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Original Article

Trends and Patterns of Cancer Burdens by Region and Income Level in Korea: A National Representative Big Data Analysis

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Purpose This study aimed to elucidate the trends and characteristics of the cancer burden in Korea by cancer site, region, and income level.

Materials and Methods Korean National Burden of Disease research methodology was applied to measure the cancer burden in Korea from 2008 to 2018. The cause of death and National Health Insurance claims data were obtained from Statistics Korea and the National Health Insurance Service, respectively. An incidence-based approach was applied to calculate the disability-adjusted life-years, which is a summary measure of population health.

Results In the past decade, the cancer burden in Korea increased from 2,088 to 2,457 person-years per 100,000 population. Among the cancer burden, the years of life lost decreased, and the years lived with disabilities increased. Cancers of the trachea, bronchus, and lung had the highest disease burden, followed by those of the stomach, colon and rectum, liver, and breast.

Conclusion The findings of this study can provide valuable quantitative data for prioritizing and evaluating cancer prevention strategies and implementing cancer policies. Estimating the difference in cancer burden according to region and income level within a country can yield useful data to understand the nature of the cancer burden and scale of the problem. In addition, the results of this study provide a better understanding of the causes of cancer patterns, thereby generating new hypotheses regarding its pathogenesis.

Key words Cancer burden, Disability-adjusted life-years, Korea

Introduction

Cancer has been the leading cause of death worldwide over the past few decades, and it remains a major barrier to increasing the life expectancy [1]. The incidence and mortality due to cancer is rapidly increasing worldwide, and the International Agency for Research on Cancer reported 19.3 million new cancer cases and 10 million deaths due to cancer worldwide in 2020 [2]. In Korea, the number of new cancer cases in 2018 was 243,837 (128,757 male, 115,080 female), and has been increasing every year since 2015 [3]. The increase in disease burden due to cancer reflects not only the aging and growth of the population, but also the increase in the prevalence of major cancer risk factors.

The Korea Central Cancer Registry (KCCR) has collected cancer incidence data nationwide since 1999 [4], presenting an opportunity to identify trends in cancer incidence and causes by periodically providing nationwide cancer statistics. However, few studies have measured the cancer burden by year using a comprehensive measure that combines morbidity and mortality, while providing information on the national cancer status for individual indicators, such as cancer incidence, prevalence, and survival. Additionally, differences in cancer morbidity and mortality exist according to region and country, mainly due to differences in population risk factors deriving from socioeconomic differences [5]. In the Global Burden of Disease (GBD) study, the disease burden was classified according to the socio-demographic index (SDI), a composite index that reflects the national income level and educational background [6]. However, to the best of our knowledge, no studies to date have calculated the differences in cancer disease burden according to individual socioeconomic factors within a country. A comprehensive assessment of the disease burden in population groups at the national level can aid in various decision-making processes, such as the prioritization of healthcare services and research, and resource allocation. Furthermore, clarifying the disease burden can provide insights to organizations and individuals committed to health policy and can be used as an evaluation tool of national cancer control programs undertaken by the Korean government.

Therefore, this study was conducted to identify trends in

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the cancer burden among Koreans according to cancer site, sex, region and income level using big data, including claims data from the National Health Insurance Service (NHIS).

Materials and Methods

1. Study design and data sources

Based on the classification system of the Korean National Burden of Diseases (KNBD), we selected 30 cancers to analyze. Among these, 25 were solid tumors, including cancers of the (1) esophagus, (2) stomach, (3) liver, (4) larynx, (5) trachea, bronchus, or lung (TBL), (6) breast, (7) cervical, (8) uterine, (9) prostate, (10) colon and rectum, (11) mouth, (12) nasopharynx, (13) other parts of the pharynx and oropharynx, (14) gallbladder and biliary tract, (15) pancreas, (16) ovary, (17) testicular, (18) kidney, (19) other urinary organs, (20) bladder, (21) brain and nervous system, (22) thyroid, (23) bone and connective tissue, (24) malignant melanoma of the skin, and (25) non-melanoma skin cancer. In addition, there were four blood cancers, including (26) Hodgkin's disease, (27) non-Hodgkin's lymphoma, (28) multiple myeloma, and (29) leukemia. Finally, (30) benign neoplasms of the brain and other parts of the central nervous system, which are benign neoplasms of other specific sites, were also included in this study.

We estimated the 2008-2018 national cancer burden in terms of years of life lost (YLL), years lived with disabilities (YLD), and disability-adjusted life years (DALYs). In this study, the GBD-based measurement methodology was modified to suit the Korean situation, and an incidence-based approach was applied to the calculation [7]. In the KNBD study, the national disease burden was measured as the DALY. The DALY is an index of the level of health measured by expressing illness and death as a single scale, along with the quality-adjusted life years (QALY). For the QALY, the individual level is the subject of analysis, and the preference for the health state is determined by weights selected by individuals. In contrast, for the DALY, preference for the health state is determined by weights according to the severity of each disease as determined by experts. Additionally, since the DALY is applied to a population group, it is more useful in measuring the national level of health [8].

For YLL measurement, we calculated the mortality rate by age, sex, and disease using the data on the cause of death by year (for 2008-2018) from Statistics Korea; for indicated causes that could not be the cause of death, garbage codes were applied and redistributed [9]. The standard expected YLLs were used to calculate the number of years lost due to premature death. The standard life expectancy was based on the 2008-2018 life table by year, sex, and age provided by Statistics Korea [10].

