Trends in regional cancer mortality in Taiwan 1992–2014

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A R T I C L E   I N F O

A B S T R A C T

Background: Although the cancer mortality rate in Taiwan has been declining in recent years, no study has yet reported any regional differences in cancer mortality rates in Taiwan. We hypothesized that regional cancer mortality rates in Taiwan, an ethnically homogeneous society, exhibited no significant variations.

Methods: We investigated the trends in Taiwan regional cancer mortality between 1992 and 2014. We analyzed regional age-standardized cancer mortality rates for lung, liver, colon, stomach, oral, breast, and prostate cancers using the Taiwan Longitudinal Health Insurance Database and Demographic Database. Furthermore, we applied Joinpoint regression analysis to evaluate the trends across different regions.

Results: There are clear regional variations in mortality rates for liver, stomach, and oral cancers, but not for lung, colon, breast, and prostate cancers. The regional death rates of oral cancer, especially for eastern Taiwan, not only elevate the fastest (APC = 14.78% per year, P < 0.001) but also show the largest disparities between men and women. Regional death rates for stomach cancer, which declined most rapidly, are converging in both general and gender groups. Liver cancer is the only one with regional variations whose trends do not all go in the same direction. We also demonstrated that northern Taiwan has significant regional advantages with respect to cancer mortality.

Conclusions: Some but not all cancers in Taiwan show regional disparities. Liver, stomach, and oral cancers in Taiwan exhibit clear regional variations in mortality rates. In particular, the regional variations in oral cancer mortality rates are consistent with those in alcohol consumption.

1. Introduction

Cancer is the leading cause of death in Taiwan [1]. Over the past 20 years the incidences of cancer—including breast, colon, lung, oral, and prostate cancers—have been climbing in Taiwan [2,3]. Both incidence and mortality rates are higher among males than females. However, due to medical advances [4], the standardized cancer mortality rate in Taiwan has decreased from 143.5 per 100,000 population in 1996 to 126.8 in 2016 [1]. The mortality rates of some cancers have dropped significantly, as was the case for liver cancer and stomach cancer which fell from 29.5 and 13.0 in 1996 to 22.2 and 5.8 in 2016, respectively [1]. Meanwhile, mortality rates of some cancers are rising. For example, the mortality rates of female breast cancer and prostate cancer have increased from 10.1 and 5.0 in 1996 to 11.8 and 6.8 in 2016 (per 100,000), respectively [1]. Although a decline in Taiwan's overall cancer mortality rate has been reported [1], a systematic study of regional cancer mortality trends in Taiwan has yet to be conducted.

Elucidation of regional variations in cancer mortality could help in the detection of risk factors, evaluation of diagnostic accuracy, and determination of the effectiveness of a particular treatment. In the United Kingdom (UK) there are significant regional variations in lung cancer mortality rates [5]. These disparities in lung cancer mortalities have been attributed to varying smoking rates in different regions. In addition to lifestyle, environmental factors such as air quality and altitude may influence cancer mortality rates. In the United States, regions with high lung cancer mortality rates have significantly higher levels of daily environmental particulate matter with a diameter < 2.5 μm (PM2.5) than those without [6]. In Germany, the regional variations in mesothelioma mortality rates are associated with asbestos exposure levels [7]. In Ecuador, altitude might be linked to regional variations in stomach cancer mortality rates [8]. Furthermore, socio-economic status, medical care standards, and urbanization might also contribute to differences in regional cancer mortality rates. For example, in Brazil cancer mortality rates in the north and the northeast—which are poor and have less well equipped medical systems—are significantly higher than those in the wealthy southern and south-eastern regions with better medical care [9]. In Mainland China, regional variations in lung cancer mortality rates among individuals over 40 have been linked to urbanization. However, the differences between urban and rural areas have diminished [10].
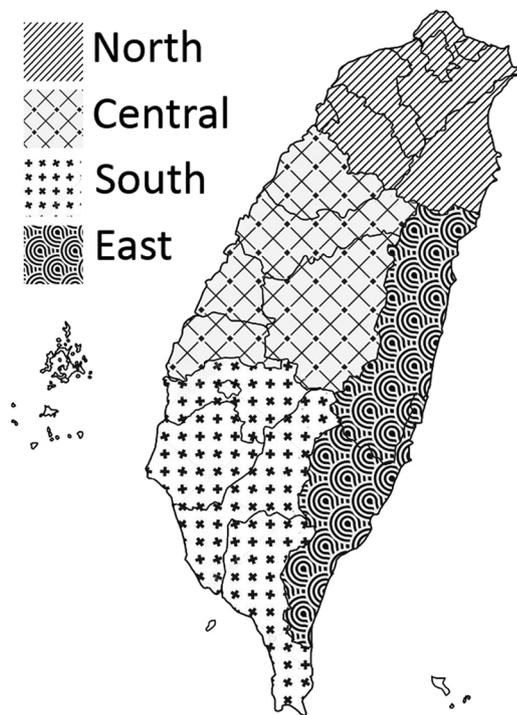

Fig. 1. The four major regions of Taiwan.

