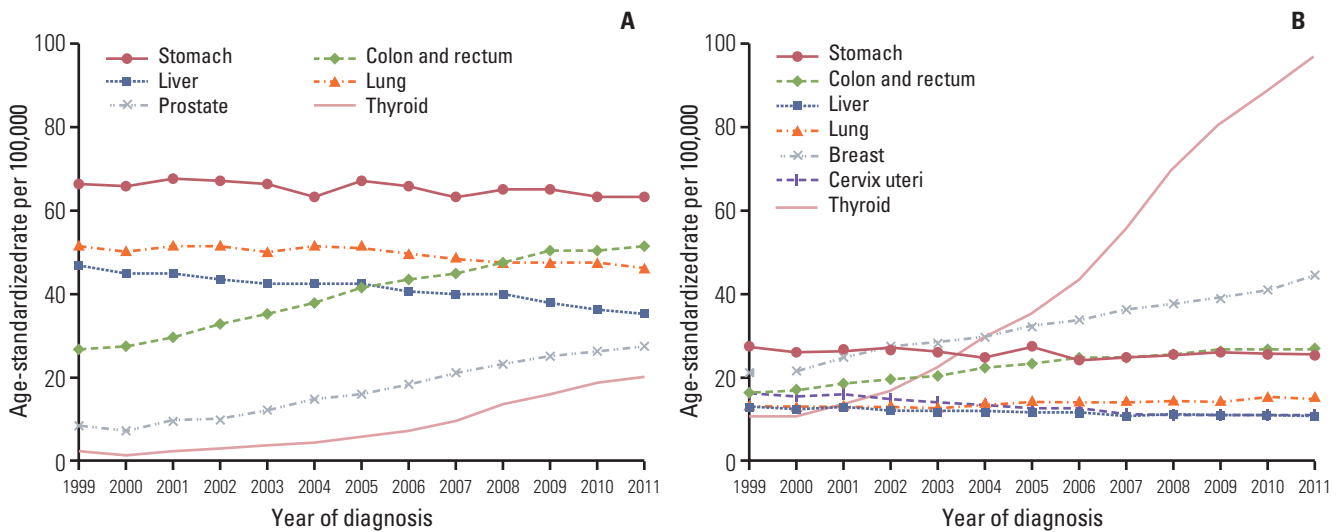


Fig. 2. Trends in age-standardized incidences of selected cancers by sex from 1999 to 2011 in Korea. Age standardization was based on the world standard population. (A) Male. (B) Female.

Table 5. Trends in cancer incidence rates for both sexes from 1999 to 2011 in Korea

Site/Type	Year											APC		
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009		2010	2011
All sites	210.5	205.1	216.7	220.1	227.6	234.8	247.7	251.8	262.9	275.2	285.9	291.5	299.8	3.4 ^{a)}
Lip, oral cavity, and pharynx	3.6	4.4	3.6	3.7	3.8	3.8	3.8	3.8	3.9	4.0	3.8	3.9	4.0	0.4
Esophagus	4.1	3.7	3.9	3.8	3.6	3.6	3.5	3.4	3.3	3.3	3.1	3.1	3.0	-2.2 ^{a)}
Stomach	43.6	42.3	44.0	43.6	43.2	41.2	44.4	42.8	41.8	42.5	43.3	42.3	42.5	-0.2
Colon and rectum	20.4	21.0	22.9	24.7	26.8	28.6	30.9	32.4	33.7	34.8	36.8	36.7	37.8	5.6 ^{a)}
Liver	27.9	26.7	27.3	26.5	25.7	25.6	25.8	24.6	24.4	24.0	23.5	22.7	22.2	-1.8 ^{a)}
Gallbladder ^{b)}	6.5	6.4	6.7	6.7	6.7	6.9	7.1	6.6	6.6	6.4	6.8	6.6	6.4	-0.1
Pancreas	5.6	5.5	5.5	5.8	5.9	6.0	6.3	6.2	6.3	6.4	6.3	6.4	6.6	1.5 ^{a)}
Larynx	2.3	2.2	2.4	2.2	2.1	1.9	2.0	1.8	1.8	1.7	1.7	1.6	1.5	-3.6 ^{a)}
Lung	28.5	27.7	28.3	28.5	27.9	28.8	29.0	28.7	28.4	28.2	28.2	28.4	28.3	0.0
Breast	10.7	10.8	12.7	13.9	14.2	15.0	16.3	16.9	18.1	18.9	19.6	20.5	22.2	6.1 ^{a)}
Cervix uteri	8.5	7.9	8.3	7.7	7.4	6.8	6.4	6.3	5.7	5.9	5.5	5.6	5.2	-4.2 ^{a)}
Corpus uteri	1.4	1.3	1.5	1.7	1.9	1.9	2.0	2.1	2.1	2.4	2.6	2.6	2.7	5.9 ^{a)}
Ovary	2.7	2.5	2.5	2.6	2.7	2.7	2.8	2.8	3.1	2.9	2.8	3.0	2.9	1.3 ^{a)}
Prostate	3.1	2.7	3.6	3.9	4.8	6.0	6.3	7.3	8.6	9.8	10.6	11.0	11.8	13.8 ^{a)}
Testis	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.5	4.3 ^{a)}
Kidney	3.0	2.9	3.3	3.4	3.5	3.7	4.1	4.4	4.8	5.0	5.2	5.3	5.6	6.0 ^{a)}
Bladder	4.6	4.6	4.9	4.7	5.1	5.1	5.1	4.9	5.0	4.8	4.6	4.6	4.6	-0.2
Brain and CNS	2.9	2.8	2.8	2.6	2.9	2.9	3.0	2.9	3.1	3.0	3.0	3.0	2.7	0.5
Thyroid	6.3	6.1	7.9	9.5	12.8	17.2	20.7	25.4	32.8	41.3	48.0	53.5	58.3	23.3 ^{a)}
Hodgkin lymphoma	0.2	0.3	0.3	0.3	0.3	0.4	0.3	0.3	0.4	0.4	0.4	0.4	0.5	4.9 ^{a)}
Non-Hodgkin lymphoma	4.5	4.2	4.5	4.6	4.9	5.3	5.3	5.5	5.6	5.6	6.1	6.1	6.5	3.5 ^{a)}
Multiple myeloma	1.0	1.0	1.1	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.5	1.5	1.4	3.6 ^{a)}
Leukemia	4.7	4.3	4.7	4.8	4.8	4.8	4.7	4.9	4.8	5.0	5.1	5.0	5.2	1.1 ^{a)}
Other and ill-defined	14.3	13.5	13.9	13.5	15.2	15.2	16.2	16.1	17.1	17.0	17.0	17.3	17.8	2.4 ^{a)}