To calculate the prevalence and incidence rates for YLD measurement, we used health insurance claims data by year (for 2008-2018). In a previous KNBD study, cancer registration data was used to calculate the cancer burden; however, as with other diseases, the data source has been changed to health insurance claims data. This is because the KCCR publishes data from the two previous years [11], while the NHIS database is updated every year, enabling the prevalence and incidence rates according to region and income levels to be calculated every year. Korea has a mandatory universal health coverage system. As of the end of 2020, a total of 52,870,968 people receive health security benefits in Korea; of these, the National Health Insurance (NHI) covers 97.1% and the remaining 2.9% comprise Medical Aid beneficiaries. The Medical Aid program is a form of public assistance [12]. The NHIS claims database contains information, such as the diagnosis name, treatment start and end dates, prescription history, and whether surgery was performed as medical treatment, with the exception of non-insured items [13]. To prevent overestimation of the incidence and prevalence rates from claims data, the prevalence was defined as ≥ 1 hospitalization or three outpatient visits, and a 5-year washout period was applied to calculate the number of occurrences.

2. Statistical analyses

YLL by cancer site was calculated by multiplying the number of deaths by sex and year by the standard life expectancy in each age group. To calculate the YLD, the incidence rate of each cancer was multiplied by the average duration and the assigned disability weight. We applied disability weights for specific causes, measured using a domestic self-report questionnaire [14]. The disease duration and average age of onset were estimated using the DisMod-II program. We measured the YLD using an incidence-based approach, with consideration of the disease prevalence, incidence, mortality, case fatality, and disability weight. In this study, when calculating the YLL and YLD, an age-weighting rate of 4% and a time discount of 3% were applied [7]. Finally, the YLL and YLD were summed to calculate cancer-site DALYs. We calculated the YLL, YLD, and DALY rates per 100,000 population by cancer type and sex, and then ranked the leading causes of disease burden.

For the regional classification, 250 municipal-level administrative districts were selected, comprising 67 cities ("Si"), 114 counties ("Gun"), and 69 districts ("Gu"). Because the NHIS calculates insurance premiums based on the wage and income of beneficiaries, insurance premiums were used as a proxy for classifying the income level of the population. Therefore, we used equivalized annual household income based on insurance premiums, divided into quintiles by sex.

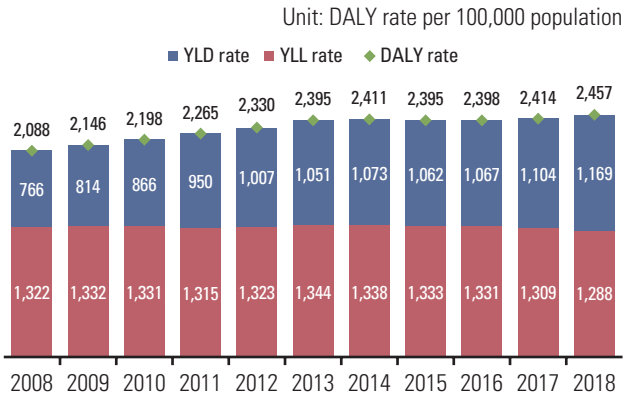


Fig. 1. Trend of burden of cancer in Korea, from 2008 to 2018. DALY, disability-adjusted life year; YLD, year lived with disability; YLL, year of life lost.

Additionally, insurance premiums for Medical Aid beneficiaries (who do not pay insurance premiums) were calculated as 0. Income levels were equally divided into five groups for all populations, including NHI beneficiaries and Medical Aid beneficiaries. The equivalized annual household income was derived as follows:

$$\textit{Equivalised annual household income} = \frac{\textit{Annual household income}}{\textit{No. of household member}^{0.5}}$$

Because it is impossible to confirm the income level from the data on the cause of death in Statistics Korea, we obtained the death rate distribution by income level from the claims data. By applying this to the YLL calculation result, YLL was distributed according to income level. We present all results