To our knowledge it has been unknown whether Taiwan, an ethnically homogeneous society, has any significant variations in regional cancer mortality rates. We thus investigated the regional mortality rates of seven cancers in Taiwan between 1992 and 2014. The seven cancers, accounting for about 70% of Taiwan's cancer mortality (Fig. S1), included the five with Taiwan's highest mortality rates and two additional cancers specific to each gender. In order by death rate from high to low were lung, liver, colon, stomach, oral, breast, and prostate cancers.

In this study we divided Taiwan into the northern, central, southern, and eastern regions, according to the main island's administrative history and its natural environment, to analyze the trends in mortality rates of these seven cancers.

2. Methods

2.1. Classification of regions

Fig. 1 shows the four regions of Taiwan—the north, the center, the south, and the east. Our regional classification is based on the administrative boundaries determined in 2005 (Method S1). Outlying islands such as Penghu and Kinmen were not included in this study.

2.2. Data source

To calculate the regional cancer mortality rates, we obtained the cancer death tolls and the population sizes for each of Taiwan's counties and cities from the Longitudinal Health Insurance Research Database [11] and the Demographic Database [12].

We examined all the cancers according to the classification of the International Classification of Diseases 10 (ICD-10). The ICD-9 classification, which was used in Taiwan until 2007, was converted to the ICD-10. The seven cancers we examined in this study were lung cancer (ICD-10 codes C33, C34), liver cancer (C22), colon cancer (C18–C21), stomach cancer (C16), oral cancer (C00–C06, C09, C10, C12–C14), female breast cancer (C50), and prostate cancer (C61).

We then used the World Health Organization 2000 standard population to calculate the age-adjusted standardized mortality rates

(ASMRs) (Method S2).

2.3. Trend analysis

We applied the joinpoint regression analysis program (Version 4.6.0.0) [13] from the American Cancer Institute to evaluate the trends in cancer mortality rates from 1992 to 2014. This non-linear regression program utilizes the slopes between the joinpoints to describe continuous trends in mortality rates [14]. In general, a positive slope means an upward trend, whereas a negative slope is a downward trend. The joinpoint regression analysis locates the optimal joinpoints via a grid-search method and determines their significance level using a permutation test. The resulting segments are formed based on the joinpoints. Assuming the *x* axis represents year and the *y* axis represents the log of the mortality rate, the slope of each segment is the annual percentage change (APC) of the ASMR.

3. Results

Taiwan's population is aging and cancer deaths are on the rise; the population's median age (Fig. S2) and age structure (Fig. S3) can vary across regions.

Table 1 shows average age-standardized cancer mortality rates in Taiwan across the four regions between 2010 and 2014. For the seven common cancers, the order of the cause of mortality (per 100,000) goes from high to low: lung cancer (25.4), liver cancer (24.3), colon cancer (14.8), breast cancer (11.4) (females only), oral cancer (7.9), stomach cancer (6.6), and prostate cancer (6.5). Among all the regional cancer mortality rates (per 100,000), liver cancer mortality in the south was the highest (30.0) and oral cancer mortality in the north was the lowest (5.5). In terms of regions, the east had the highest rate in four cancers—lung cancer (27.1), oral cancer (15.5), stomach cancer (9.0), and breast cancer (6.1)—out of the seven. The northern region had the lowest mortality rates for five of these cancers, including lung cancer (24.2), liver cancer (18.6), colon cancer (13.9), oral cancer (5.5), and prostate cancer (6.0). Assuming each region has an equal probability of being ranked the highest or lowest, the odds of at least five of these seven cancers being ranked lowest for a region is significant (P = 0.01). In other words, the north has a significant regional advantage with respect to cancer mortality rates. On the other hand, whether the east could have regional disadvantages is not statistically significant (P ≥ 0.05).

3.1. Overview of trends

Table 2 reveals the regional trends among the seven cancer mortality rates using joinpoint regression analyses. Generally speaking, the trends in the regional mortality rates for these seven cancers between 1992 and 2014 were consistent with the mortality trends observed for Taiwan as a whole (Fig. S4). However, there were some exceptions from the overall trend: for example, the colon cancer mortality rate in the north dropped between 1999 and 2014. Like the overall trends (Fig. S4), the regional colon, oral, female breast, and prostate cancer mortality rates climbed over the years; the regional lung, liver, and stomach cancer mortality rates declined. Figs. S5–S11 further illustrate the regional cancer mortality rates for four subgroups of ages (20–39, 40–59, 60–79, 80 +), and Figs. S12–S17 present those rates by sex focusing only on liver, oral, and stomach cancers. In addition, mortality rates in males across all regions were higher than those in females for all seven cancers (Fig. 3).