APC was calculated using age-standardized incidence data based on the world standard population. APC, annual percentage change; CNS, central nervous system. ^{a)}Significantly different from zero ($p < 0.05$). ^{b)}Includes the gallbladder and other / unspecified parts of the biliary tract.

Table 6. Trends in cancer incidence rates in males from 1999 to 2011 in Korea

Site/Type	Year											APC		
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009		2010	2011
All sites	285.0	276.7	288.3	290.0	294.8	299.4	311.3	310.0	316.4	323.3	329.8	329.7	332.9	1.6 ^{a)}
Lip, oral cavity, and pharynx	6.1	7.1	6.0	6.2	6.5	6.2	6.1	6.1	6.3	6.5	6.1	6.1	6.3	0.3
Esophagus	8.8	8.0	8.3	8.2	7.7	7.7	7.6	7.2	7.0	7.0	6.6	6.5	6.2	-2.6 ^{a)}
Stomach	66.2	65.0	67.2	66.6	65.9	62.3	66.9	65.4	63.1	64.4	64.9	63.1	63.3	-0.4 ^{a)}
Colon and rectum	26.2	27.2	29.6	32.9	35.3	37.9	41.1	43.3	45.3	46.9	49.8	49.7	51.4	6.1 ^{a)}
Liver	46.8	44.7	45.1	43.9	42.3	42.1	42.6	40.2	39.7	39.4	38.1	36.7	35.6	-2.1 ^{a)}
Gallbladder ^{b)}	8.1	7.8	8.2	8.1	7.8	8.4	8.7	8.1	7.9	7.6	8.1	8.2	7.6	-0.2
Pancreas	7.8	7.6	7.6	7.9	7.7	8.0	8.3	8.0	8.2	8.4	8.1	8.0	8.5	0.7 ^{a)}
Larynx	4.9	4.5	5.1	4.7	4.5	4.1	4.3	3.8	3.8	3.5	3.6	3.4	3.1	-3.7 ^{a)}
Lung	51.4	49.8	51.1	51.0	50.0	50.8	50.9	49.2	48.7	47.6	47.4	47.2	46.0	-0.8 ^{a)}
Breast	0.2	0.3	0.2	0.3	0.2	0.2	0.2	0.2	0.1	0.3	0.2	0.2	0.2	-0.9
Prostate	8.4	7.2	9.5	10.1	12.4	15.1	15.7	17.9	20.9	23.4	25.1	25.9	27.4	12.3 ^{a)}
Testis	0.6	0.5	0.6	0.6	0.6	0.6	0.6	0.7	0.7	0.7	0.8	0.8	0.9	4.2 ^{a)}
Kidney	4.5	4.4	4.9	5.0	5.2	5.5	6.0	6.5	7.1	7.4	7.6	7.9	8.1	5.7 ^{a)}
Bladder	9.0	9.0	9.4	9.0	9.7	9.8	9.8	9.6	9.4	9.1	8.7	8.8	8.7	-0.4
Brain and CNS	3.2	3.1	3.1	2.9	3.3	3.3	3.3	3.1	3.4	3.4	3.4	3.4	3.0	0.6
Thyroid	2.1	1.9	2.4	2.7	3.7	4.8	5.9	7.5	10.0	13.3	15.6	18.5	20.2	24.2 ^{a)}
Hodgkin lymphoma	0.4	0.4	0.4	0.3	0.4	0.5	0.4	0.4	0.5	0.5	0.5	0.6	0.6	3.9 ^{a)}
Non-Hodgkin lymphoma	5.8	5.5	5.8	5.8	6.2	6.6	6.5	6.9	7.0	6.8	7.4	7.3	7.7	2.7 ^{a)}
Multiple myeloma	1.2	1.3	1.4	1.4	1.4	1.4	1.6	1.5	1.6	1.7	1.9	1.8	1.8	3.3 ^{a)}
Leukemia	5.5	5.0	5.4	5.8	5.5	5.7	5.6	5.6	5.7	5.8	5.9	6.0	6.1	1.1 ^{a)}
Other and ill-defined	17.9	16.5	16.8	16.5	18.5	18.2	19.2	18.8	20.2	19.7	19.9	19.6	20.3	1.7 ^{a)}

APC was calculated using age-standardized incidence data based on the world standard population. APC, annual percentage change; CNS, central nervous system.

^{a)}Significantly different from zero ($p < 0.05$). ^{b)}Includes the gallbladder and other / unspecified parts of the biliary tract.