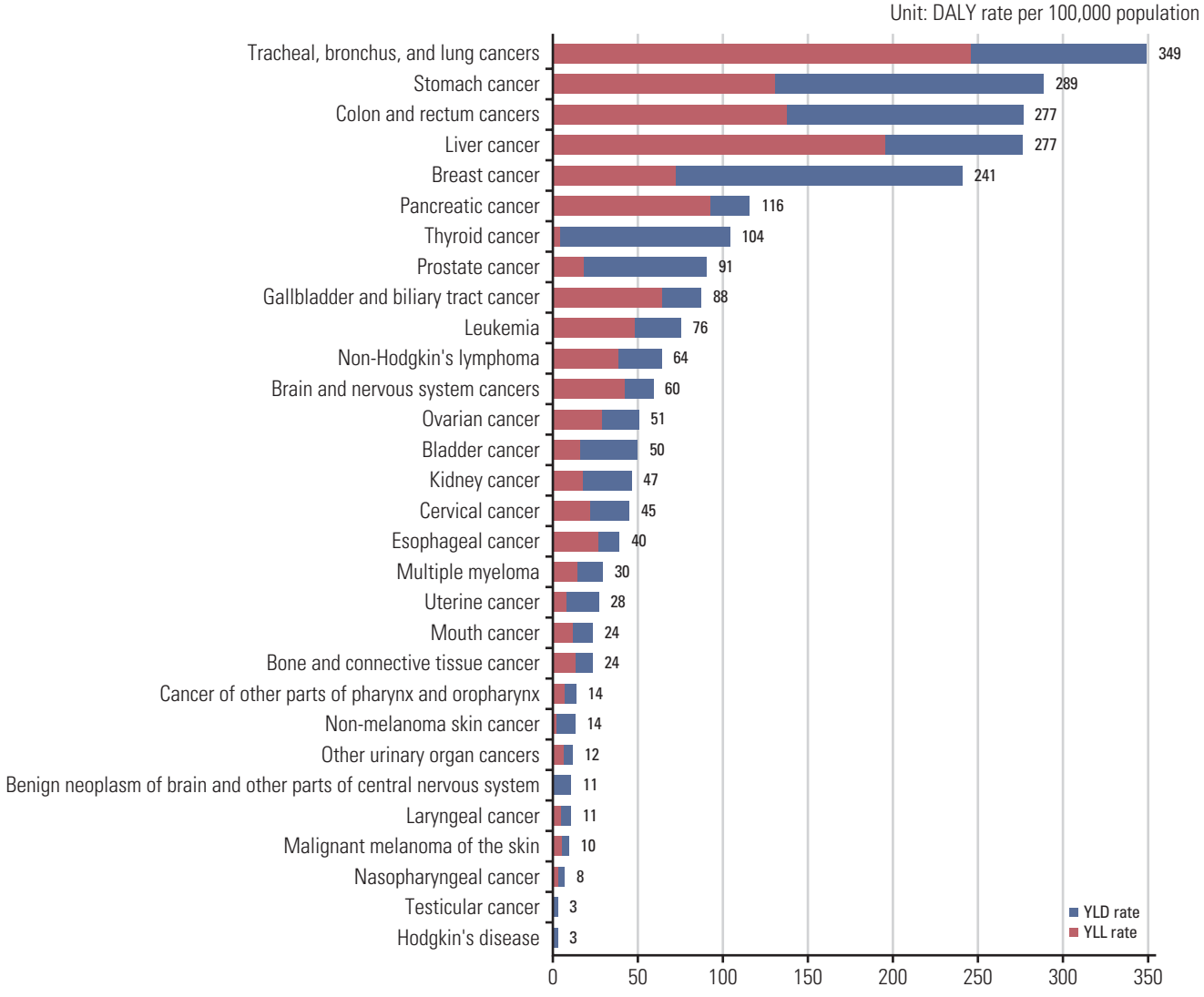


Fig. 2. DALYs by cancer site in Korea, 2018. DALY, disability-adjusted life year; YLD, year lived with disability; YLL, year of life lost.

Table 1. DALYs (unit: DALY rate per 100,000 population) by cancer site and sex in Korea, 2018

Rank	Men				Women			
	% of total DALY rates	No. of DALYs	DALY rate	Cancer site	Cancer site	DALY rate	No. of DALYs	% of total DALY rates
1	17.7	121,300	482	TBL cancers	Breast cancer	474	120,427	21.6
2	15.7	107,332	426	Liver cancer	Colon and rectum cancers	226	57,548	10.3
3	14.0	96,022	381	Stomach cancer	TBL cancers	218	55,505	9.9
4	12.1	82,668	328	Colon and rectum cancers	Stomach cancer	198	50,214	9.0
5	6.7	46,031	183	Prostate cancer	Thyroid cancer	162	41,072	7.4
6	4.8	32,548	129	Pancreatic cancer	Liver cancer	129	32,692	5.9
7	3.5	23,781	94	Gallbladder and biliary tract cancer	Pancreatic cancer	103	26,103	4.7
8	3.2	22,030	87	Leukemia	Ovarian cancer	102	25,898	4.6
9	3.0	20,478	81	Bladder cancer	Cervical cancer	90	22,926	4.1
10	2.8	19,106	76	Non-Hodgkin's lymphoma	Gallbladder and biliary tract cancer	81	20,662	3.7
11	2.5	17,085	68	Esophageal cancer	Leukemia	64	16,301	2.9
12	2.4	16,251	65	Kidney cancer	Brain and nervous system cancers	56	14,279	2.6
13	2.3	15,926	63	Brain and nervous system cancers	Uterine cancer	55	13,939	2.5
14	1.7	11,741	47	Thyroid cancer	Non-Hodgkin's lymphoma	53	13,509	2.4
15	1.2	8,016	32	Multiple myeloma	Kidney cancer	29	7,414	1.3
16	1.1	7,313	29	Mouth cancer	Multiple myeloma	28	7,188	1.3
17	1.0	6,846	27	Bone and connective tissue cancer	Bone and connective tissue cancer	20	5,148	0.9
18	0.9	6,029	24	Cancer of other part of pharynx and oropharynx	Bladder cancer	20	5,065	0.9
19	0.7	4,945	20	Laryngeal cancer	Mouth cancer	19	4,804	0.9
20	0.6	3,957	16	Other urinary organ cancers	Non-melanoma skin cancer	14	3,447	0.6
21	0.5	3,417	14	Non-melanoma skin cancer	Benign neoplasm of brain and other parts of central nervous system	13	3,304	0.6
22	0.4	2,808	11	Nasopharyngeal cancer	Esophageal cancer	12	3,029	0.5
23	0.4	2,530	10	Malignant melanoma of the skin	Malignant melanoma of the skin	10	2,478	0.4
24	0.3	2,329	9	Benign neoplasm of brain and other parts of central nervous system	Other urinary organ cancers	8	2,053	0.4
25	0.3	1,713	7	Testicular cancer	Cancer of other part of pharynx and oropharynx	4	1,049	0.2
26	0.2	1,610	6	Breast cancer	Nasopharyngeal cancer	4	992	0.2
27	0.2	1,058	4	Hodgkin's disease	Hodgkin's disease	3	645	0.1
28	0.0	-	-	Cervical cancer	Laryngeal cancer	2	570	0.1
29	0.0	-	-	Uterine cancer	Prostate cancer	-	-	0.0
30	0.0	-	-	Ovarian cancer	Testicular cancer	-	-	0.0

