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ORIGINAL ARTICLE

Thyroid cancer: incidence and mortality trends in China, 2005–2015

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Abstract

Purpose Understanding secular trends of thyroid cancer is critical to plan strategies for cancer prevention and control. Our aim was to estimate the incidence and mortality trends of thyroid cancer in China during 2005–2015.

Methods A retrospective cohort evaluation of thyroid cancer cases and deaths during 2005–2015 was performed using population-based data from the *Chinese Cancer Registry Annual Report*. The incidence and mortality rates of thyroid cancer were stratified by gender, age group (0, 1–4, 5–9, 10–14…80–84, 85–), and area (urban or rural). A Joinpoint regression model was used to examine secular trends.

Results In China, the age-standardized incidence was $3.21/10^5$ in 2005, and increased to $9.61/10^5$ in 2015. Besides, a significant increase incidence rate was observed with the average annual percent change (AAPC) of 12.4% (95% CI: 10.5%–14.4%) in the period 2005–2015. The age-standardized mortality was $0.30/10^5$ in 2005 and $0.35/10^5$ in 2015, and the AAPC was 2.9% (95% CI: 1.3%–4.5%). For both incidence and mortality, the rates of thyroid cancer were much higher in females than in males, and in urban areas rather than rural areas; however, the rates of increasing trends showed no significant differences. With respect to the highest age-specific rates, it appeared in the age group of 50–54 years old for incidence and in the age group of 80–84 years old for mortality. Notably, the rate of increasing incidence trend was lower in older age groups, especially for people aged 70–79 years old.

Conclusion A rapid increase in incidence and a moderate increase in mortality of thyroid cancer were observed from 2005 to 2015 in our study. Effective measures and tailored programs should be taken to curb the growth trend and reduce the disease burden.

Keywords Thyroid cancer · Incidence · Mortality · Trends · Joinpoint · China

Introduction

Although thyroid cancer is a relatively rare neoplasm worldwide, it is the most frequent endocrine cancer. According to the International Agency for Research on Cancer's GLOBOCAN 2012 [1], 298,000 thyroid cancer cases were diagnosed worldwide, accounting for 2.1% of the total estimated new cases. The age-standardized incidence rate was $4.0/10^5$, with 3-times more common in women ($6.1/10^5$) than that in men ($1.9/10^5$). Relative to cases, deaths of the thyroid cancer are much lower (40,000 or 0.5% of all cancer deaths). The age-standardized mortality rate (ASMR) was $0.5/10^5$, and there is no difference between men ($0.4/10^5$) and women ($0.6/10^5$).

In China, the crude incidence rate and ASIR of thyroid cancer were $13.17/10^5$ and $9.61/10^5$ in 2015 [2], respectively, which have increased markedly compared with that in 2005 ($4.30/10^5$ and $3.21/10^5$). Several countries have reported a rapid increase in the incidence rate of thyroid cancer over the past few decades, including the United States [3], Canada [4], Lithuania [5], Sri Lanka [6], and China [7]. However, until now, substantial share of causes of this increasing trend remain unknown or not fully identified. Exposure to ionizing radiation is the best established

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risk factor for thyroid cancer, especially for children [8]. Some other potential factors, such as female hormones [9] and iodine deficiency [10], may be partly responsible for the observed increase although the extents of these contributions are unclear. In addition, whether the mortality rate of thyroid cancer is stable or increasing is controversial [11, 12]. Thus, the current hypothesis is that the increase is mainly due to improved sensitivity of diagnostic tools [13], especially that of ultrasonography (US) and fine needle aspiration biopsy (FNAB), leading to an increased detection of small sub-clinical tumors. However, others argued that over-diagnosis cannot explain the observed increase fully [14]. For instance, a study found an increased incidence rates in differentiated thyroid cancer of all sizes in both men and women on basis of the surveillance epidemiology and end results (SEER) data [15].

However, a comprehensive epidemiology description of thyroid cancer during a long period has not yet been conducted in China. To bridge this gap, our study sought to describe and analyze the trends in incidence and mortality rates of thyroid cancer in China during 2005–2015 based on data from the *Chinese Cancer Registry Annual Report*. We reported the estimated number of new cases and deaths, as well as the corresponding incidence and mortality, age-standardized rates (ASRs), and the annual percent change (APC), describing variations by gender, age, and area.

Methods

Data source

The analysis data of thyroid cancer including cancer cases, deaths, incidence, mortality, and the ASRs during 2005–2015 were derived from the *Chinese Cancer Registry Annual Report*. They were collected from local population-based cancer registries, and then submitted to the National Central Cancer Registry (NCCR). After careful checks and evaluation, the data meet the requirements would be used for the analysis. Thyroid cancer (C73) cases were identified by the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). The resource was all individual cases diagnosed with or died of thyroid cancer between the 1st January and the 31st December in one year.

Statistical analysis

Crude incidence and mortality rates of thyroid cancer were classified by gender, age groups (0, 1–4, 5–9, 10–14… 80–84, 85–), and areas (urban or rural). The number of new cases or deaths of every age group were estimated using the 5-year age-specific incidence or mortality and the populations corresponded. The pooled age-specific rates calculated by Joinpoint Regression Program were also analyzed from 2005 to 2015. The Chinese population structure in 1982 (2005–2009) or 2000 (2010–2015) and Segi's world population structure were applied for ASRs. And all the rates were expressed as per 100,000 person-year.

Joinpoint regression analysis were performed to identify calendar years, where occurred a statistically significant change. For each period of the identified trends, an estimated APC was calculated by means of generalized linear models assuming a Poisson distribution [16]. Using Segi's world population, the average annual percent change (AAPC), APC, and corresponding 95% confidence intervals (95% CI) were calculated to quantify changes in incidence and mortality, and by gender, age group, and area. Joinpoint Regression Program Version 4.7.0.0. was used for analysis. Significance level α was set at 0.05 for two sides.