Table 7. Trends in cancer incidence rates in females from 1999 to 2011 in Korea

Site/Type	Year											APC		
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009		2010	2011
All sites	61.1	157.4	169.0	174.6	184.3	193.4	207.8	16.4	232.0	249.0	263.0	273.6	286.2	5.4 ^{a)}
Lip, oral cavity, and pharynx	1.6	2.4	1.7	1.7	1.7	1.9	1.9	1.8	1.9	1.9	1.8	2.2	2.1	1.2
Esophagus	0.6	0.6	0.6	0.5	0.6	0.5	0.4	0.5	0.5	0.5	0.4	0.4	0.4	-2.6 ^{b)}
Stomach	26.7	25.2	26.2	26.3	25.9	24.7	26.8	25.1	24.8	25.1	25.7	25.2	25.1	-0.4
Colon and rectum	16.4	16.4	17.9	18.8	20.5	21.5	23.0	24.1	24.5	25.1	26.3	26.0	26.4	4.5 ^{a)}
Liver	12.3	11.8	12.2	11.8	11.5	11.3	11.4	11.1	11.1	10.7	10.6	10.3	10.3	-1.5 ^{a)}
Gallbladder ^{b)}	5.3	5.5	5.7	5.8	5.8	5.9	6.0	5.5	5.6	5.5	5.8	5.4	5.5	-0.1
Pancreas	4.0	4.0	4.0	4.2	4.5	4.5	4.7	4.7	4.8	4.9	4.9	5.0	5.1	2.2 ^{a)}
Larynx	0.4	0.3	0.3	0.3	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2	-7.6 ^{a)}
Lung	12.4	12.5	12.3	12.6	12.4	13.0	13.5	14.0	13.9	14.2	14.1	14.6	15.1	1.7 ^{a)}
Breast	20.9	20.9	24.7	27.2	27.8	29.3	32.0	33.3	35.6	37.1	38.7	40.4	43.8	6.3 ^{a)}
Cervix uteri	16.3	15.1	15.8	14.8	14.2	13.1	12.4	12.2	11.1	11.5	10.6	10.8	10.1	-4.0 ^{a)}
Corpus uteri	2.8	2.6	3.0	3.3	3.8	3.7	3.9	4.0	4.2	4.7	5.1	5.1	5.3	6.1 ^{a)}
Ovary	5.0	4.8	4.8	5.0	5.1	5.2	5.4	5.4	5.9	5.6	5.4	5.8	5.7	1.6 ^{a)}
Kidney	1.7	1.8	1.9	2.0	2.1	2.2	2.5	2.7	2.8	3.0	3.2	3.0	3.4	6.0 ^{a)}
Bladder	1.6	1.6	1.7	1.7	1.8	1.7	1.7	1.6	1.7	1.6	1.6	1.5	1.5	-0.8
Brain and CNS	2.6	2.5	2.5	2.4	2.5	2.6	2.8	2.7	2.9	2.7	2.6	2.7	2.4	0.3
Thyroid	10.4	10.1	13.2	16.2	21.8	29.5	35.3	43.3	55.6	69.4	80.6	88.6	96.8	23.3 ^{a)}
Hodgkin lymphoma	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3	0.3	0.4	6.3 ^{a)}
Non-Hodgkin lymphoma	3.4	3.2	3.4	3.5	3.9	4.1	4.4	4.4	4.4	4.7	5.1	5.1	5.5	4.5 ^{a)}
Multiple myeloma	0.8	0.8	0.9	0.8	1.0	1.0	1.2	1.1	1.2	1.2	1.2	1.3	1.1	3.9 ^{a)}
Leukemia	3.9	3.8	4.1	4.0	4.1	4.1	4.0	4.4	4.2	4.3	4.2	4.1	4.5	0.9 ^{a)}
Other and ill-defined	11.8	11.5	11.8	11.5	12.8	13.1	13.9	14.1	14.8	14.9	14.8	15.5	15.7	3.0 ^{a)}

APC was calculated using age-standardized incidence data based on the world standard population. APC, annual percentage change; CNS, central nervous system. ^{a)}Significantly different from zero ($p < 0.05$). ^{b)}Includes the gallbladder and other / unspecified parts of the biliary tract.

In contrast, the incidences of liver cancer in both sexes, lung cancer in males, and cervical cancer in females have decreased. Notably, thyroid cancer increased by 23.3% per year rapidly in both sexes, and became the most common cancer since 2009. Improvements in the sensitivity of diagnostic techniques for thyroid cancer, such as the advent of ultrasound and fine-needle aspiration, have enabled the detection of small-sized thyroid cancers. Furthermore, screening rates have increased. Therefore, the increased incidence of thyroid cancer might reflect the identification of previously undetected diseases rather than a true increase in the occurrence of thyroid cancer [13-16]. Furthermore, due to the construction of a 1999-2011 KNCI DB, the completeness of the Korean cancer registry data has improved gradually, and this may have contributed, in part, to the gradual overall increases in cancer incidence, particularly among elderly patients.

4. Age-specific incidence rates

The most common cancer sites by sex and age group in 2011 are shown in Table 8. Leukemia and thyroid cancer were the most common cancer in both sexes in patients aged

0-14 and 15-34 years, respectively. For males, stomach cancer was the most common cancer in those aged 35-64, while lung cancer was more frequent among patients aged 65 and over. Thyroid cancer was the most common cancer in females aged 35-64 years, and colorectal cancer was the most common cancer among older females aged 65 and over.

The age-specific incidence rates for selected cancers in males and females in 2011 are shown in Fig. 3. The graphs show that the incidences of stomach, lung, liver, and colorectal cancers increased gradually with age. Incidences of breast and thyroid cancers in females were highest among patients in their late 40s and early 50s, respectively, and leveled off thereafter. The age-specific pattern of breast cancer is different from those in Western countries [17].