DALY, disability-adjusted life year; TBL, trachea, bronchus, and lung.

in units per 100,000 population, as the YLL, YLD, and DALY rates. SAS ver. 9.4 (SAS Institute Inc., Cary, NC) was used for statistical analysis.

Results

From 2008 to 2018, the DALY rate increased approximately 17.7% (from 2,088 to 2,457, respectively). In 2018, 52.4% of the Korean cancer DALY rates stemmed from the YLL (1,288) and 47.6% from the YLD (1,169). Between 2008 and 2018, the YLL rate decreased by 2.6% (from 1,322 to 1,288), whereas the YLD rate increased by 52.6% (from 766 to 1,169) (Fig. 1).

The leading causes of cancer DALYs for both sexes in 2018 were TBL cancers (n=349), stomach cancer (n=289), colon and rectum cancers (n=277), liver cancer (n=277), and breast cancer (n=241), which accounted for 58.3% of the total cancer burden in Korea. The proportion of the YLL in the DALY was the highest (≥ 70%) in pancreatic cancer, gallbladder and biliary tract cancer, brain and nervous system cancers, liver cancer, and TBL cancers, and the lowest in thyroid cancer and benign neoplasms of the brain and other parts of the central nervous system (< 10%) (Fig. 2). There was a difference in the cancer ranking between males and females: in males, the DALY rate was the highest for TBL cancers (n=482), liver cancer (n=426), stomach cancer (n=381), colon and rectum cancers (n=328), and prostate cancer (n=183); in females, it was the highest for breast cancer (n=474), colon and rectum cancers (n=226), TBL cancers (n=218), stomach cancer (n=198), and thyroid cancer (n=162). The five major cancers accounted for 66.2% and 58.2% of the total cancer burden in males and females, respectively (Table 1).

Trends over the past decade varied by cancer type. Between 2008 and 2018, the DALY rates for prostate cancer, multiple myeloma, testicular cancer, other urinary organ cancers, uterine cancer, and breast cancer significantly increased by more than 60%. Prostate cancer remained in the top 15 in 2008 but rose to the top eight in 2018. In contrast, the DALY rates of laryngeal, cervical, stomach, liver, and nasopharyngeal cancers decreased. Both the YLL and YLD rates decreased in cervical and laryngeal cancers. However, for stomach, liver, and nasopharyngeal cancers, the YLL rate decreased while the YLD rate increased, revealing that a decrease in the YLL rate contributed to a decrease in the DALY rate. As shown in Fig. 3, the rankings of TBL cancers and colorectal cancer have risen over the past 10 years, while those of stomach and liver cancers have declined slightly.

The distribution and difference in cancer burden by region were examined. The region with the highest DALY rate was Gunwi-gun, Gyeongsangbuk-do (n=4,312), which had a rate 2.61 times higher than that in the lowest region, Yeongtong-gu, Suwon-si, Gyeonggi-do (n=1,650). Further, the highest regional YLL rate (Gunwi-gun, Gyeongsangbuk-do; n=2,702) was 3.65 times higher than the lowest regional YLL rate (Yeongtong-gu, Suwon-si, Gyeonggi-do; n=740). Additionally, the highest regional YLD rate (Goesan-gun, Chungcheongbuk-do; n=1,787) was 1.96 times higher than the lowest regional YLD rate (Yeongtong-gu, Suwon-si, Gyeonggi-do; n=910). Regions with an overall low disease burden tended to be distributed in Seoul and the Gyeonggi Province. Furthermore, the gap in the burden of cancer death was larger than that of the cancer incidence (Fig. 4).

The gap in the DALY rate according to income level decreased from 2008 to 2012 and then increased. In 2008, the cancer DALY rate was 1.71 times higher in the Q1 group (lowest income level) than in the Q5 group (highest income level). This decreased to 1.60 times in 2012, but then increased again to 1.81 times in 2018. However, the difference in disease burden between the Q1 and Q2 groups was in the range of 1.38 to 1.47, indicating a significant difference between Q1 and the other groups. In addition, in terms of the rate of DALY rate increase over the past 10 years, the Q3-Q5 group showed an increase rate of around 15%, whereas the Q1 and Q2 groups showed relatively higher increase rates of 21.3% and 20.5%, respectively (Fig. 5).