Results

Population data

The number of cancer registries increased from 45 to 501 during 2005–2015, covering a total population of 69–388 million and accounting for 5.31–28.22% of the overall national population. After quality evaluation, data from 34 to 388 cancer registries were accepted for this study from 2005 to 2015, covering a total population of 55 million to 321 million and accounting for 4.20–23.35% of the whole national population. The number of registers and coverage population were shown in Table 1.

Incidence and mortality rates of thyroid cancer

In 2015, there were 42,249 new thyroid cancer cases estimated occurred from 321 million people in Chinese accepted registries, with a higher frequent in women (10,178 for males and 32,071 for females), accounting for 4.58% of overall new cancer cases. The crude incidence rate of thyroid cancer was $13.17/10^5$ ($6.25/10^5$ in males and $20.28/10^5$ in females). The ASIRs were $11.05/10^5$ and $9.61/10^5$ after being standardized by the age structure of Chinese population and the world population, respectively. Compared with previous years, all indicators were increased both in overall population and in male or female population, which showed the growing disease burden caused by thyroid cancer. Meanwhile, the annual burden was markedly higher among female population than male population at approximately three times greater in terms of new cases (Table 2).

Table 1 The exact information of cancer registries in China during 2005–2015

Year	No. registries (urban/rural)	Population (millions)	Ratio (%)	Accepted registries (urban/rural)	Population (millions)	Ratio (%)
2005	45 (20/25)	69	5.31	34 (16/18)	55	4.20
2006	49 (21/28)	76	5.80	34 (15/19)	60	4.53
2007	48 (20/28)	71	5.36	38 (17/21)	60	4.53
2008	56 (26/30)	82	6.21	41 (20/21)	66	4.98
2009	104 (46/58)	109	8.20	72 (31/41)	85	6.40
2010	219 (92/127)	207	15.42	145 (63/82)	158	11.86
2011	234 (98/136)	221	16.43	177 (77/100)	175	13.01
2012	261 (100/161)	239	17.65	193 (74/119)	198	14.63
2013	347 (126/221)	287	21.11	255 (88/167)	226	16.65
2014	449 (160/289)	346	25.27	339 (129/210)	288	21.07
2015	501 (174/327)	388	28.22	388 (142/246)	321	23.35

The estimated number of thyroid cancer deaths from 321 million people covered by the accepted registries was 1865 (712 for males and 1153 for females), accounting for 0.33% of overall cancer deaths in 2015. The crude mortality rate was $0.58/10^5$ ($0.44/10^5$ in males and $0.73/10^5$ in females). The ASMR China and ASMR world were $0.36/10^5$ and $0.35/10^5$, respectively. Year-by-year crude and ASMR are detailed in Table 3. Notably, similar to the incidence, female population was also the remaining larger contributors to the mortality.

With regard to gender and area, the ASIR was greatest for females in urban areas, followed by females in rural areas, males in urban areas and males in rural areas. Broadly, thyroid cancer occurred more often among females than males, urban areas than rural areas. Besides, the incidence rate for females in urban areas increased more sharply than those in other groups (Fig. 1a). When assessed on both gender and area, the ASMR all remained stable in four groups, with slight fluctuations. Similarly, the greatest mortality burden for thyroid cancer was observed in females of urban areas, while the difference was not obvious compared with the ASIR (Fig. 1b).

Age-specific incidence and mortality rates of thyroid cancer

Age-specific incidence and mortality rates of thyroid cancer for different years were compared. Generally, the incidence was relatively low in the population younger than 14 years old. However, the rate dramatically increased from 15 years old and peaked at age group of 50–54 years, then gradually decreased and leveled off at age group of 75–79 years and even older. The trend of age-specific incidence rate in 2005–2015 was similar except for the gradual growing rates, especially in the age group of 30–69 years. Different from the incidence rates, before 40 years old, the mortality rates were very low. From the age group of 55–59 years and above, the mortality rate increased very quickly, reached highest at the age group of older than 80 years or 75–79 years and then slightly dropped after that. Moreover, the differences of mortality rates among 11 years were negligible (Fig. 2).

Stratified by gender, the spectrum of age groups observed in 11 years differed. Overall, 40–59 years was the most common age group in terms of incidence rate, accounting for ~50% of the new thyroid cancer cases. For males, the proportion of new cases showed a slight decrease at age groups of 0–24 years and older than 70 years and increased at age group of 25–39 years during 2005–2015. And for females, the proportion of new cases showed a decrease at the same age groups and increased slightly at age group of 55–64 years. In terms of cancer deaths, the age group profile according to different years was heterogeneous. Both in males and in females, the burden of cancer deaths mainly occurred in patients aged 70 years or older, and there is almost no deaths before 30 years. The proportions of age group of 20–39 years and older than 80 years gradually increased in males, whereas, the proportion of age group of 70–79 years reduced. A similar transition was observed when females were assessed. (Fig. 3).

After stratified by gender and area, the age-specific trends of male, female, urban, and rural groups were similar to overall population, which reached the peak in patients aged 50–54 years. In addition, the age-specific rates were highest in females, followed by urban areas, rural areas, and males. Importantly, the speed of rise and decline in female and urban groups were faster than that in male and rural groups. In terms of mortality rate, the trends of four groups were also similar. However, there was no significant difference between them. It's worth noting that only the age-specific rate of rural area declined at the age group of 75–79 years or older (Fig. 4).