5. Trends in cancer mortality

The trends in cancer deaths for all sites combined and for selected sites are shown in Figs. 1 and 4. ASRs of mortality for all sites combined decreased 2.7% per year in both sexes since 2002. Lung cancer surpassed stomach cancer as the leading cause of cancer death in 1999 and is expected to account for 22.2% of all cancer deaths in 2011. However, the

Table 8. The five major sites of cancer incidence by age group and sex for 2011 in Korea

Rank	Age group (yr)			
	0-14	15-34	35-64	≥65
Male				
1	Leukemia (5.0)	Thyroid (12.8)	Stomach (99.4)	Lung (449.8)
2	Non-Hodgkin lymphoma (2.0)	Colon and rectum (3.3)	Colon and rectum (78.6)	Stomach (438.4)
3	Brain and CNS (1.9)	Leukemia (3.2)	Liver (66.5)	Colon and rectum (355.9)
4	Kidney (0.5)	Non-Hodgkin lymphoma (3.2)	Thyroid (47.7)	Prostate (298.1)
5	Liver (0.3)	Stomach (3.0)	Lung (44.1)	Liver (202.1)
Female				
1	Leukemia (4.6)	Thyroid (65.1)	Thyroid (234.1)	Colon and rectum (181.1)
2	Brain and CNS (1.7)	Breast (11.0)	Breast (117.8)	Stomach (157.8)
3	Non-Hodgkin lymphoma (1.4)	Cervix uteri (5.4)	Stomach (43.8)	Lung (129.0)
4	Ovary (0.8)	Stomach (3.7)	Colon and rectum (43.6)	Thyroid (93.6)
5	Thyroid (0.8)	Ovary (3.1)	Cervix uteri (22.0)	Liver (77.4)

CNS, central nervous system.

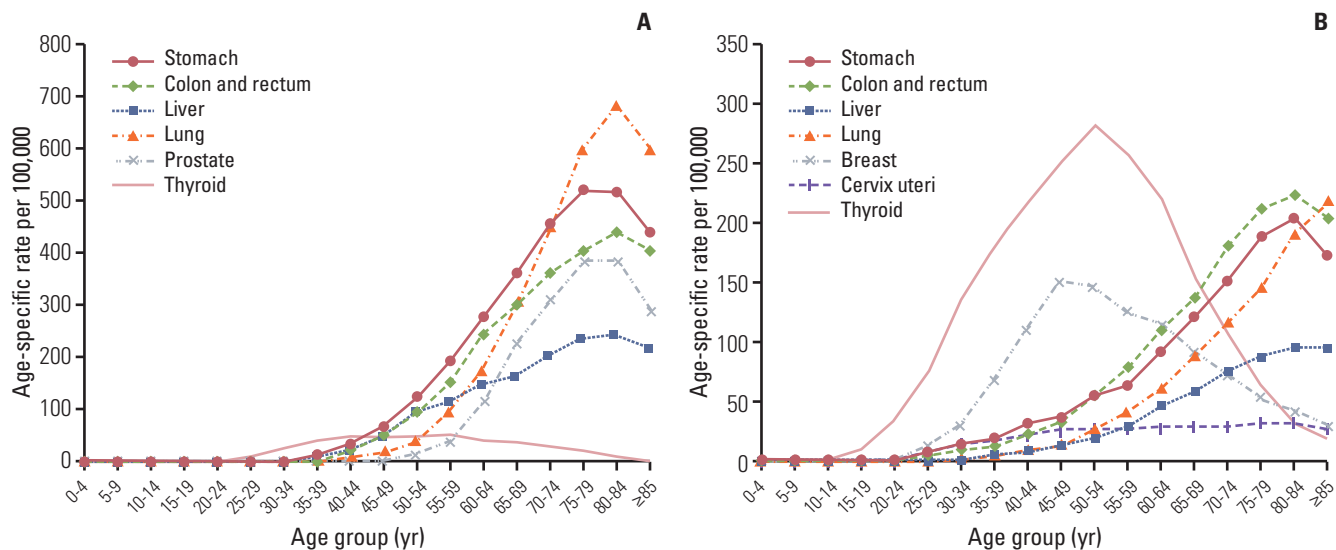


Fig. 3. Age-specific incidence rates of major cancers for 2011 in Korea. (A) Male. (B) Female.