3.2. Regional trends by cancer type

3.2.1. Lung cancer

No substantial regional variations in lung cancer mortality rates were detected (Fig. 2). Table 1 indicates that between 2010 and 2014

Table 1
Average age-standardized and crude Taiwan regional mortality rates for lung, liver, colon, oral, stomach, breast and prostate cancers (2010–2014).

	Lung				Liver				Colon				Oral				Stomach				Breast[a]			Prostate	
	Crude[b]	ASMR (WHO)			Crude[b]	ASMR (WHO)			Crude[b]	ASMR (WHO)			Crude[b]	ASMR (WHO)			Crude[b]	ASMR (WHO)			Crude[b]	ASMR (WHO)		Crude[b]	ASMR (WHO)
		All	Male	Female		All	Male	Female		All	Male	Female		All	Male	Female		All	Male	Female		All	Female		Male
Taiwan	37.2	25.4	34.8	16.8	34.6	24.3	35.3	14.0	22.0	14.8	18.0	12.0	11.0	7.9	15.2	1.1	9.9	6.6	8.8	4.6	8.2	5.8	11.4	9.8	6.5
North	33.9	24.2	33.1	16.1	25.5	18.6	27.4	10.7	19.8	13.9	16.8	11.3	7.5	5.5	10.6	0.9	10.3	7.2	9.7	4.8	8.1	5.9	11.3	9.0	6.0
Center	38.6	26.2	36.8	16.7	38.7	27.1	39.3	15.3	22.2	14.9	17.9	12.1	13.5	9.9	19.0	1.1	8.9	5.9	7.8	4.3	8.0	5.9	11.7	10.3	7.1
South	40.3	26.2	35.2	18.0	44.8	30.0	43.2	17.3	25.4	16.4	20.1	12.9	13.6	9.5	18.1	1.2	9.4	6.1	8.0	4.3	8.4	5.8	11.4	10.5	6.8
East	45.2	27.1	37.5	17.1	39.9	25.5	35.5	15.3	23.3	14.0	17.4	10.6	22.5	15.5	26.7	4.0	15.5	9.0	11.7	6.4	9.1	6.1	12.6	12.5	6.8

ASMR, age-standardized mortality rate per 100,000 population.
[a] Male rates were not calculated due to rarity.
[b] Crude rates were calculated per 100,000 population.

the north and the east had the lowest and highest average lung cancer mortality rates (24.2 and 27.1 per 100,000 population), respectively. With the exception of the east, all regions have sloped downward since 1997 (Table 2). Between 1997 and 2014, the north declined the most with –0.96% APC (P < 0.001). Although all regions experienced up-ward trends before 1998, only the east maintained a steady but statistically non-significant increase (0.29% per year, P = 0.27) throughout the study period. Furthermore, the gap between male and female mortality rates diminished for all regions because male mortality rates decreased while female mortality increased (Fig. 3).

3.2.2. Liver cancer

Fig. 2 illustrates the regional differences in liver cancer mortality. From 2010 to 2014 the north and the south had the lowest and highest average mortality rate for liver cancer (18.6 and 30.0 per 100,000 population), respectively (Table 1). Only the north maintained a significant decline (APC = –1.33% per year, P < 0.001) throughout the study period (Table 2). Meanwhile, the center and the south rose before 2004 and fell afterward. The center and the south had similar mortality rates, but a significant gap separated them from the north. Although the liver cancer mortality rate in the east was growing, its magnitude was small and non-significant (APC = 0.30% per year, P = 0.29). Also, with the exception of the east, year-over-year differences between the male and female liver cancer mortality rates fell because of the decline in male liver cancer mortality (Fig. 3).

3.2.3. Colon cancer

Colon cancer showed no significant regional variations (Fig. 2). Table 1 indicates that between 2010 and 2014 the north and the south had the lowest and highest regional colon cancer mortality rates (13.9 and 16.4 per 100,000 population) respectively. The rates in all regions escalated during the 1990s. After 2000 the growth slowed and even decreased in the north. Between 1999 and 2014 the north was the only region in which colon cancer mortality dropped (APC = –0.65% per year, P < 0.001, Table 2); the gender differences in colon cancer mortality rates across regions were smaller than those for lung or liver cancer mortality rates, and male and female colon cancer mortality rates in the east even crossed over each other (Fig. 3).

3.2.4. Stomach cancer

There were clear regional differences in stomach cancer mortality rates, although the differences are diminishing (Fig. 2). Since 2004, all regions displayed a steady decline in stomach cancer mortality; despite falling steadily in the east (APC = –3.33% per year, P < 0.001, Table 2), stomach cancer mortality rates remained the highest of all (Table 1). In contrast to the center, for example, the difference in deaths per 100,000 population between the center and the east was 5.0 in 1992, dropping to 3.1 during the period 2010–2014; in 1992 the east and the center experienced 15.3 and 10.3 deaths per 100,000 population, respectively, falling to 9.0 and 5.9 during the period 2010–2014. Furthermore, the difference between male and female stomach cancer mortality rates also shrank, especially in the north and the east, where male stomach cancer mortality rates dropped (Fig. 3). Since 2014, the center had the most impressive decline in both male and female stomach cancer mortality rates (APC = –5.18% per year, P < 0.001, Table S1, and APC = –4.53% per year, P < 0.001, Table S2, respectively).