Table 2 Incidence of thyroid cancer in registration areas of China, 2005–2015

Year	Gender	No. cases	Crude rate ($1/10^5$)	Ratio (%)	ASR China ($1/10^5$)	ASR world ($1/10^5$)
2005	Both	2361	4.30	1.66	2.78	3.21
	Male	550	1.98	0.69	1.25	1.49
	Female	1811	6.68	2.91	4.35	4.97
2006	Both	2977	5.00	1.83	3.22	3.68
	Male	659	2.20	0.72	1.41	1.63
	Female	2318	7.84	3.23	5.06	5.76
2007	Both	3212	5.37	1.94	3.48	3.97
	Male	732	2.42	0.79	1.57	1.80
	Female	2480	8.38	3.40	5.42	6.17
2008	Both	4435	6.71	2.24	4.20	4.81
	Male	993	2.98	0.90	1.88	2.15
	Female	3442	10.49	3.92	6.55	7.50
2009	Both	5607	6.56	2.29	4.21	4.80
	Male	1344	3.11	0.98	1.97	2.29
	Female	4263	10.09	3.99	6.50	7.36
2010	Both	7740	6.21	2.21	5.13	4.56
	Male	1806	2.86	0.91	2.38	2.12
	Female	5934	9.64	3.93	7.93	7.03
2011	Both	11,431	7.84	2.77	6.53	5.75
	Male	2816	3.82	1.21	3.24	2.83
	Female	8615	11.95	4.79	9.86	8.72
2012	Both	17,162	8.67	3.09	7.20	6.34
	Male	4097	4.08	1.31	3.45	3.02
	Female	13,065	13.37	5.36	11.02	9.72
2013	Both	23,011	10.16	3.57	8.43	7.37
	Male	5591	4.87	1.55	4.13	3.57
	Female	17,420	15.60	6.14	12.80	11.24
2014	Both	35,435	12.29	4.29	10.22	8.93
	Male	8846	6.05	1.93	5.18	4.46
	Female	26,589	18.72	7.25	15.36	13.49
2015	Both	42,249	13.17	4.58	11.05	9.61
	Male	10,178	6.25	1.99	5.42	4.63
	Female	32,071	20.28	7.77	16.79	14.68

Data were obtained from the *Chinese Cancer Registry Annual Report*

ASIR China age-standardized incidence rate by Chinese population, *ASIR world* age-standardized incidence rate by world population

Table 3 Mortality of thyroid cancer in registration areas of China, 2005–2015

Year	Gender	No. cases	Crude rate ($1/10^5$)	Ratio (%)	ASR China ($1/10^5$)	ASR world ($1/10^5$)
2005	Both	248	0.45	0.27	0.22	0.30
	Male	91	0.33	0.16	0.17	0.23
	Female	157	0.58	0.45	0.26	0.36
2006	Both	219	0.37	0.21	0.17	0.23
	Male	75	0.25	0.11	0.12	0.16
	Female	144	0.49	0.37	0.22	0.30
2007	Both	247	0.41	0.23	0.18	0.26
	Male	97	0.32	0.15	0.16	0.22
	Female	150	0.51	0.38	0.20	0.30
2008	Both	331	0.50	0.27	0.21	0.29
	Male	120	0.36	0.16	0.17	0.23
	Female	211	0.64	0.46	0.25	0.34
2009	Both	455	0.53	0.29	0.23	0.32
	Male	160	0.37	0.17	0.17	0.24
	Female	295	0.70	0.51	0.29	0.40
2010	Both	546	0.44	0.25	0.29	0.28
	Male	199	0.32	0.14	0.22	0.22
	Female	347	0.56	0.42	0.36	0.34
2011	Both	777	0.53	0.30	0.35	0.34
	Male	254	0.34	0.15	0.24	0.24
	Female	523	0.73	0.54	0.46	0.44
2012	Both	1032	0.52	0.30	0.34	0.33
	Male	364	0.36	0.17	0.24	0.24
	Female	668	0.68	0.52	0.44	0.42
2013	Both	1153	0.51	0.29	0.33	0.32
	Male	410	0.36	0.16	0.23	0.23
	Female	743	0.67	0.50	0.42	0.40
2014	Both	1612	0.56	0.32	0.36	0.35
	Male	587	0.40	0.19	0.27	0.26
	Female	1025	0.72	0.56	0.45	0.43
2015	Both	1865	0.58	0.33	0.36	0.35
	Male	712	0.44	0.20	0.28	0.27
	Female	1153	0.73	0.56	0.45	0.43

Data were obtained from the *Chinese Cancer Registry Annual Report*

ASMR China age-standardized mortality rate by Chinese population, *ASMR world* age-standardized mortality rate by world population

Temporal trend of thyroid cancer incidence and mortality rates

During 2005–2015, AAPC in the age-adjusted incidence rate was 12.4% (95% CI: 10.5–14.4%). When gender-specific trends were analyzed, the incidence rate of thyroid cancer increased regardless of gender. The AAPC was higher in males (13.3%, 95% CI: 11.2–15.6%) than in females (10.7%, 95% CI: 8.3–13.1%) during the whole study period. In females, the Joinpoint regression analysis showed two-time periods with joinpoint in the year 2010. APC were 6.4% (95% CI: 1.3%, 11.8%) in the period 2005–2010, 15.1% (95% CI: 12.2%, 18.1%) in the period 2010–2015, respectively (Fig. 5). When age-specific trends were explored, increasing trends were observed in all age groups except for the population aged 80 years or older. The significant increase was also detected, being highest in the