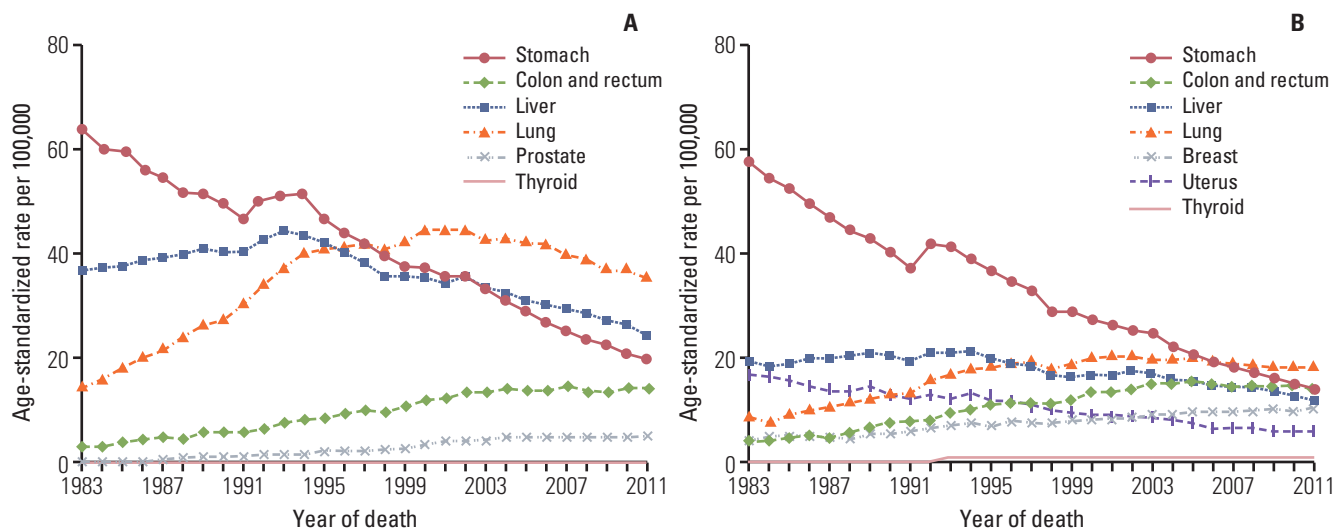


Fig. 4. Annual age-standardized cancer mortalities of selected cancers by sex from 1983 to 2011 in Korea. Age standardization was based on the world standard population. (A) Male. (B) Female.

ASRs of mortality due to lung cancer have decreased slightly in both males and females since 2002. The ASRs of mortality due to stomach and uterus cancers also have decreased continuously. Along with significant increases in colorectal, prostate, and female breast cancer incidence rates, mortality rates of these cancers have also continued to increase.

6. Survival rates

The trends in relative survival for all sites combined among both sexes by year of diagnosis from 1999 to 2011 are shown in Fig. 5. The relative survival for all sites combined

Table 9. Trends in the 5-year relative survival rates (%) by year of diagnosis from 1993 to 2011 in Korea

Site/Type	Both			Male			Female								
	1993-1995	1996-2000	2001-2005	2007-2011	Change ^{a)}	1993-1995	1996-2000	2001-2005	2007-2011	Change ^{a)}	1993-1995	1996-2000	2001-2005	2007-2011	Change ^{a)}
All sites	41.2	44.0	53.8	66.3	25.1	31.7	35.3	45.2	57.6	25.9	53.4	55.3	64.0	75.2	21.8
Lip, oral cavity, and pharynx	41.1	46.7	54.1	61.6	20.5	35.8	41.1	49.3	57.3	21.5	58.1	63.8	67.7	73.2	15.1
Esophagus	12.7	15.2	21.2	30.2	17.5	11.8	14.3	20.4	29.7	17.9	23.7	24.2	29.5	35.4	11.7
Stomach	42.8	46.6	57.7	69.4	26.6	43.0	46.9	58.4	70.1	27.1	42.6	46.0	56.4	67.9	25.3
Colon and rectum	54.8	58.0	66.6	73.8	19.0	55.3	59.0	68.5	75.8	20.5	54.2	56.8	64.1	70.7	16.5
Liver	10.7	13.2	20.2	28.6	17.9	9.9	12.9	20.1	28.5	18.6	13.6	14.2	20.3	28.7	15.1
Gallbladder ^{b)}	17.3	19.7	22.8	27.5	10.2	16.6	20.3	23.3	29.0	12.4	18.0	19.1	22.3	26.1	8.1
Pancreas	9.4	7.6	8.0	8.7	-0.7	8.8	7.3	8.0	8.1	-0.7	10.1	8.1	8.1	9.5	-0.6
Larynx	59.7	62.3	66.1	71.7	12.0	60.2	62.8	66.7	72.0	11.8	55.4	57.8	58.2	68.1	12.7
Lung	11.3	12.7	16.2	20.7	9.4	10.4	11.6	15.0	18.3	7.9	14.2	16.2	19.7	26.8	12.6
Breast	77.9	83.2	88.5	91.3	13.4	75.1	85.6	87.0	88.7	13.6	78.0	83.2	88.5	91.3	13.3
Cervix uteri	77.5	80.0	81.3	80.1	2.6	-	-	-	-	-	77.5	80.0	81.3	80.1	2.6
Corpus uteri	81.5	81.8	84.6	86.5	5.0	-	-	-	-	-	81.5	81.8	84.6	86.5	5.0
Ovary	58.7	58.9	61.4	61.6	2.9	-	-	-	-	-	58.7	58.9	61.4	61.6	2.9
Prostate	55.9	67.2	80.1	92.0	36.1	55.9	67.2	80.1	92.0	36.1	-	-	-	-	-
Testis	85.4	90.4	90.6	93.2	7.8	85.4	90.4	90.6	93.2	7.8	-	-	-	-	-
Kidney	62.0	66.1	73.3	78.8	16.8	60.8	64.4	72.8	78.4	17.6	64.5	69.7	74.5	79.5	15.0
Bladder	69.1	73.1	75.5	75.4	6.3	70.0	74.8	77.3	77.4	7.4	65.5	66.3	68.5	67.0	1.5
Brain and CNS	38.5	39.0	40.6	41.4	2.9	37.2	37.5	40.0	39.3	2.1	40.2	40.7	41.4	43.9	3.7
Thyroid	94.2	94.9	98.3	100.0	5.8	87.2	89.5	95.8	100.1	12.9	95.4	95.9	98.7	99.9	4.5
Hodgkin lymphoma	68.0	71.2	76.7	81.1	13.1	67.6	68.1	74.7	81.1	13.5	68.6	77.4	80.6	81.2	12.6
Non-Hodgkin lymphoma	46.6	50.8	59.9	65.8	19.2	45.3	48.9	58.0	63.9	18.6	48.7	53.5	62.3	68.2	19.5
Multiple myeloma	22.1	19.8	29.3	34.6	12.5	21.1	17.8	29.6	34.6	13.5	23.3	22.1	28.9	34.7	11.4
Leukemia	26.5	33.3	41.8	48.0	21.5	26.2	32.3	41.6	47.3	21.1	26.8	34.6	42.0	48.7	21.9
Other and ill-defined	42.1	45.9	55.8	66.3	24.2	37.4	42.4	52.1	62.4	25.0	47.4	50.0	59.8	70.3	22.9

CNS), central nervous system. ^{a)}Percentage change in 5-year relative survival from 1993 to 1995 and 2007 to 2011, ^{b)}Includes the gallbladder and other/ unspecified parts of the biliary tract.