TBL cancers had the highest DALY rate among groups Q1 to Q5. In addition, the types of cancer ranked in the top five were the same. However, cancers with the second highest disease burden were stomach cancer in the Q2-Q4 groups, liver cancer in the Q1 group, and breast cancer in the Q5 group. Overall, the disease burden tended to decrease with increasing income level. Conversely, there were cases where the disease burden was greater in the high-income group than in the low-income group. For thyroid cancer, the DALY rate gradually increased as the income level increased, and the gap between Q1 and Q5 was 32 (Q1: 87, Q5: 119). In the case of prostate cancer, there was no constant increase according to income level, but among the groups, the DALY rate (107) was the highest in the Q5 group (S1 Table).

Discussion

This study was conducted to quantify the burden of premature death and disability according to cancer site, sex, region, and income level by applying the GBD methodology to the situation in Korea. The cancer burden among Koreans has increased as a whole over the past decade. Further, the cancer burden due to death has decreased and the cancer burden due to disability has increased. Key findings from this study may help in understanding cancer patterns in Korea.

In 2008, the importance of preventing premature death

Rank, 2008	Rank, 2018	Cancer site	DALY rate (2008)	DALY rate (2018)	Percentage change in DALY rate, 2008-2018	YLL rate (2008)	YLL rate (2018)	Percentage change in YLL rate, 2008-2018	YLD rate (2008)	YLD rate (2018)	Percentage change in YLD rate, 2008-2018
3	1	Tracheal, bronchus, and lung cancers	290	349	20.5%	236	246	4.1%	54	104	91.8%
1	2	Stomach cancer	333	289	–13.3%	200	131	–34.4%	134	158	18.2%
4	3	Colon and rectum cancers	234	277	18.5%	131	138	4.8%	102	139	36.0%
2	4	Liver cancer	316	277	–12.3%	254	196	–23.0%	61	81	32.0%
5	5	Breast cancer	149	241	62.4%	59	73	22.8%	89	169	88.6%
6	6	Pancreatic cancer	80	116	45.7%	67	93	38.4%	12	23	84.8%
7	7	Thyroid cancer	76	104	36.6%	5	5	–11.4%	71	100	40.2%
15	8	Prostate cancer	33	91	176.4%	12	18	48.3%	20	73	254.3%
8	9	Gallbladder and biliary tract cancer	73	88	20.7%	56	64	15.3%	17	24	38.2%
9	10	Leukemia	69	76	9.5%	56	48	–13.9%	13	27	109.2%
12	11	Non-Hodgkin's lymphoma	51	64	26.3%	33	38	17.6%	18	26	41.5%
10	12	Brain and nervous system cancers	55	60	9.5%	41	43	4.7%	14	17	23.4%
13	13	Ovarian cancer	38	51	35.3%	21	29	35.3%	17	22	35.3%
14	14	Bladder cancer	37	50	36.5%	14	16	18.3%	23	34	47.3%
17	15	Kidney cancer	31	47	53.0%	14	18	27.0%	16	29	75.7%
11	16	Cervical cancer	52	45	–13.7%	25	23	–9.6%	28	23	–17.4%
16	17	Esophageal cancer	32	40	23.1%	24	27	10.7%	8	13	61.7%
21	18	Multiple myeloma	15	30	95.5%	12	15	25.7%	4	15	314.7%
20	19	Uterine cancer	17	28	63.0%	6	8	31.3%	11	19	81.6%
19	20	Mouth cancer	18	24	29.8%	11	12	13.8%	8	12	51.3%
18	21	Bone and connective tissue cancer	20	24	21.2%	12	14	16.5%	8	10	28.3%
24	22	Cancer of other part of pharynx and oropharynx	10	14	44.4%	6	7	19.0%	4	7	88.0%
23	23	Non-melanoma skin cancer	11	14	26.5%	2	2	6.4%	8	11	31.8%
28	24	Other urinary organ cancers	7	12	70.4%	4	6	60.8%	3	5	83.6%
25	25	Benign neoplasm of brain and other parts of central nervous system	8	11	32.8%	1	1	–42.8%	7	10	46.1%
22	26	Laryngeal cancer	13	11	–17.9%	6	5	–19.4%	7	6	–16.5%
26	27	Malignant melanoma of the skin	8	10	20.1%	5	6	1.8%	3	4	55.6%
27	28	Nasopharyngeal cancer	8	8	–7.2%	5	4	–18.6%	3	4	9.9%
30	29	Testicular cancer	2	3	86.9%	1	1	49.6%	1	3	103.4%
29	30	Hodgkin's disease	2	3	47.4%	1	1	0.3%	1	2	110.4%

Fig. 3. Cancer rankings by DALYs in 2018 and percentage change from 2008 to 2018 (unit: DALY rate per 100,000 population). Cancers are ordered by rank in 2018 and are linked to their ranking in 2008. Color refers to the change in DALY rate from 2008 to 2018: red signifies an increase of more than 60%, gray signifies an increase of less than 60%, and blue signifies a decrease. DALY, disability-adjusted life year; YLD, year lived with disability; YLL, year of life lost. Rankings are by DALY rate.