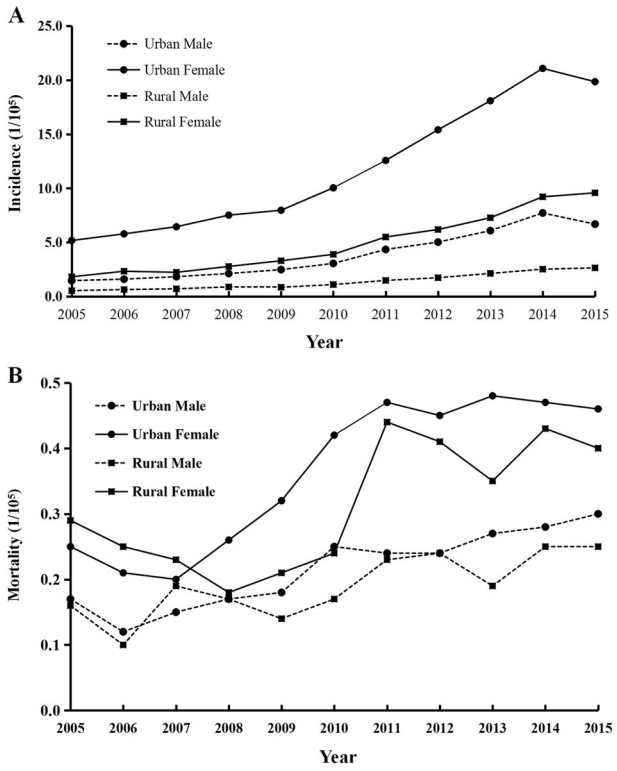

Fig. 1 ASIR world (**a**) and ASMR world (**b**) of thyroid cancer by gender in urban and rural areas, 2005–2015

age group of 30–39 years (AAPC: 16.7%, 95% CI: 14.5–19.0%). And the incidence rate increased slightly among patients aged 70–79 years (AAPC: 2.1%, 95% CI: 0.3–4.1%). When area-specific trends were analyzed, the incidence rate was increased at an AAPC of 14.8% (95% CI: 12.9–16.7%) in urban areas and 15.0% (95% CI: 12.3–17.7%) in rural areas, with no obvious disparity between different areas in temporal trends (Table 4). In rural areas, the Joinpoint regression analysis also showed two-time periods with joinpoint in the year 2010. APC were 10.2% (95% CI: 4.2%, 16.6%) in the period 2005–2010, 20.0% (95% CI: 18.2%, 21.8%) in the period 2010–2015, respectively (Fig. 5).

In terms of mortality, the Joinpoint regression analysis revealed an AAPC of 2.9% (95% CI, 1.3–4.5%) in the period 2005–2015. In all subgroups, thyroid cancer mortality trends had a increase in males (AAPC: 2.9%, 95% CI: 1.6–4.2%), females (AAPC: 2.6%, 95% CI: 1.2–4.1%), urban areas (AAPC: 3.6%, 95% CI: 1.9–5.4%), people aged 20–39 years (AAPC: 14.2%, 95% CI: 8.1–20.7%) and 40–59 years (AAPC: 6.2%, 95% CI: 2.9–9.6%). No significant trends were identified in other groups. Similar to the incidence trends, the highest AAPC was observed in the age group of 20–39 years. And there was also no significant difference in temporal trends between males and females (Table 4).

Discussion

In our study, the incidence rate of thyroid cancer appeared to increase at a substantial rate (AAPC: 12.4%), while the mortality rate increased moderately (AAPC: 2.9%) in China during 2005–2015. The results were a little different from the prevailing notion that there is a relatively stable or even decreased trend in mortality rate [11, 17, 18], but in accordance with some other studies. A significant increase in thyroid cancer incidence-based mortality was found during 1994–2013 (approximately 1.1% per year, 95% CI: 0.6–1.6%) using data from the SEER-9 cancer registry program [19]. Thyroid cancer mortality in Korea increased from 1985 to 2004 (APC: 7.94%, 95% CI: 6.43–9.46%) and then continuously decreased until 2015 (APC: −4.10%, 95% CI: −5.76%, −2.40%) [20]. Similarly, mortality has been declining up to the middle 1980s in men and late 1980s in women and has been moderately increasing thereafter in the United States [21]. Although the number of cancer registries have changed from 2005 to 2015, the quality of NCCR data remained good in terms of reliability and representativeness. And the improved quality of death cause registration could be a potential explanation for the increasing trend of thyroid cancer mortality.

Female individuals experienced higher both rates compared with male patients, with a fairly consistent ratio of female to male is 3:1. With respect to the highest age-specific rates, it appeared in the age group of 50–54 years old for incidence rate and 80–84 years old for mortality rate. In addition, both incidence and mortality rates were greater in urban areas than those in rural areas in terms of regional variations. These findings were consistent with some other studies [22, 23]. Thyroid cancer cases during recent decades are mainly attributable to urban females in the age group of 50–54 years old. Because of the presented heterogeneity in results, the variations of lifestyles, socioeconomic status, health resources in the subgroups of genders, areas, and ages should be concerned about. Therefore, adopting a "one size fits all" method for thyroid cancer prevention and control is unlikely to present good results [24]. Considering these individuals have a large proportion of their expected lifespans remaining, contribute substantially to the economy, and play a major role in caring for their families, it is necessary to allocate more health resources to high-risk populations and develop tailored programs that can realistically reduce the burden of thyroid cancer.

Because we used the ASR world for the Joinpoint regression analysis, the change in Chinese population structure (1982 and 2000) would not affect the temporal trend analysis. In Joinpoint regression analysis, of note was the rate of increasing incidence trend in males (AAPC: 13.3%) was higher than that in females (AAPC: 10.7%). However, considering the large number of female cancer