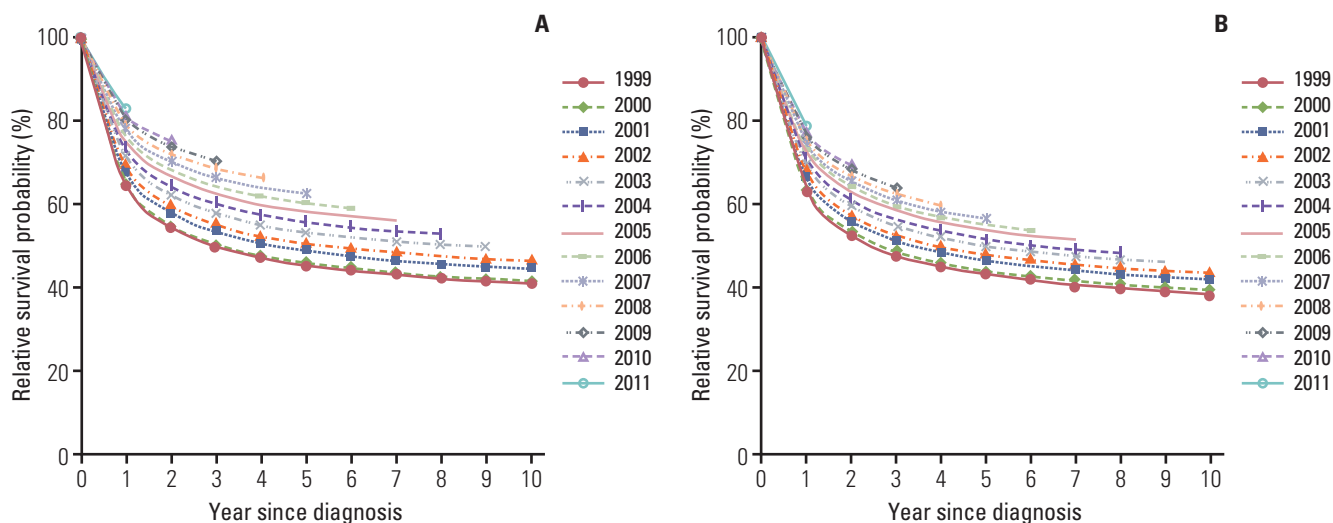
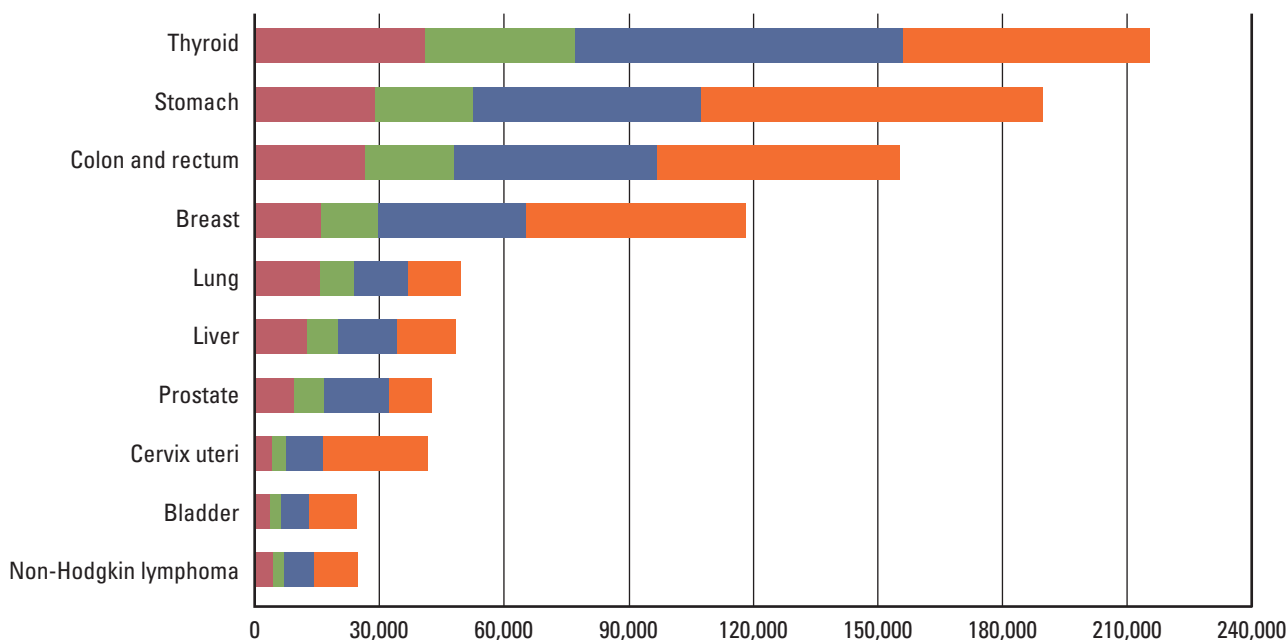


Fig. 5. Trends in relative survival by year of diagnosis from 1999 to 2011. (A) All sites for both sexes. (B) All sites except thyroid cancer for both sexes.