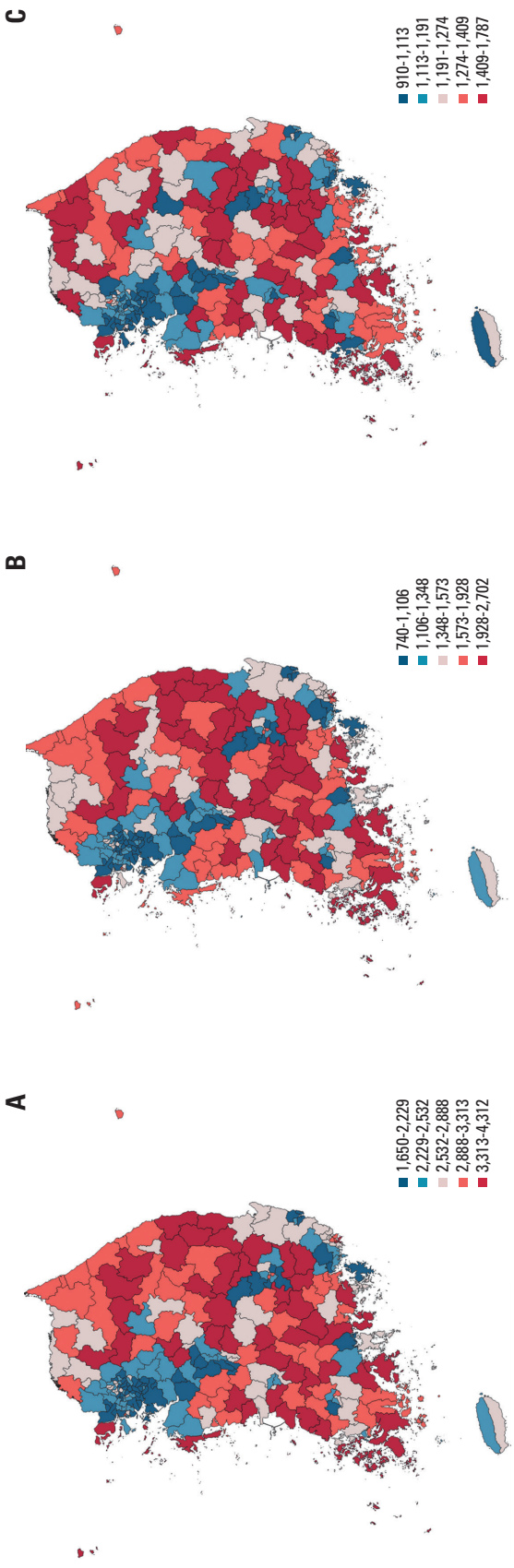
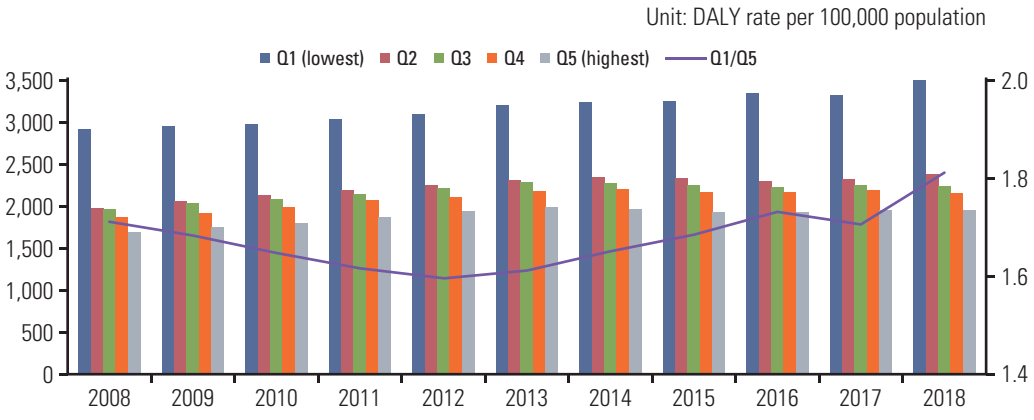


Fig. 4. Cancer burden by region, 2018. (A) DALY rate per 100,000 population by region. (B) YLL rate per 100,000 population by region. (C) YLD rate per 100,000 population by region. DALY, disability-adjusted life year; YLD, year lived with disability; YLL, year of life lost.

was emphasized, as the YLL accounted for approximately 63% of the total DALY; since then, the YLD has steadily increased and YLL has decreased, resulting in a YLL:YLD ratio of 52:48 in 2018. This appears to reflect a situation in which advances in early detection, diagnosis, and treatment technologies for various cancers and improvements in cancer management have been effective in reducing the YLL. However, a reduction in the YLD rate due to primary prevention has not been adequately achieved, and as cancer survival rate is increasing, the overall cancer burden is still inevitably increasing. Continuous efforts are needed to reduce cancer mortality through early diagnosis, treatment, and prevention, with minimal sequelae. However, primary prevention efforts also need to be emphasized to reduce the cancer incidence through a reduction in cancer risk factors. In Korea, as interest and demand for specialized cancer treatment have increased, large cancer hospitals have been established and cancer treatments have diversified. Although treating cancer is naturally of importance, active investment in multidisciplinary research on the nature of cancer is essential. Furthermore, research focused on identifying cancer risk factors and understanding preventive effects should be actively pursued. It is necessary to develop cancer prevention practice guidelines that reflect such research results and strengthen publicity so that they can be put into practice in daily life. Above all else, there is a need for more specialized primary care services that can lead to overall lifestyle changes, such as appropriate physical activity and nutrition for cancer survivors and healthy people before the onset of cancer. The establishment and generalization of these primary medical services is very important for reducing the cancer incidence.