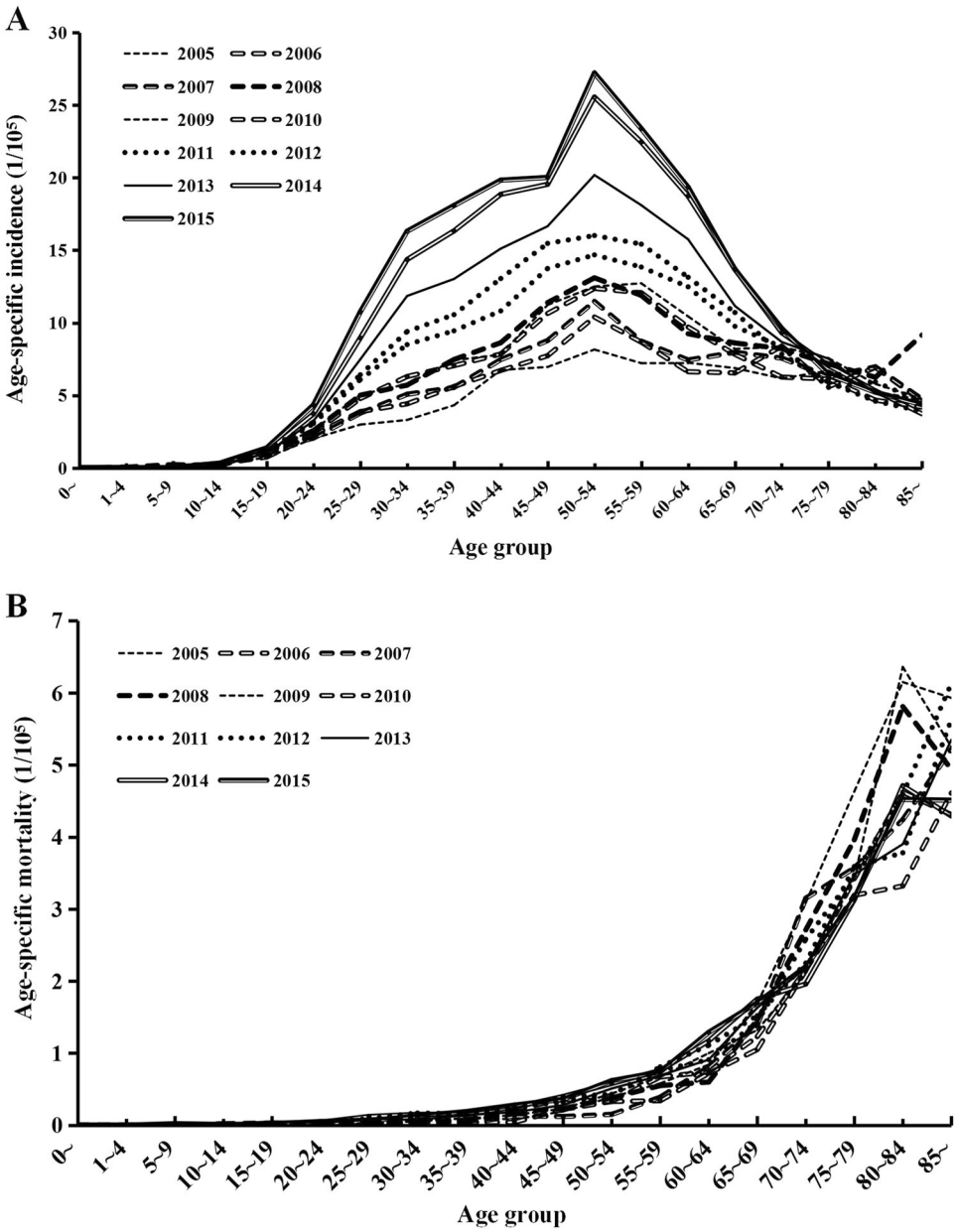

Fig. 2 Age-specific incidence rates (**a**) and mortality rates (**b**) of thyroid cancer, 2005–2015

cases, it didn't have any significant effect on differences between males and females. Moreover, the speed of increasing trend was lower in the age group of 70 years or older compared with other groups both in incidence and mortality rates. Finally, unfortunately, mortality rate increased sharply in the younger age groups, with an AAPC of 14.2% in the age group of 20–39 years and 6.2% in the age group of 40–59 years. But in general, survival of thyroid cancer is very good with a 5-year relative survival of about more than 90% and even better for younger age groups. Besides, the gap of mortality rates between different years in these age groups was small. Such an abnormal result may be due to the very low mortality, so even small changes can cause large fluctuations of AAPC. The potential reasons underlying these changes warrant investigation in further studies. As for the extraordinarily high APC (21.1%) for short time periods (2013–2015) in the age group of 20–29 years old, it was unlikely to be real sustained incidence changes for the slowly developing cancer. Even if they are statistically significant, we use AAPC to describe the temporal trend.

It is unclear whether the observed increase in thyroid cancer incidence is real or due to over-diagnosis. Currently, the increase of diagnostic activity has been suspected to be of great importance, especially the spread use of US and FNAB. On one hand, with the improvement of living level, people tend to take the physical examination far more seriously. A study conducted in Hangzhou, the capital city in