	Cancer prevalent cases										
	Thyroid	Stomach	Colon and rectum	Breast	Lung	Liver	Prostate	Cervix uteri	Bladder	Non-Hodgkin lymphoma	All sites
Under 1 yr	40,354	28,319	25,848	15,779	15,040	11,685	8,659	3,556	3,207	3,754	190,797
1-2 yr	36,163	23,434	21,585	14,013	8,265	7,782	7,294	3,438	2,736	2,944	153,306
2-5 yr	79,195	55,099	49,063	35,129	12,972	14,613	15,802	9,186	6,729	6,825	340,723
5-13 yr	59,466	82,143	58,320	52,731	12,518	13,608	10,402	24,897	11,107	10,104	412,457
Total	215,178	188,995	154,816	117,652	48,795	47,698	42,157	41,077	23,779	23,627	1,097,253

Fig. 6. Prevalence of major cancer sites by time since diagnosis on January 1, 2012 in Korea.

Table 10. Crude and age-standardized rates of cancer prevalence by sex on January 1, 2012 in Korea

Site/Type	Crude prevalence rate per 100,000 ^{a)}			Age-standardized prevalence rate per 100,000 ^{b)}		
	Both	Male	Female	Both	Male	Female
All sites	2,189.6	1,959.6	2,420.1	1,514.1	1,488.7	1,618.5
Lip, oral cavity, and pharynx	31.0	41.9	20.0	21.7	31.4	13.4
Esophagus	13.6	24.5	2.6	9.1	18.6	1.5
Stomach	377.1	500.5	253.6	252.7	372.7	154.9
Colon and rectum	308.9	367.7	250.0	206.3	276.4	150.7
Liver	95.2	142.3	48.0	66.2	105.6	31.0
Gallbladder ^{c)}	27.0	27.5	26.5	17.7	20.8	15.4
Pancreas	12.7	14.0	11.5	8.6	10.6	7.0
Larynx	16.2	30.5	2.0	10.9	23.2	1.2
Lung	97.4	127.0	67.7	65.1	96.2	41.3
Breast	234.8	2.1	468.0	161.1	1.6	316.3
Cervix uteri	82.0	-	164.1	55.8	-	108.4
Corpus uteri	27.1	-	54.2	18.9	-	37.1
Ovary	25.8	-	51.6	18.9	-	37.4
Prostate	84.1	168.1	-	53.0	129.0	-
Testis	3.9	7.9	-	3.6	7.1	-
Kidney	46.0	62.0	30.1	32.5	46.4	20.3
Bladder	47.5	77.2	17.7	30.6	58.7	9.6
Brain and CNS	16.0	16.6	15.4	14.2	15.1	13.3
Thyroid	429.4	132.0	727.4	304.2	94.7	512.0
Hodgkin lymphoma	3.6	4.6	2.6	3.1	3.9	2.3
Non-Hodgkin lymphoma	47.1	51.2	43.1	35.3	40.8	30.6
Multiple myeloma	6.8	7.3	6.3	4.7	5.5	4.0
Leukemia	27.3	30.0	24.6	26.5	29.4	23.6
Other and ill-defined	129.0	124.7	133.2	93.3	100.9	87.2

CNS, central nervous system. ^{a)}Crude prevalence rate: number of prevalent cases divided by the corresponding person-years of observation. Prevalent cases were defined as patients who were diagnosed between January 1, 1999 and December 31, 2011 and who were alive on January 1, 2012. Multiple primary cancer cases were counted multiple times, ^{b)}Age-adjusted using the world standard population, ^{c)}Includes the gallbladder and other/unspecified parts of the biliary tract.

increased with year of diagnosis, and also increased when we excluded thyroid cancer cases in our analysis.

Table 9 shows the 5-year relative survival rates for four diagnosis periods: 1993-1995, 1996-2000, 2001-2005, and 2007-2011. Patients who were diagnosed with cancer in the most recent period (2007-2011) had a 5-year relative survival rate of 66.3% for all sites combined in both sexes (57.6% in males and 75.2% in females). When compared with earlier periods, notable improvements in the 5-year relative survival rates were observed for all sites combined. The higher cancer survival rate in females might be partly explained by cancers common in females (e.g., thyroid, breast, and cervix uteri cancers) having relatively good prognoses.

When examined by year of diagnosis and cancer site, the 5-year relative survival rates appeared to be higher for most major cancers in patients diagnosed from 2007 to 2011

compared with those diagnosed from 1993 to 1995, with the exception of pancreatic cancer. The greatest improvements were seen in cancers of the prostate, stomach, leukemia, lip/oral cavity/pharynx, and non-Hodgkin lymphoma. The improving survival rates could be attributable to early detection and improved treatments [18,19], but this requires further evaluation. Only pancreatic cancer showed no improvement in 5-year relative survival rate compared with 1993-1995. A lack of progress in early detection and treatment could explain the observed absence of improvement in the survival rate for pancreatic cancer [20].