3.2.5. Oral cancer

There were significant regional variations in oral cancer mortality rates (Fig. 2). As shown in Table 1, between 2010 and 2014 the north had the lowest average oral cancer mortality rate (5.5 per 100,000) and the south had the highest (15.5 per 100,000). This 2.8-fold difference is the largest regional variation (Fig. 2). Between 1992 and 2014, oral cancer mortality rates increased in all regions. The east was consistently high, the center and the south were similar, and the north was the

Table 2
Joinpoint regression analysis of trends in breast, colon, liver, lung, oral, stomach and prostate cancer mortality rates by region (1992–2014).

	Trend 1			Trend 2			Trend 3			Trend 4			Trend 5		
	Years	APC	P	Years	APC	P	Years	APC	P	Years	APC	P	Years	APC	P
Breast															
North	1992–1995	9.00	0.08	1995–2014	0.69[a]	2.4×10^{-3}									
Center	1992–2014	2.03[a]	$< 1.0 \times 10^{-8}$												
South	1992–2014	1.54[a]	2.5×10^{-7}												
East	1992–2014	2.72[a]	5.2×10^{-4}												
Colon															
North	1992–1999	3.62[a]	4.1×10^{-4}	1999–2014	−0.65[a]	5.9×10^{-4}									
Center	1992–1998	6.34[a]	5.0×10^{-4}	1998–2014	0.18	0.47									
South	1992–1997	7.99[a]	2.3×10^{-4}	1997–2014	0.60[a]	4.6×10^{-3}									
East	1992–2000	4.64[a]	0.01	2000–2014	0.25	0.65									
Liver															
North	1992–2014	−1.33[a]	$< 1.0 \times 10^{-8}$												
Center	1992–2003	1.19[a]	0.01	2003–2014	−1.57[a]	3.5×10^{-4}									
South	1992–1996	5.48[a]	2.7×10^{-3}	1996–1999	−3.03[a]	0.45	1999–2004	2.84[a]	0.04	2004–2014	−2.11[a]	3.5×10^{-6}			
East	1992–2014	0.30	0.29												
Lung															
North	1992–1997	3.24[a]	4.1×10^{-3}	1997–2014	−0.96[a]	2.7×10^{-7}									
Center	1992–1996	8.95[a]	4.6×10^{-5}	1996–2014	−0.46[a]	1.7×10^{-3}									
South	1992–1997	5.57[a]	1.3×10^{-4}	1997–2014	−0.67[a]	1.1×10^{-4}									
East	1992–2014	0.29	0.27												
Oral															
North	1992–1996	14.59[a]	0.01	1996–2014	2.43[a]	3.1×10^{-7}									
Center	1992–2004	5.68[a]	$< 1.0 \times 10^{-8}$	2004–2014	0.04	0.91									
South	1992–2003	8.09[a]	$< 1.0 \times 10^{-8}$	2003–2014	0.29	0.54									
East	1992–1998	14.78[a]	4.4×10^{-3}	1998–2014	1.76[a]	0.02									
Stomach															
North	1992–1996	0.38	0.80	1996–2014	−4.06[a]	$< 1.0 \times 10^{-8}$									
Center	1992–1996	3.01	0.11	1996–2001	−4.76[a]	0.01	2001–2004	2.76	0.60	2004–2008	−7.58[a]	0.01	2008–2014	−3.51[a]	2.7×10^{-3}
South	1992–1998	0.03	0.99	1998–2014	−3.75[a]	$< 1.0 \times 10^{-8}$									
East	1992–2014	−3.33[a]	$< 1.0 \times 10^{-8}$												
Prostate															
North	1992–2001	6.34[a]	1.2×10^{-6}	2001–2014	0.12	0.70									
Center	1992–1996	17.59[a]	0.03	1996–2014	0.94[a]	0.04									
South	1992–1997	16.47[a]	3.2×10^{-3}	1997–2014	1.06[a]	0.02									
East	1992–2007	6.43[a]	3.5×10^{-5}	2002–2014	−2.84	0.27									