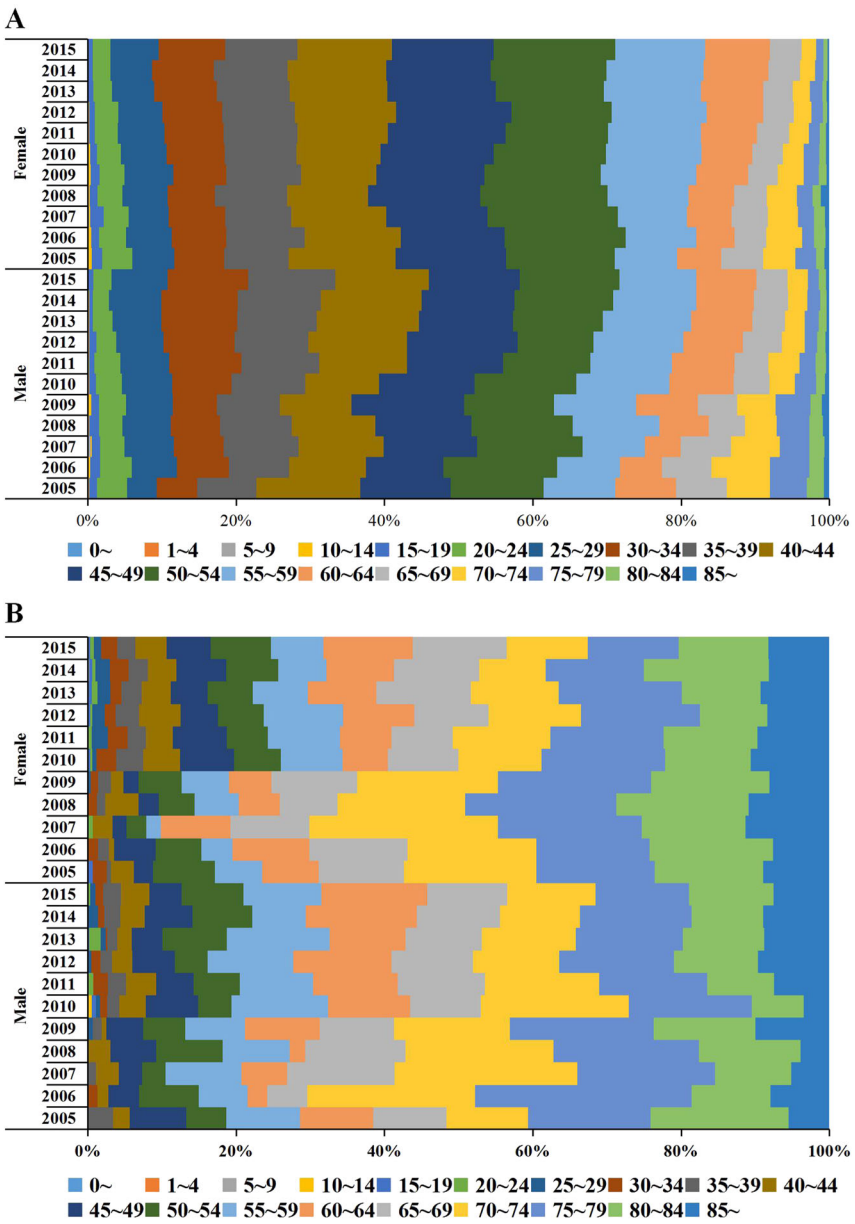

Fig. 3 Age groups distribution for estimated new cases (**a**) and deaths (**b**) of thyroid cancer, 2005–2015

Zhejiang province of China, has shown that more than 80% of the thyroid cancer cases were detected due to routine physical examinations [25]. This also is a possible explanation for the higher incidence in urban areas than in rural areas, as people live in urban areas pay much more attention to their own health. On the other hand, many tumors which otherwise would not be diagnosed are detected with the help of the improved sensitivity of diagnostic tools, especially thyroid nodules smaller than 1 cm in diameter. For instance, the increased incidence rate of thyroid cancer was mainly caused by the increase in papillary thyroid cancer (PTC) and in stage I thyroid cancer in Lithuania [5]. Grodski et al. [26] also concluded that an increase in the incidence of thyroid cancer was attributable largely to an increase in the diagnosis of papillary micro-carcinoma based on a cohort of 13,793 patients. The size distribution of thyroid cancer has shifted toward smaller lesions due to the use of US in cancer screening [27].

Nevertheless, proponents of a true increase in incidence argue that the detection of large tumors also has increased. A population-based analysis indicated that large well-differentiated thyroid cancers, including those >4 cm or >6 cm, have more than doubled in incidence [14]. Besides, based on the SEER data, a significant increase (2.9% per year) for thyroid cancer incidence-based mortality from 1994 to 2013 was observed in the patients who were diagnosed with advanced-stage PTC, which appeared to be associated with the increasing incidence of advantage-stage

