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Global, regional, and national thyroid cancer age-period-cohort modeling and Bayesian predictive modeling studies: A systematic analysis of the global burden of disease study 2019

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ABSTRACT

Objective: To analyze the changing trend of the global burden of thyroid cancer (TC) and its associated risk factors using data from the Global Burden of Disease study 2019 (GBD 2019).
Methods: This study utilized the GBD 2019 database to analyze the burden trend of TC in various regions and countries from 1990 to 2019, while also examining the age-period-cohort (APC) effect. Additionally, the study used Bayesian age-period-cohort (BAPC) and predictive models to forecast TC incidence up until 2030.
Results: According to data from 2019, there were 233,846.64 (95 % UI 211,636.89–252,806.55) cases of TC worldwide. The burden of TC varies among regions and countries, with higher incidence rates observed in moderate and above SDI regions. Age and gender also play a role, with incidence rates peaking in the >95 age group for men and the 70–74 age group for women. Additionally, women have a higher incidence than men. The APC model revealed that the impact of age was most significant among individuals aged 95 years and older, while it was lowest among those aged 0–14 years. Additionally, the period effect showed a relatively low risk of morbidity with a Period RR < 0 during 1990–2004 and a high relative risk of morbidity with a Period RR > 0 during 2005–2019. Furthermore, the cohort effect demonstrated that the relative risk of developing the disease was lower before 1950 and higher after 1950. Predicted values show an increasing trend in thyroid incidence over the next 30 years.
Conclusions: The findings of this study highlight the continued significance of thyroid cancer as a global public health issue. It is crucial to develop targeted interventions that address the specific risk factors associated with thyroid cancer. Furthermore, health policies should be customized and adapted to the unique needs of different regions and populations.

1. Introduction

Malignancies have become a significant component of the burden of chronic non-communicable diseases. Thyroid cancer is a

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malignant tumor that originates from follicular epithelial cells or parietal thyroid gland cells, and is one of the most common endocrine malignancies [1], accounting for 3%–4% of all cancers [2]. Currently, there is significant research being conducted in the field of thyroid cancer, particularly focusing on nanocarriers for treatment and factors influencing thyroid hormone secretion [3]. While there have been remarkable advancements in the treatment of thyroid cancer, there is comparatively less emphasis on epidemiological studies. According to recent studies, thyroid cancer is becoming a global public health problem [4]. It ranks ninth in incidence among all cancers. The incidence of thyroid cancer has increased rapidly in recent years, with a relatively stable rate of about 5/100,000 until the mid-1990s and a significant increase to 15/100,000 by 2014, particularly in women, as noted in one study [4]. Thyroid cancer has become a significant contributor to the disease burden in some developed countries due to socioeconomic development.

While known risk factors such as age, gender, race, and family history are not modifiable, there are some modifiable factors that influence the incidence, death, and Disability-adjusted life years (DALY) rate of thyroid cancer. These factors include obesity, cancer diagnosis, iodine intake, and ionizing radiation [2]. Numerous studies have extensively examined the correlation between obesity and thyroid cancer [5,6]. The incidence of thyroid cancer is influenced by obesity due to various factors such as low-grade chronic inflammation, altered cytokine levels, insulin resistance, oxidative stress, and hormonal changes, all of which are prevalent in obese individuals [7]. Research suggests that with every 5-point increment in body mass index and 0.1-point increment in waist-to-hip ratio, the risk of developing thyroid cancer increases by 30 % and 14 % respectively [7].

GBD studies provide a more comprehensive analysis of the global health challenges posed by thyroid cancer [8]. However, there are currently few studies that have analyzed GBD data on thyroid cancer. Therefore, it is necessary to evaluate the global dynamics and age-period-cohort effects o thyroid cancer to make adjustments to health policies. This study aims to assess the global burden of thyroid disease and compare age- and gender-related indicators across regions and 204 countries. The findings could be valuable for governments at various levels of economic development in mitigating the unnecessary burden of thyroid cancer.