APC, annual percentage change.
[a] Significantly different from 0 (P < 0.05).
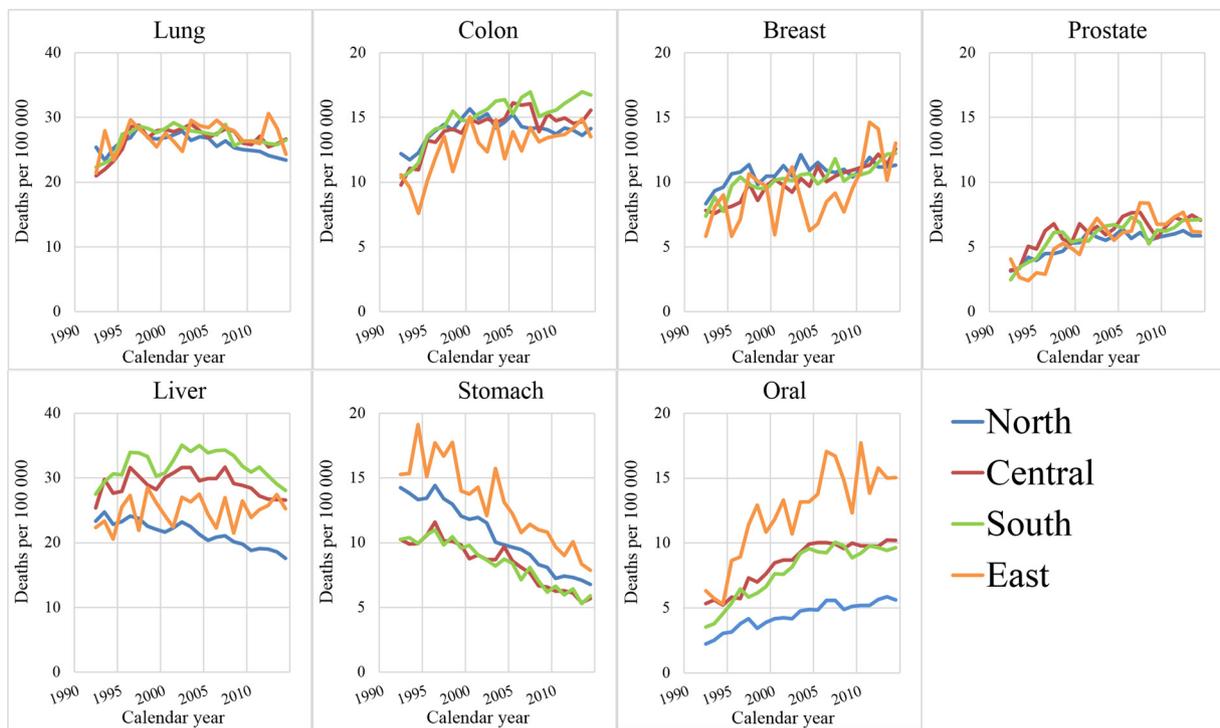
Fig. 2. Regional age-standardized mortality rates (ASMRs) for lung, liver, colon, stomach, oral, breast, and prostate cancers (1992–2014). The lower three panels show significant regional variations; the upper four do not. ASMR unit: deaths per 100,000 population standardized to the world standard population.

lowest. Since the mid-1990s, oral cancer mortality rates have soared, particularly in the east (APC = 14.78% per year, P < 0.001, Table 2). After 2004, the increases in all regions decelerated. For example, the east was left with a growth rate of only 1.76% per year (P = 0.02). Also, regional differences have expanded more in recent years than they did during the period 1992–1996. Likewise, for each region the differences between male and female oral cancer mortality rates have grown over time (Fig. 3); the male oral cancer mortality rates rose, especially in the east from 1992 to 1997 (APC = 20.87% per year, P < 0.01, Table S1), while the female rates remained steady (Table S2). Since 1992, the oral cancer mortality rate for males in the east has undergone more than a three-fold increase, resulting in the greatest gender variation (Fig. 3).

3.2.6. Breast cancer

As shown in Fig. 2, there were minor or no significant regional variations in breast cancer. All regions experienced an increase in breast cancer mortality rates, while the east exhibited a great variability (Fig. 4). Between 2010 and 2014, the south had the lowest breast cancer mortality rate (5.8 per 100,000) while the east had the highest (6.1 per 100,000) (Table 1). Despite being statistically non-significant, a surge for breast cancer mortality developed in the north between 1992 and 1995 (APC = 9.00% per year, P = 0.08, Table 2). Afterwards its growth gradually leveled out (APC = 0.69% per year, P < 0.01). Meanwhile, the south (APC = 2.03% per year, P < 0.001), the center (APC = 1.54% per year, P < 0.001), and the east (APC = 2.72% per year, P < 0.001) exhibited trends of continuous growth (Table 2).

3.2.7. Prostate cancer

No significant regional variations in prostate cancer mortality were seen (Fig. 2). As shown in Table 1, between 2010 and 2014 the center had the highest prostate cancer mortality rate, followed by the south, the east, and then the north with the lowest (7.1, 6.8, 6.8, 6.0 per 100,000, respectively). The rates of all regions escalated between 1992 and 1996, especially in the center (APC = 17.59% per year, P = 0.03); however, since 2001 they have slowed. With regards to APC, the center and the south experienced similar regional changes (Table 2). All

regions experienced an increase during the study period, with the exception of the east which displayed a statistically non-significant decline from 2007 to 2014 (Fig. 4).