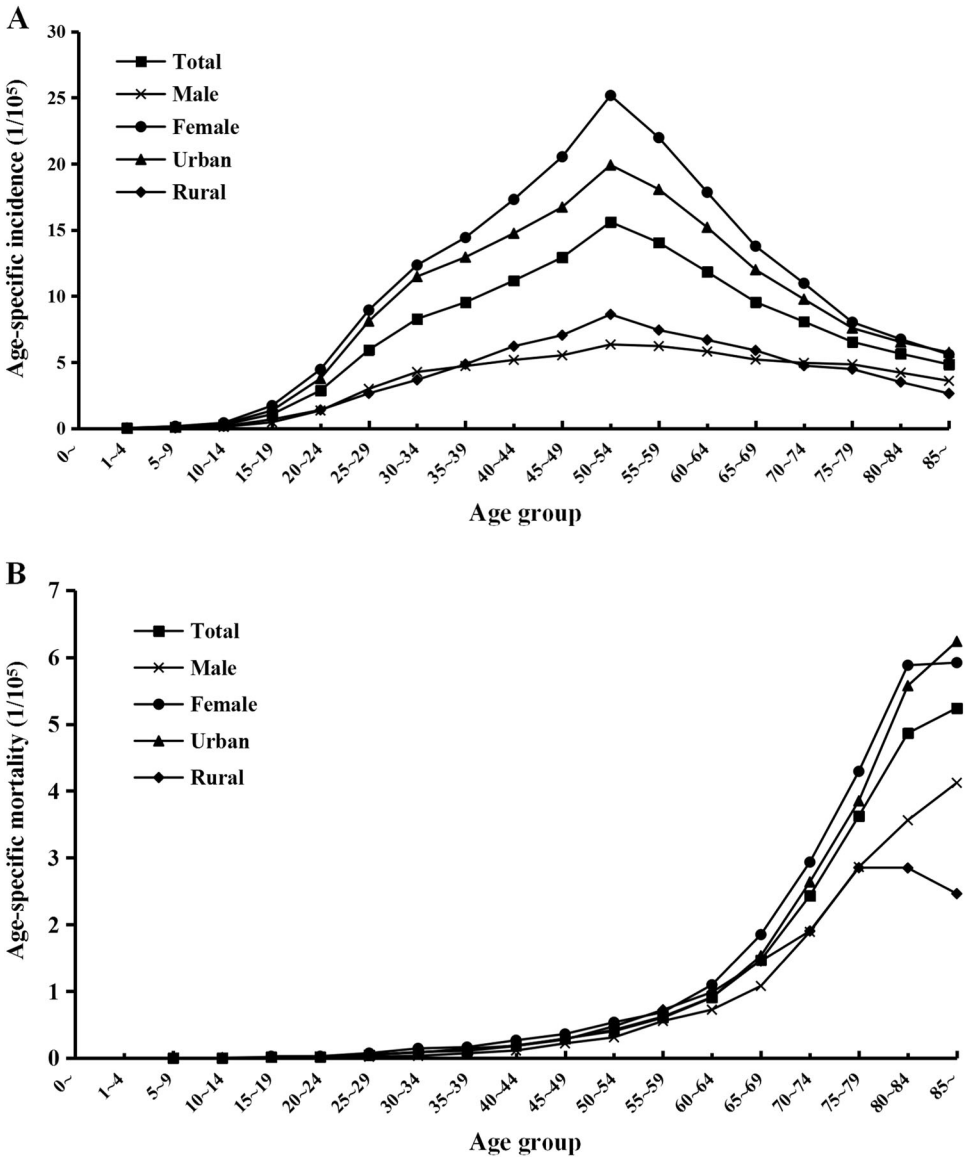

Fig. 4 Age-specific incidence rates (**a**) and mortality rates (**b**) of thyroid cancer stratified by gender and area, 2005–2015

PTC (3.5% per year since 1981) [20]. These results also reflect a true increase in the occurrence of thyroid cancer in the United States. Furthermore, PTC accounts for a large proportion in the thyroid cancer, with a good prognosis compare with other histologic sub-types [28]. Thus, the moderately increased mortality rate in our study may supports the notion that there has been a real increase.

Over-diagnosis is unlikely to be the only reason for the increased incidence rate of thyroid cancer, and some additional factors may play important roles in the observed increase to a certain extent. Firstly, thyroid cancer is one of cancers that shown a female dominance, suggesting some role of sex hormones, particularly estrogen, in favoring the malignant progression of thyroid tissue to cancer [29]. This also explains why the highest incidence of female thyroid cancer is established in the age group of 50–55 years old. An experimental study noted that estradiol, the most potent form of estrogen, promoted motility and tumorigenicity of cancer stem cells. And compared with control mice, estradiol-treated mice inoculated with thyroid cancer stem cell-enriched cells developed larger tumor masses [30].

Secondly, to date, exposure to ionizing radiation is a recognized risk factor for thyroid cancer, especially during childhood and adolescence. Their tissues are growing and cells are dividing more rapidly, making them more sensitive to ionizing radiation [31]. For instance, after the Chernobyl accident, a drastic increase in thyroid cancer incidence was observed among those who were children or adolescents in the areas contaminated with ^{131}I [32]. A survey study investigated 3087 atomic bomb survivors (aged 0 to <10 years) at exposure found that the prevalence of all nodules were significantly associated with the thyroid radiation

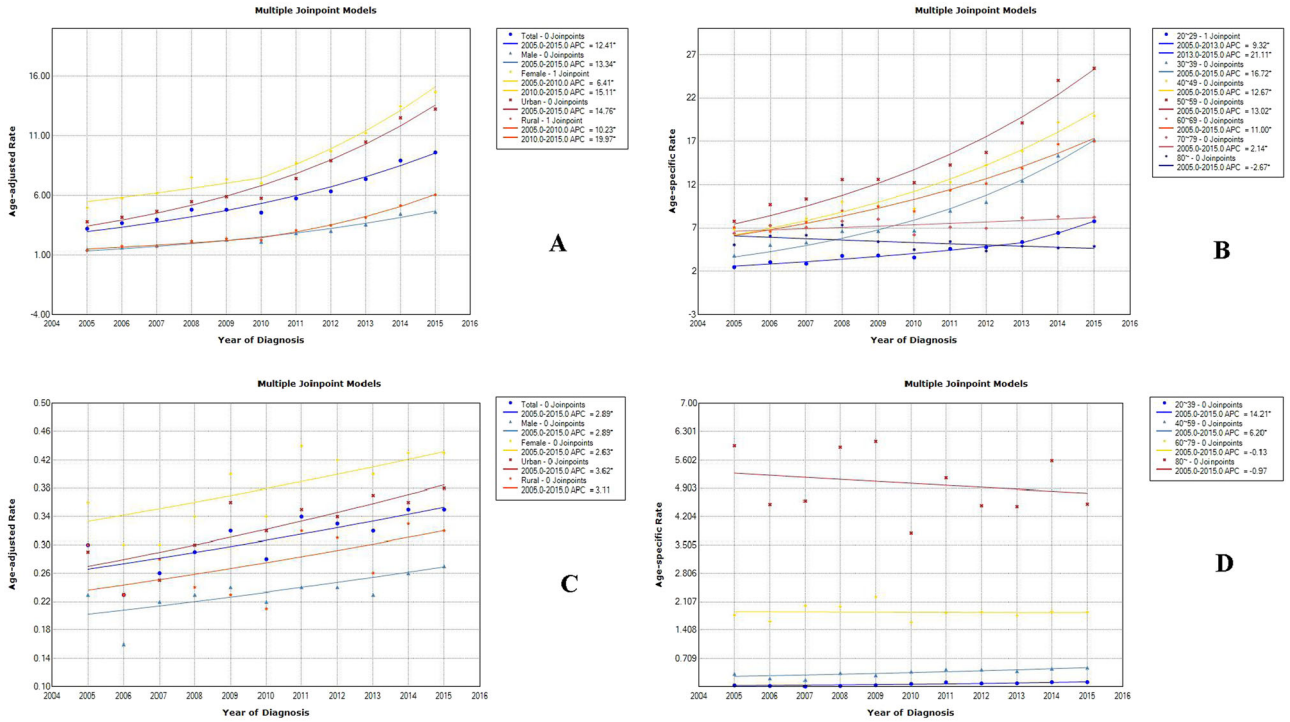

Fig. 5 Trends in thyroid cancer during 2005–2015; (**a**) stratified by gender and area in incidence; (**b**) stratified by age group in incidence; (**c**) stratified by gender and area in mortality; (**d**) stratified by age group in mortality