A decrease in the age-standardized mortality rate for many cancers in Korea over the past several decades can be observed from the main information annually published in the National Cancer Registry. Nevertheless, when examined by cancer site, the share of the YLL for pancreatic cancer, gallbladder and biliary tract cancer, brain and nervous system cancers, liver cancer, and TBL cancers was over 70%, suggesting that these cases reflect a poor prognosis after cancer diagnosis.

Regarding the cancer burden ranking results, the DALY rate was highest in the order of TBL cancers, stomach, colorectal, liver, and breast cancers, which was slightly different from the 2019 GBD order of lung, liver, stomach, colorectal, and pancreatic cancers [6]. This seems to be due to differences in methodologies. In the GBD study, the burden of disease was calculated through an estimation based on published papers and the numerical values extracted therefrom. Epidemiological indicators collected by the Institute for Health Metrics and Evaluation, which served as data input in the GBD study, may not be the most useful and up-to-date infor-



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Q1 (lowest)	2,919	2,954	2,976	3,036	3,109	3,200	3,250	3,264	3,352	3,333	3,541
Q2	1,981	2,067	2,131	2,194	2,256	2,314	2,347	2,332	2,303	2,328	2,386
Q3	1,965	2,035	2,084	2,147	2,219	2,287	2,284	2,261	2,227	2,262	2,240
Q4	1,868	1,922	1,993	2,074	2,118	2,183	2,204	2,179	2,170	2,192	2,159
Q5 (highest)	1,704	1,752	1,805	1,875	1,947	1,987	1,967	1,938	1,936	1,953	1,955
Q1/Q5	1.71	1.69	1.65	1.62	1.60	1.61	1.65	1.68	1.73	1.71	1.81

Fig. 5. Difference in cancer burden according to income level, 2018. DALY, disability-adjusted life year.

mation at the national level. In addition, multiple assumptions and methodological choices, often compromises, are required to integrate different types of information. Most importantly, there is a difference in the DALY measurement perspective. In the GBD study, a prevalence-based approach was applied. In contrast, in the present study, disease burden was measured using epidemiological indicators extracted from NHIS claims data, with information on the actual medical use of Koreans. In addition, the KNBD study, which is the basis of the present study, adopted an incidence-based approach that is useful for cohort-based data [7].

TBL cancers in men and breast cancer in women were found to be major causes of the cancer burden, which is consistent with the ranking of cancer burden by sex published in the 2019 GBD study [6]. Furthermore, a research team from the Alberta Department of Health in Canada analyzed premenopausal and postmenopausal breast cancer cases from 44 populations in 41 countries, including Asia, Europe, and the United States, and found that Korean women had the highest average annual growth rate of breast cancer [15]. However, the breast cancer incidence rate is higher at a younger age in Korea than in Western countries. Contrary to the epidemiology of female breast cancer in the West, where the incidence rapidly increases in women in their 60s and 70s, the breast cancer incidence rate in Korean women is highest in women aged 45-50 years [16]. The reasons for this increase in breast cancer incidence in young women are presumed to be early menarche, decreased breastfeeding, obesity, late marriage, and low fertility [17-19]. Although it is impossible to completely avoid situational factors with long-term exposure in women, such as the active entry of women into society and delays in marriage and childbirth, it is necessary to try to improve the prognosis by promoting self-examinations and managing individually controllable factors. On the other hand, TBL cancers have the highest cancer burden among all people and men, and the importance of management has been emphasized, as TBL cancers have ranked first in the country's cancer mortality rate for the past 10 years. As can be seen from the results of the present study, with an YLL as high as 70%, TBL cancers are deadly, with a low survival rate. This is also supported by the 2018 National Cancer Registry statistics [20], which reported the 5-year relative survival rate of lung cancer as 32.4%, representing the second poorest prognosis, after gallbladder and other biliary tract and pancreatic cancers. The increased recognition of the need for early TBL cancer screening was reflected by its addition to the national health screening list in July 2019 [21]. The introduction and implementation of this TBL cancer screening program is expected to yield significantly improved survival rates.

The cancer burden trend over the past 10 years differed according to cancer site, and both the YLL and YLD decreased in laryngeal and cervical cancers. Laryngeal cancer, along with nasopharyngeal cancer, is a representative disease caused by smoking, and as the smoking rate of adults has continuously decreased over the last decade [22], it can be inferred that reductions in the burden of laryngeal and nasopharyngeal cancers are an effect of the reduction in the

smoking rate. In addition, the incidence of cervical cancer has gradually decreased since the human papillomavirus vaccine was introduced in Korea in 2006 [23], and this effect may have reduced the burden of cervical cancer. In addition, cervical cancer screening is expected to further reduce the burden of cervical cancer through continuous efforts to improve screening rates, as this not only reduces mortality, but also lowers the incidence of cancer itself [24] by detecting factors of cancer.

The decreases in the DALY rate for stomach and liver cancers were confirmed to be due to decreases in the YLL. For stomach cancer, the National Cancer Screening Program seems to be effective in reducing the death rate. A study by Jun et al. [25] demonstrated that regular gastroscopy could reduce the risk of stomach cancer death by 81%. The effect of early screening for stomach cancer in reducing the risk of death was also reflected in the results of the present study. On the other hand, mortality rates in stomach and liver cancers are almost entirely attributable to modifiable risk factors [26]. Thus, the decreases in the DALY rate for stomach and liver cancers may be attributed to improvements in the smoking rate [22], which is a modifiable risk factor.