2. Sources and methods

2.1. Data sources

Thyroid cancer disease burden and risk factors data from 1990 to 2019 were gathered from the GBD 2019 database, which can be found on the official website of the Institute for Health Metrics and Evaluation (IHME). Previous studies have provided comprehensive information on the process of integrating GBD data [9,10]. The data can be accessed through the following webpage: https://vizhub.healthdata.org/gbd-results; [11]. The variables obtained from the database included incident cases, prevalent cases, YLDs numbers, and their corresponding age-standardized rates (ASRs) at the global, regional, and national levels. These data were stratified by age (5–9, every 5-year age group up to 95 years, and 95 years and older), calendar year (1990–2019), region, and country (or territory). Geographically, the world was divided into 21 GBD regions. Moreover, the 204 countries and territories were categorized into five groups based on their socio-demographic index (SDI): high, high-middle, middle, low-middle, and low SDI quintile. The data sources obtained from GBD 2019 included screening criteria such as GBD Estimate, Cause of death or injury, Risk factor, prevalence, deaths, DALYs, YLDs, YLLs, Number and Rate, Cause (thyroid cancer), Location (Global, all locations, all countries and territories, all GBD regions), Age (All ages, Age-standardized), Sex (both, Female, Male), and Year. Diseases other than thyroid cancer were excluded. The subject search terms used in electronic databases such as PubMed were 'GBD', '2019′, 'Thyroid cancer', and 'Risk factor'. The search period ranged from 2019 to 2023.

The GBD 2019 database is a comprehensive and extensive global observational epidemiological survey database that covers 369 diseases or injuries and 87 behavioral, environmental, and additional risk factor disease burdens for 204 countries and territories. It is based on multiple global data sources and employs a uniform and comparable methodology, taking into account age, year, sex, and other classifications. This database is the largest of its kind to date, and its data spans from 1990 to 2019 [8,12,13]. The 2019 GBD study presents data on the prevalence and incidence rates, as well as the number of deaths, YYLs, YLDs, and DALYs associated with thyroid cancer from 1990 to 2019. Disease burden was estimated using DALYs, which represent the sum of years of life lost due to disease and one year of healthy life lost equals one DALY [14]. In GBD 2019, years of life were estimated by taking into account various factors such as cause, location, age group, sex, and year.

2.2. Statistical methods

This study presents a descriptive analysis of the trends in global thyroid disease burden from 1990 to 2019. The data extracted on the incidence and Death rates of thyroid cancer, DALYs, and DALY rates were analyzed comparatively, taking into account important indicators such as gender, age, region, and country. Furthermore, the study examines the correlation between the global thyroid cancer burden and socioeconomic development status. To compare incidence rates across different populations or time periods, we utilized age-standardized rates as a comprehensive metric to examine age-specific correlated incidence rates over the years.

The Socio-Demographic Index (SDI) is a novel measure that combines social and demographic development factors. It was initially introduced by researchers from the Global Burden of Disease (GBD) study in 2015 [15]. The Social Development Index (SDI) is a measure of population health levels that takes into account critical factors such as a country's per capita income, average educational attainment, and fertility rates. It is calculated as the geometric mean of the normalized regional per capita revenue, years of schooling at age 15 and older, and total fertility rate (TFR) for women under the age of 25 [16]. The use of Social Determinants of Health Index (SDI) can aid researchers in exploring the correlation between disease burden and key socioeconomic factors that promote overall population health. This can provide valuable insights for policymakers to make informed decisions.

Table 1

Incidence cases, deaths, and disability-adjusted life years (DALYs) for thyroid cancer in 2019 and age standardized rates (ASRs) per 100,000，by SID and global burden of disease region.