4. Discussion

This study of age-adjusted mortality rates demonstrates that some cancers in Taiwan have clear regional variations. Oral, stomach, and liver cancers exhibit clear regional variations based on the magnitude of changes in regional mortality rates, but lung, colon, breast, and prostate cancers do not. With the exception of oral cancer, mortality rates for which have shown increasing regional variation, each cancer across the four regions in Taiwan exhibits an even or converging temporal trend. This suggests that Taiwan is moving in the direction of health equality for all cancer patients.

Not all of the seven cancers exhibited a monotonic decline in mortality rates between 1992 and 2014. Despite a global downward trend in cancer mortality [15], in Taiwan only liver and stomach cancers had lower mortality rates in 2014 than in 1992. During this period, lung cancer in all regions except the east, liver cancer in the center and the south, and colon cancer in the north rose and then declined, yet the others exhibited upward regional trends. Oral, breast, and prostate cancers, as well as colon cancer (except in the north), rose continually across all regions. Among these, oral cancer mortality increased the most.

The regional differences in oral cancer mortality rates correlate with those of the increasing incidence rates, thereby also correlating with those of oral cancer risk factors such as alcohol consumption [16] in Taiwan. Surprisingly, oral cancer death rates across all regions in Taiwan have continued to rise, and their regional gaps are expanding as well. The increase in mortality across all regions has been decelerating since 2004, corresponding to the beginning of the biennial Taiwanese statewide oral cancer screening program in that same year [2]. This may have aided early diagnosis and reduced mortality. However, the steadily rising trends and gaps are causes for alarm, particularly for males in the east, which had Taiwan's highest alcohol consumption
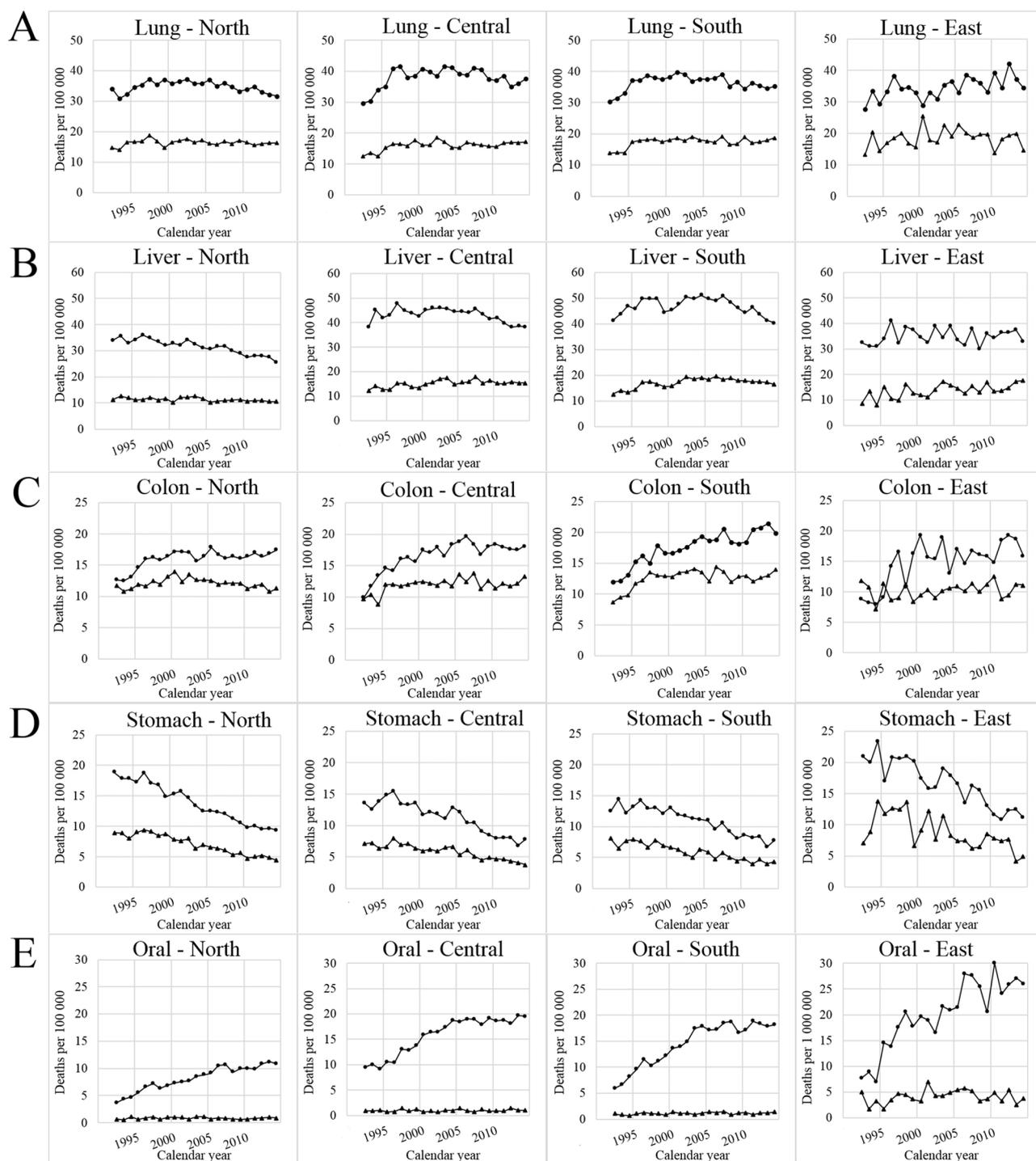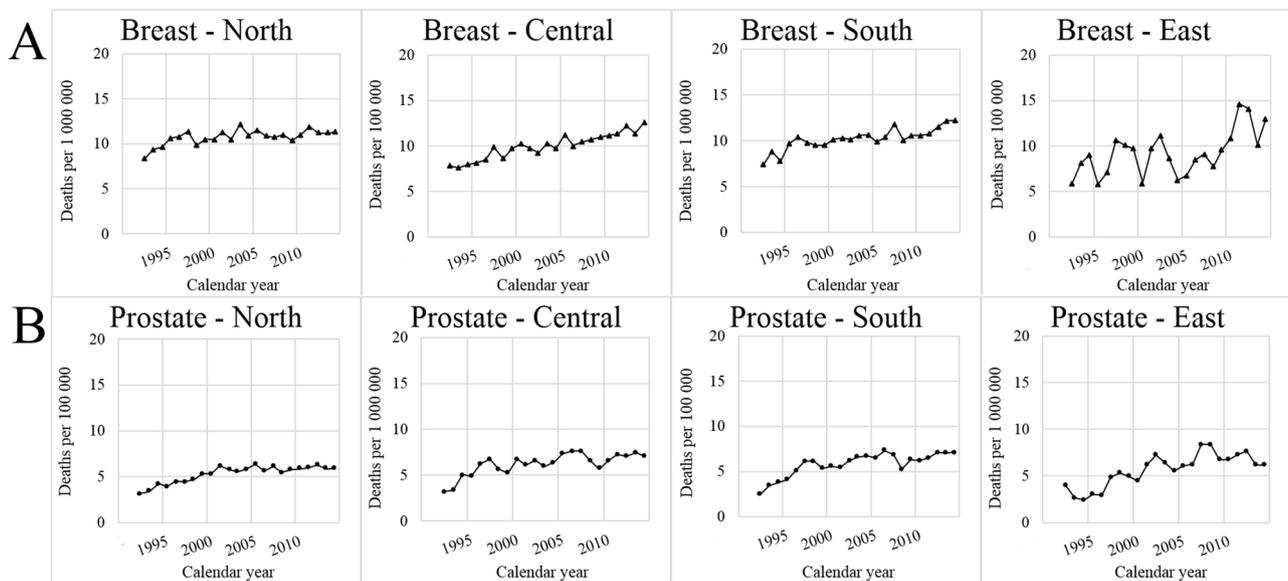
Fig. 3. Trends in age-standardized mortality rates (ASMRs) of five common cancers across four regions of Taiwan (1992–2014). (A) Lung cancer, (B) liver cancer, (C) colon cancer, (D) stomach cancer, and (E) oral cancer. Circles represent men; triangles represent women. ASMR unit: deaths per 100,000 population standardized to the world standard population.