In contrast, in cancers for which the cause has not yet been clearly identified, such as prostate cancer, multiple myeloma, testicular cancer, other urinary organ cancers (including renal pelvic and ureteric orifice cancers), uterine cancer, and kidney cancer, the rate of increase in disease burden tended to exceed 50%. Although chemical substances and genetic factors have been mentioned as causes of these diseases, the causal relationship between these factors and disease onset has not been clearly identified. Therefore, research that can improve the understanding of the causes of these diseases, as well as the causes of this increase in disease burden, is needed.

Because NHIS claims data were used as the main data source in the present study, the health insurance premium variables and regional variables in the Qualification and Premium Database were used to identify differences in income level and regional cancer burden and its characteristics. According to the regional results, there were many regions with relatively low disease burden in Seoul and Gyeonggi-do, the metropolitan areas, which may reflect the differences in medical access and imbalances. Health disparities generally arise from a complex combination of socioeconomic, biological, behavioral, and structural barriers [27], with lower socioeconomic groups more likely to engage, and persist, in unhealthy behaviors [28]. In addition, these groups may have relatively fewer opportunities for early detection and timely treatment, and have a higher risk of serious comorbidities, than high socioeconomic groups [29].

As revealed by the GBD study [30], the cancer burden was high in the low-income group within the country, with a higher rate of increase over the past 10 years. In contrast, the burden of most cancers decreased as income level increased, with the exception of thyroid and prostate cancers, which had a higher disease burden in higher income groups. This is similar to the results of a previous study in which the screening prevalence, incidence rate, and postoperative complication rate of thyroid cancer were higher in the high-income group than in other groups [31]. Controversy over the overdiagnosis of thyroid cancer has been growing in Korea since around 2014, and the claim that overdiagnosis is the cause of the rapid increase in thyroid cancer, based on the research published by Ahn et al. [32], has spread throughout the world. Proponents of this claim have publicly pointed out problems with thyroid cancer screening and argued that the Korean government and medical community should refrain from overdiagnosis and take preventive measures. In other words, because thyroid cancer screening is an opportunistic health checkup, it may be affected by the financial ability of service users [31]. On the other hand, other studies indicate that the risk of developing prostate cancer is increased in high socioeconomic groups [33]. In Korea, as with thyroid cancer, it is presumed that this is the result of active participation by the high-income group in screening rather than an actual difference in cancer risk. However, since there are few studies that have identified a consistent cause in this regard, additional research is needed to determine the relationship between prostate cancer and income level. Finally, although the top five cancer types remained the same among all income groups, there were slight differences in the rankings. Thus, it is necessary to consider these results when setting cancer management priorities.

Combining the above results, there was a gap in the cancer burden according to sex, region, and income level. Additionally, there was a difference in the ranking of the cancer types accounting for the most cancer burden according to sex and income level. The findings from the present study can be used as a basis for establishing cancer management programs tailored to the characteristics of cancer burden by region or income level in the future. Most importantly, since the top five cancers (such as TBL and breast cancers) accounted for more than 50% of the cancer burden for both men and women, cancer management policies and health resource allocation that prioritize these cancers are required. In addition, it is necessary to identify rapidly increasing cancer types or specific issues by continuously monitoring the cancer burden, and efforts are needed to identify the causes and prepare countermeasures.

The present study has several limitations. Although the cancer burden was examined at various levels, its association with risk factors was not confirmed. It is necessary to

quantify the attributable burden of risk factors such as smoking, drinking, and obesity, which are generally identified as being related to cancer. Because the frequency and level of exposure and the dangerousness of a risk factor may differ by age group, income level, etc., future studies should evaluate the attributable burden by various subgroups to provide useful evidence for cancer management. Another limitation is the uncertainty of the duration of each cancer. Although we used DisMod-II to estimate the duration of each cancer, it does not reflect differences in the duration of the disease according to the healthcare environment and the country's level of development. In the future, it is necessary to develop and establish a methodology that can directly estimate the duration of each disease using real-world data, including information on actual medical use in Korea. Finally, although the NHIS claims data is useful for examining the overall distribution and long-term trend of the cancer burden, it does not reflect non-used medical services, unmet needs for medical services, and misdiagnoses because it only covers cases diagnosed at medical institutions.

Our findings on the cancer burden provide valuable and quantitative data for the prioritization and evaluation of prevention strategies and implementation of cancer policies with a focus on cancer prevention and early diagnosis. Estimating the difference in cancer burden according to region and income level within a country can help elucidate the nature of the cancer burden and scale of the problem. In addition, the results of this study provide clues to understand the patterns in cause of cancer. Such understanding helps generating new hypothesis about its pathogenesis. However, in the case of carcinoma, the cause of which remains unknown despite its large cancer burden, it is necessary to continuously conduct research to determine its etiology and lay the foundation for prevention.

Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (https://www.e-crt.org).

Ethical Statement

This study was approved by the Institutional Review Board (IRB) of Korea University (IRB No. KUIRB-2018-0024-01). Due to the study's retrospective nature, informed consent was not required.

Author Contributions

Conceived and designed the analysis: Jung YS, Yoon SJ.
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Contributed data or analysis tools: Jung YS, Yoon SJ.
Performed the analysis: Jung YS, Yoon SJ.
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Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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