	Incidence (95%UI)		Deaths (95%UI)		DALYs (95%UI)	
	number	age-standardized rate	number	age-standardized rate	number	age-standardized rate
Low SDI	11679.79 (9586.02–13741.22)	1.63 (1.34–1.90)	3881.04 (3179.29–4501.51)	0.72 (0.59–0.84)	130894.05 (107450.69–153143.26)	19.57 (16.03–22.66)
High-middle SDI	57964.73 (52409.06–64001.37)	3.06 (2.76–3.38)	9449.4 (8562.41–10154.20)	0.47 (0.43–0.51)	240968.71 (220217.20–262040.13)	12.35 (11.27–13.41)
Middle SDI	65559.09 (57598.70–73072.17)	2.49 (2.19–2.77)	13968.2 (12460.07–15490.18)	0.59 (0.53–0.66)	385510.67 (341357.91–426263.99)	15.02 (13.35–16.61)
High SDI	68405.44 (62052.62–74858.09)	4.59 (4.17–5.03)	9376.03 (8004.76–10012.26)	0.47 (0.42–0.50)	204881.75 (183508.18–221175.97)	12.29 (11.13–13.31)
Low-middle SDI	30106.98 (25984.46–33693.92)	1.91 (1.66–2.13)	8872.73 (7802.38–9842.78)	0.66 (0.58–0.73)	268798.51 (234450.57–297878.98)	17.75 (15.52–19.65)
Global	233846.64 (211636.89–252806.55)	2.83 (2.56–3.06)	45575.96 (41289.61–48775.34)	0.57 (0.51–0.61)	1231841.05 (1113585.39–1327064.40)	14.98 (13.55–16.14)
Andean Latin America	2145.16 (1658.96–2687.75)	3.63 (2.79–4.54)	623.86 (760.65–475.58)	1.13 (0.86–1.38)	15341.03 (11920.54–18812.80)	26.74 (32.71–20.77)
Southern Latin America	2001.78 (1560.97–2561.62)	2.58 (2.00–3.31)	482.06 (517.86–443.35)	0.58 (0.53–0.62)	11410.94 (10559.20–12385.54)	14.25 (15.48) 13.18)
Tropical Latin America	4527.53 (4245.92–5027.41)	1.82 (1.71–2.02)	1236.73 (1367.64–1132.64)	0.52 (0.48–0.58)	31370.65 (29438.93–35742.19)	12.82 (14.57–12.02)
High-income Asia Pacific	15659.75 (13134.42–18056.29)	4.98 (4.19–5.79)	2754.35 (3071.31–2127.72)	0.53 (0.43–0.58)	49019.24 (41648.17–54668.39)	12.46 (13.99–10.69)
Eastern Sub-Saharan Africa	5342.68 (4113.90–6791.94)	2.19 (1.72–2.72)	1795.26 (2198.71–1402.67)	1.04 (0.80–1.26)	62598.6 (49514.64–77614.49)	27.78 (34.10–21.85)
South Asia	31533.9 (26591.47–36439.30)	1.9 (1.61–2.19)	9195.55 (10476.58–7978.03)	0.65 (0.56–0.74)	291574.64 (254403.38–330796.42)	18.33 (20.88–15.98)
Western Sub-Saharan Africa	1083.13 (857.10–1325.20)	0.43 (0.34–0.52)	429.29 (505.69–334.45)	0.23 (0.18–0.27)	13431.80 (10647.73–15986.55)	5.67 (6.70–4.43)
North Africa and Middle East	19253.48 (15675.27–22281.23)	3.46 (2.89–3.96)	2289.52 (2668.57–1981.44)	0.54 (0.47–0.66)	74180.39 (62526.30–86119.46	14.88 (17.09–12.81)
Central Latin America	7183.16 (6143.08–8403.89)	2.90 (2.49–3.40)	1909.52 (2187.37–1634.19)	0.82 (0.71–0.94)	48382.39 (41445.82–56012.25)	20.04 (23.15–17.11)
Eastern Europe	12257.15 (10669.34–14145.94)	4.25 (3.70–4.93)	1870.38 (2088.36–1655.98)	0.55 (0.49–0.62)	49426.13 (43997.00–55523.68)	15.82 (17.81–14.08)
High-income North America	28296.42 (24460.56–32790.23)	5.40 (4.64–6.27)	2754.08 (2886.70–2490.00)	0.43 (0.40–0.45)	69048.12 (62829.86–74873.99)	12.23 (13.34–11.10)
Oceania	161.67 (113.90–219.59)	1.80 (1.30–2.40)	50.2 (68.12–37.29)	0.78 (0.59–1.04)	1576.43 (1156.35–2176.44)	19.04 (25.95–14.17)
Australasia	1737.85 (1359.22–2228.20)	4.44 (3.47–5.72)	235.78 (256.66–198.65)	0.48 (0.40–0.51)	5591.76 (4760.09–6245.13)	12.94 (14.56–10.98)
Southern Sub-Saharan Africa	738.68 (633.41–859.42)	1.13 (0.97–1.30)	259.00 (292.87–218.58)	0.48 (0.40–0.54)	7497.15 (6317.24–8624.38)	11.96 (13.61–10.11)
Central Sub-Saharan Africa	519.62- (363.26–728.66)	0.8 (0.54–1.14)	241.64 (343.06–168.05)	0.49 (0.33–0.71)	7385.34 (5265.39–10251.43)	11.63 (16.52–8.08)
Central Asia	1467.37 (1305.66–1649.90)	1.69 (1.51–1.89)	308.74 (340.85–278.41)	0.45 (0.40–0.49)	9231.3 (8202.92–10321.49)	11.46 (12.79–10.27)
Southeast Asia	25581.44 (20569.12–29885.75)	3.72 (3.01–4.32)	5862.06 (6646.13–4999.36)	1.02 (0.88–1.15)	164303.52 (136533.58–187955.55)	25.34 (28.88–21.37)
East Asia	41579.53 (34750.62–50204.07)	2.11 (1.77–2.54)	7620.95 (8874.16–6346.14)	0.40 (0.33–0.46)	197337.06 (165223.90–228530.15)	9.86 (11.35–8.30)
Caribbean	1246.22 (1044.92–1481.60)	2.43 (2.04–2.89)	322.00 (373.49–268.84)	0.62 (0.52–0.72)	8611.52 (7132.39–10142.31)	16.77 (19.77–13.87)
Western Europe	26217.36 (22591.16–30005.05)	3.93 (3.40–4.50)	4308.75 (4614.46–3775.76)	0.46 (0.41–0.48)	90232.9 (81224.88–98005.77)	11.66 (12.79–10.59)
Central Europe	5312.74 (4617.70–6120.29)	3.09 (2.67–3.57)	1026.26 (1180.26–899.52)	0.48 (0.42–0.56)	24290.14 (21221.42–28011.79)	12.73 (14.75–11.04)