levels [17,18]. To reduce the oral cancer mortality rates, prevention and improved treatments are both needed.

The most encouraging finding is perhaps the downward and converging regional death rates for stomach cancer. This notable decline corresponding with global trends in stomach cancer mortality indicates improvement in medical diagnosis, treatment, and early prevention, including the reduction in *Helicobacter pylori* infection and improved food storage and preservation [19]. However, it remains unclear what contribution each improvement—prevention through better hygiene, food preservation, or improved stomach cancer surgery—made to the

decrease in mortality. The diminishing regional differences may well have been the combined results of concurrent hygiene improvement and balanced health care across all regions [20].

Among those cancers with regional variations, liver cancer exhibits the most peculiar pattern in mortality rates. Those in the center and the south rose and then fell; those in the north steadily declined, while those in the east slowly increased but not statistically significantly. This large and uncommon regional difference would mean that if the regional population sizes were the same, the south would experience 1.6 times more liver cancer deaths than the north. The drop in liver cancer

Fig. 4. Trends in age-standardized mortality rates (ASMRs) of two other cancers across four regions of Taiwan (1992–2014). (A) Breast cancer, and (B) prostate cancer. Circles represent men; triangles represent women. ASMR unit: deaths per 100,000 population standardized to the world standard population.

mortality is attributable to both hepatitis B vaccination (hepatitis B is one of the primary causes of liver cancer [21]) since 1986 [22] and the higher survival rates of modern hepatectomies [23]. However, the causes of the regional variation remain to be elucidated. The prevalence of hepatitis C in the center and the south [24], the implementation of advanced hepatitis screening in the north since 2003 [25], and alcohol usage rates [17,18] in the east may each contribute to the regional variation. The variation in liver cancer mortality has recently been linked to PM2.5 exposure [26]. However, further investigation is required to identify the mechanisms behind this pattern.