Table 4 Trends in thyroid cancer incidence and mortality rates by gender, age group and area, China, 2005–2015 (AAPC (95% CI))

Variable	Incidence	Mortality
Total	12.4[a] (10.5, 14.4)	2.9[a] (1.3, 4.5)
Gender		
Male	13.3[a] (11.2, 15.6)	2.9[a] (1.6, 4.2)
Female	10.7[a] (8.3, 13.1)	2.6[a] (1.2, 4.1)
Age group		
20–29	11.6[a] (8.6, 14.6)	14.2[a] (8.1, 20.7)
30–39	16.7[a] (14.5, 19.0)	
40–49	12.7[a] (10.6, 14.7)	6.2[a] (2.9, 9.6)
50–59	13.0[a] (10.5, 15.6)	
60–69	11.0[a] (9.2, 12.9)	−0.1 (−2.0, 1.8)
70–79	2.1[a] (0.3, 4.1)	
80–	−2.7[a] (−5.2, −0.1)	−1.0 (−4.3, 2.5)
Area		
Urban	14.8[a] (12.9, 16.7)	3.6[a] (1.9, 5.4)
Rural	15.0[a] (12.3, 17.7)	3.1 (−0.3, 6.6)

AAPC average annual percent change

[a]Indicates that the average annual percent change (AAPC) is significantly different from zero at the alpha = 0.05 level

dose. Excess odds ratios per gray unit were 4.40 for malignant tumors, 2.07 for benign nodules, and 1.11 for cysts [33]. Notably, the radiation effects on thyroid nodules still exist even after 62–66 years. In a case-control study, radiation exposure during dental X-rays was associated with an increased risk of thyroid cancer significantly [34]. Patients with Hodgkin lymphoma, leukemia, or central nervous system tumors were more likely to develop into thyroid cancer after radiation treatment [35].

Thirdly, in population studies, U-shaped curves were shown for the relationship between the iodine intake level and the risk of thyroid disease [36]. In other words, both low and high iodine intakes increased the risk of thyroid disease. Another study shown that long-term high or low iodine intake led to excessive secretion of thyroid stimulating hormone by the hypophysis cerebri, which would cause significant proliferation of thyroid follicular epithelial cells, resulted in goiter and mutated into thyroid cancer eventually [37]. Iodine intake was also related to the pathological types of thyroid cancer, for example, the incidence of papillary cancer was high in iodine-rich areas and follicular cancer was high in iodine deficiency areas [38].

Finally, some researchers presented the viewpoint that obesity could be related to the incidence of thyroid cancer. A large prospective cohort study carried out in Denmark proved that greater body mass index (BMI) during childhood was associated with an increasing risk of thyroid cancer [39]. A positive association of BMI as related to papillary, follicular, and anaplastic thyroid cancer but not

related to medullary thyroid cancer was observed in a cohort study conducted in the United States of America. And it also reported an adverse effect of adiposity on risk for thyroid cancer, with the multivariate relative risks for BMI values of 18.5–24.9 (reference), 25.0–29 and 30 kg/m^2 were 1.0, 1.27, and 1.39, respectively [40]. Besides, a cohort of French women covering teachers with the age of 40–65 years indicated a dose-effect relationship between thyroid cancer risk and BMI. And women had a 21% increased risk of thyroid cancer per 5 kg/m^2 increase in BMI [41]. Further, some other risk factors, such as familial inheritance [42], alcohol drinking [43, 44], dietary [45], smoking [46, 47], and income level [48] were also the contributors to the thyroid cancer burden.

This study also has several limitations. First, since the coverage of cancer data and diagnostic tools had been changed over the study period, the accuracy of these analyses might be lowered. Second, unavailability of detailed information about clinical–pathological characteristics of thyroid cancer, including tumor type, stage, and size, from population-based cancer registries. Thus, we could not confirm the specific risk factors, which could affect prognosis and recurrence of thyroid cancer. Regardless, the NCCR data are functional and reliable for the reason that it is the largest and most comprehensive database of thyroid cancer in China.

Conclusion

In summary, we found a rapid increase in incidence and a moderate increase in mortality of thyroid cancer from 2005 to 2015 in China. For both of incidence and mortality, the rates of thyroid cancer were much higher in females than in males, and in urban areas than in rural areas. With respect to the highest age-specific rates, it appeared in the age group of 50–54 years old for incidence and in the age group of 80–84 years old for mortality. Effective measures and tailored programs that focuses on the target population, especially females in urban areas, could substantially reduce the burden caused by thyroid cancer. Meanwhile, the rate of increasing trend was similar between males and females, urban areas and rural areas both in incidence and mortality. However, it was much higher in younger age groups but lower in older age groups, especially for people aged 70–79 years in incidence. Therefore, additional population-based studies are required to explore the real contributors to changes in thyroid cancer incidence and mortality trends in China.

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Author contributions LL and ZP conceived and designed the study. JW and YS analyzed the data. JW, FY and LL interpreted the data. JW drafted the manuscript. All authors reviewed and approved the final version manuscript. JW and ZP had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human or participants or animals performed by any of the authors.

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