Thyroid cancer is influenced by a range of complex and diverse pathogenic factors. As such, research into demographic factors such as age, period, and birth cohort are important areas to explore. The limitations of traditional methods in dealing with the interactions among age, period, and cohort factors can be addressed by using the age-period-cohort (APC) model. This model allows for adjusting and controlling these three factors, thereby reducing the mutual effects among them. To achieve this, the study employed a web-based APC analysis tool developed by the National Cancer Institute, which is based on the R language. The APC model considers age as a factor that affects vital rates, while time represents the various historical and environmental factors that influence different generations exposed to various risk factors. Cohort effects refer to differences between groups of individuals born in the same period but with different lifestyles [14]. The study included participants from various age groups (10–95+ years) and time periods, The model's estimable function was determined using a two-sided Wald chi-square test, with a statistically significant difference being defined as $P < 0.05$. This study utilized Office Excel 2019 to compile the data. The Global Burden of Disease (GBD) standardized the data by age (i.e., age-standardized rate) and provided 95 % uncertainty intervals. Statistical analysis and plotting were conducted using the R language, with packages such as ggplot2 and maps installed and loaded. We used GraphPad Prism 8.0 (GraphPad Software Inc., San Diego, CA, USA) to generate charts and used R version 4.2.1 (R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.https://www.R-project.org/.) for data analyses.

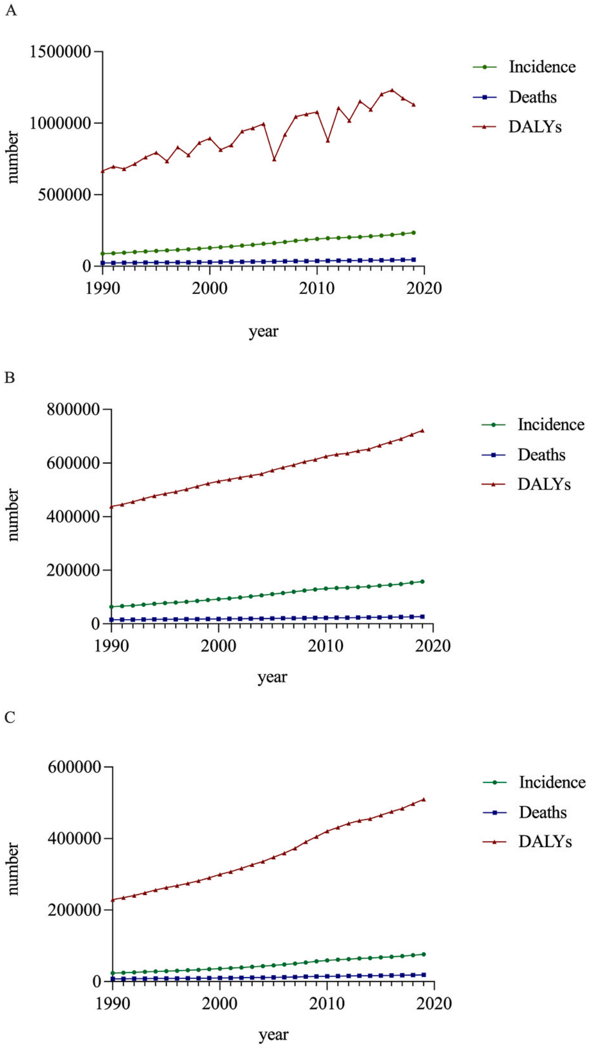

Fig. 1. Global trends in disease burden from 1990 to 2019 (A: both; B: females; C: males).