7. Prevalence rates

The cancer prevalence rates by sex and cancer site on

January 1, 2012 in Korea are shown in Table 10. The CRs per 100,000 of cancer prevalence for all sites combined were 1,959.6 and 2,420.1 in males and females, respectively, and the ASRs per 100,000 of cancer prevalence for all sites combined were 1,488.7 and 1,618.5 in males and females, respectively. In males, the five leading primary sites of cancer for prevalence were stomach (CR, 500.5; ASR, 372.7), colon and rectum (CR, 367.7; ASR, 276.4), prostate (CR, 168.1; ASR, 129.0), liver (CR, 142.3; ASR, 105.6), and thyroid (CR, 132.0; ASR, 94.7), which together accounted for 66.9% of all prevalent cancer cases. In females, the most common cancer site was thyroid (CR, 727.4; ASR, 512.0), followed by breast (CR, 468.0; ASR, 316.3), stomach (CR, 253.6; ASR, 154.9), colon and rectum (CR, 250.0; ASR, 150.7), and cervix uteri (CR, 164.1; ASR, 108.4), which together accounted for 77.0% of all prevalent cancer cases.

The prevalence by time since diagnosis is shown in Fig. 6. For all cancers combined, the 2-year prevalence constituted 31.4% of all prevalent cases. The 2-year prevalence, as a percentage of the total prevalence, was highest for thyroid (22.2%), followed by stomach (15.0%) and colon and rectum (13.8%), which had high incidence rates and good prognoses. For all cancers combined in both sexes, the 2-5-year and >5-year prevalences accounted for 31.1% and 37.6% of the total prevalence, respectively. The long-term prevalences for lung

and liver cancers were relatively low due to low survival rates of lung cancer patients.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

Acknowledgments

This work was supported by a research grant from the National Cancer Center (No. 1310220), Republic of Korea. The authors are indebted to Korea Central Cancer Registry (KCCR)-affiliated hospitals, non-KCCR-affiliated hospitals, 11 regional cancer registries (the Busan, Daegu & Gyeongbuk, Gwangju & Jeonnam, Incheon, Daejeon & Chungnam, Ulsan, Gangwon, Chungbuk, Jeonbuk, Gyeongnam and Jeju-do cancer registries), the National Health Insurance Service and Statistics Korea for data collection.

References

1. Statistics Korea [Internet]. Daejeon: Statistics Korea; 2014 [cited 2014 Jan 4]. Available from: <http://kosis.kr>.
2. Yoon SJ, Bae SC, Lee SI, Chang H, Jo HS, Sung JH, et al. Measuring the burden of disease in Korea. *J Korean Med Sci*. 2007;22:518-23.
3. Jung KW, Won YJ, Kong HJ, Oh CM, Seo HG, Lee JS. Cancer statistics in Korea: incidence, mortality, survival and prevalence in 2010. *Cancer Res Treat*. 2013;45:1-14.
4. Shin HR, Won YJ, Jung KW, Kong HJ, Yim SH, Lee JK, et al. Nationwide cancer incidence in Korea, 1999-2001: first result using the national cancer incidence database. *Cancer Res Treat*. 2005;37:325-31.
5. Ajiki W, Tsukuma H, Oshima A. Index for evaluating completeness of registration in population-based cancer registries and estimation of registration rate at the Osaka Cancer Registry between 1966 and 1992 using this index. *Nihon Koshu Eisei Zasshi*. 1998;45:1011-7.
6. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, et al. International classification of diseases for oncology. 3rd ed. Geneva: World Health Organization; 2000.
7. World Health Organization. International statistical classification of diseases and related health problems. 10th rev. Geneva: World Health Organization; 1994.
8. Segi M. Cancer mortality for selected sites in 24 countries (1950-1957). Sendai: Tohoku University School of Medicine; 1960.
9. Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, et al. SEER cancer statistics review, 1975-2010. Bethesda: National Cancer Institute; 2013.
10. National Cancer Institute. SEER*Stat Program, version 6.6.1 [Internet]. Bethesda: National Cancer Institute; 2013 [cited 2013 Jan 4]. Available from: <http://seer.cancer.gov/seerstat/>.
11. Ederer F, Heise H. Instructions to IBM 650 programmers in processing survival computations. Methodological note. No. 10. Bethesda: National Cancer Institute; 1959.
12. Paul Dickman [Internet]. Stockholm: PaulDickman.com; 2014 [cited 2014 Jan 14]. Available from: <http://www.pauldickman.com>.
13. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. *JAMA*. 2006;295:2164-7.
14. Enewold L, Zhu K, Ron E, Marrogi AJ, Stojadinovic A, Peoples GE, et al. Rising thyroid cancer incidence in the United States by demographic and tumor characteristics, 1980-2005. *Cancer Epidemiol Biomarkers Prev*. 2009;18:784-91.
15. Han MA, Choi KS, Lee HY, Kim Y, Jun JK, Park EC. Current status of thyroid cancer screening in Korea: results from

- a nationwide interview survey. *Asian Pac J Cancer Prev.* 2011; 12:1657-63.
16. Kim SY. Study to provide evidence of health screening service for thyroid cancer. Seoul: National Evidence-based Healthcare Collaborating Agency; 2012.
17. Forman D, Bray F, Brewster DH, Gombe Mbalawa C, Kohler B, Pineros M, et al. Cancer incidence in five continents. Vol. 10 (electronic version). Lyon: IARC Press; 2013.
18. Jung KW, Yim SH, Kong HJ, Hwang SY, Won YJ, Lee JK, et al. Cancer survival in Korea 1993-2002: a population-based study. *J Korean Med Sci.* 2007;22 Suppl:S5-10.
19. Gondos A, Bray F, Hakulinen T, Brenner H; EUNICE Survival Working Group. Trends in cancer survival in 11 European populations from 1990 to 2009: a model-based analysis. *Ann Oncol.* 2009;20:564-73.
20. Dickman PW, Adami HO. Interpreting trends in cancer patient survival. *J Intern Med.* 2006;260:103-17.