Among those cancers without significant regional variations, lung cancer had the highest regional mortality rates; this was despite a decline in the rates. The downward trends in regional lung cancer mortality rates were correlated with the decline in smoking across all regions among adults [27]. Unlike the situation in the UK [5], however, a slight regional variation in smoking rates [17] did not lead to significant regional variation in lung cancer mortality in Taiwan. Neither did the slight decline in female smoking rates [17] explain the slight upward trend in regional female lung cancer mortality rates. Instead, the rising female lung cancer mortality may be more closely related to cooking practices [28] and air pollution [29].

There was no clear regional variation in colon cancer mortality rates. While both the overall incidence [3] and mortality rates were on the rise, the slowdown in the increase of colon cancer mortality rates across all regions (Table 2) may be attributable to the introduction of colon cancer screening in 1999 [2]. Extended colon cancer screening in 2004 [30], which may have enhanced awareness, early diagnosis, and treatment (especially in the north) may have further reduced mortality. In recent years, colon cancer screening has become even more thorough, and the latest study has showed a drop in overall colon cancer mortality [1].

Likewise, breast cancer mortality rates across four regions showed similar and gradual increases, while the incidence rates spiked [3]. The breast cancer mortality-to-incidence ratio, which was roughly 1:3 in the 1990s, has become 1:5 in the 2010s. Because the mortality-to-incidence ratio can be used as an indicator for the efficacy of cancer screening [31], the declining mortality-to-incidence ratio suggests that biannual breast cancer screenings and mammograms since 2002 [2] may have contributed to early diagnosis, thus suppressing the growth in breast cancer mortality [32]. To effectively suppress the growing mortality rates, however, it would be necessary to thwart breast cancer at any

onset ages.

Prostate cancer in Taiwan exhibited no significant regional differences in mortality rates. Unlike the downward trend in most European countries, such as the UK [5], the gradual rise in mortality may have been the result of spiking incidence [3].

This study has also revealed regional health disparities in Taiwan. We demonstrated statistically that the north had a regional advantage with regard to cancer mortality rates. Of the seven cancers, the five lowest mortality rates were in northern Taiwan. The north was also the only region to show a decline in the four major cancer mortality rates (lung, liver, colon, and stomach cancers) in recent years. This advantage may be due to lower cancer incidence rates in the north [33]. Different degrees of palliative care utilization [34] might also further the differences, as palliative care may benefit survival rates. Besides, the superior socioeconomic status of the north [35] could allow cancer patients to receive better care; individuals with higher educational levels in the north may take more appropriate actions and hold more favorable attitudes toward their treatment. The above factors must be considered to explain how northern Taiwan exhibits such an advantage with respect to cancer.

Cancers which have regional variations or not might be universal. We compared our results with the UK regional cancer study of lung, colon, breast, and prostate cancers [5]. Both studies showed that colon, breast, and prostate cancers consistently displayed minor regional variations, with the exception of lung cancer in England. This may mean that, by default, cancer mortality rates should behave similarly under conditions of similar genetic makeup, physical environment, demographic conditions, socioeconomic status, access to health care, and risk-factor exposure.

This study has some limitations. First, this is an observational study at the regional level, so we cannot determine the causes of the variations in locations smaller than the regions, such as cities and counties. Second, deaths involve multiple aspects. Inaccurate death certificates could be recorded, and determining the causes of death in elderly cancer patients is especially difficult. Third, the change of ICD codes in 2007 from ICD-9 to ICD-10 could lead to code comparability issues. However, the conversion between ICD-9 and ICD-10 is rather stable for cancer because its comparability ratio is 1.0068 [36].

To our knowledge, however, this is the first comprehensive study of Taiwan's regional cancer mortality rates. Previous reports have documented mortality statistics of individual cancers, but none has

addressed regional variation. The present study examines seven common cancers across four regions over 23 years, making its findings more robust than studies not accounting for regional trends.

5. Conclusions

Each of the seven cancers exhibits a congruent trend in mortality rates across regions, albeit with some regional variations. Oral, liver, and stomach cancers in Taiwan exhibit significant regional variations in mortality rates; lung, colon, breast, and prostate cancers do not. The striking regional disparities in oral cancer mortality rates could be a red flag to oral cancer patients in afflicted regions. Regional variations could raise public awareness, draw attention to healthcare policies, and reveal underlying cancer risk factors.

Conflict of interest statement

The authors declare no potential conflicts of interest.

Authors' contributions

YRH and KYC conceived of the study and participated in its design, implementation of the experiments and coordination. YRH collected the data. YRH and KYC performed the statistical analyses and interpretation. YRH, SPM, and KYC drafted the manuscript, read, and approved the final manuscript.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.02.005.

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