3. Results

3.1. Analysis of the current global thyroid cancer disease burden

3.1.1. Global level

The Global Burden of Disease Study 2019 reported that there were 233,846.64 newly diagnosed cases of thyroid cancer with a global age-standardized incidence rate that increased from 2.01 in 1990 to 2.83 in 2019. The number of deaths due to thyroid cancer was 45,575.96 with an age-standardized death rate that decreased from 0.60 in 1990 to 0.57 in 2019. The age-standardized DALYs rate increased slightly from 15.55 (95 % UI 14.40–17.02) in 1990 to 14.98 (95 % UI 13.55–16.14) in 2019, resulting in a total of 231,841.05 (95 % UI 1327064.40–1113585.39) DALYs. The age-standardized incidence rate also increased slightly from 14.62 (95 % UI 13.59–15.98) in 1990 to 13.61 (95 % UI 12.48–14.64) in 2019. However, there was no significant increase in age-standardized death and DALYs rate during this time period. Although thyroid cancer DALYs remained predominantly YLLs, the change was not significant over the last 30 years, while YLDs increased from 0.94 (95 % UI 0.65–1.26) in 1990 to 1.37 (95 % UI 0.95–1.87) in 2019 (Table 1).

From 1990 to 2019, there was a noticeable increase in the number of thyroid cancer incidences and DALYs worldwide, with a slow increase in death cases (Fig. 1A). Notably, women had a significantly higher prevalence of thyroid cancer incidences and DALYs compared to men (Fig. 1B and C). YLDs showed an overall increase over time, while age-standardized rates decreased for the entire population and women in YLLs （Fig. 2A and B). However, there was a steady growth in men (Fig. 2A).

3.1.2. Regional level

The region with the highest number of thyroid cancer incidences in 2019 was High SDI, while the lowest was Low SDI. The highest number of deaths occurred in Middle SDI, while the lowest was in Low SDI. Additionally, Middle SDI had the highest number of DALYs, while Low SDI had the lowest (Table 1). Interestingly, Low SDI areas had the highest age-standardized incidence rate, while high SDI areas had the lowest. The areas with Low SDI had the highest age-standardized death rates and age-standardized DALYs rates, while the areas with High-middle SDI had the lowest death rates and the areas with High SDI had the lowest DALYs rates (Table 1 and Fig. 3). Among the 21 disease-burden regions, East Asia had the highest number of incidences while Oceania had the lowest. On the other hand, South Asia had the highest number of deaths and Oceania had the lowest. Moreover, South Asia had the highest DALYs, while Oceania had the lowest (Table 1). In terms of age-standardized morbidity, high-income North America had the highest rates while Western Sub-Saharan Africa had the lowest. On the other hand, Andean Latin America had the highest age-standardized death rates

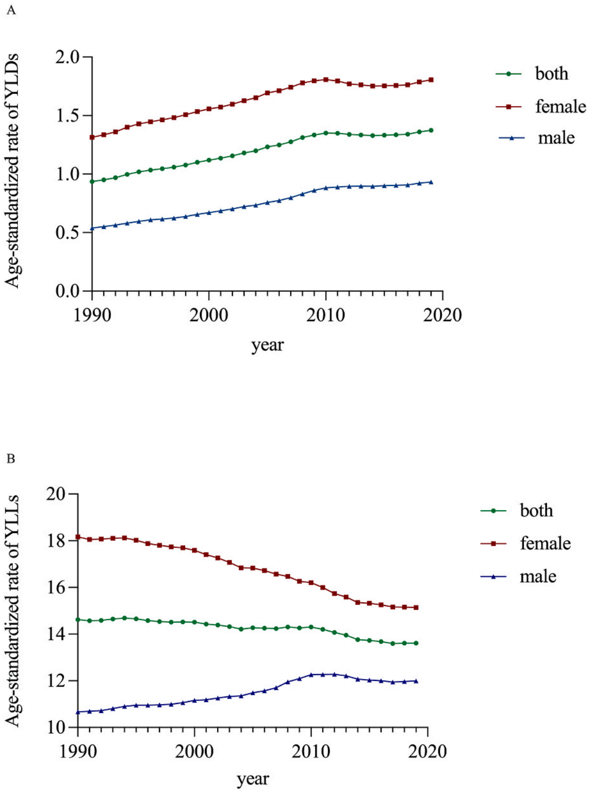

Fig. 2. Global trends in YLLs and YLDs from 1990 to 2019 (A: YLDs; B: YLLs).

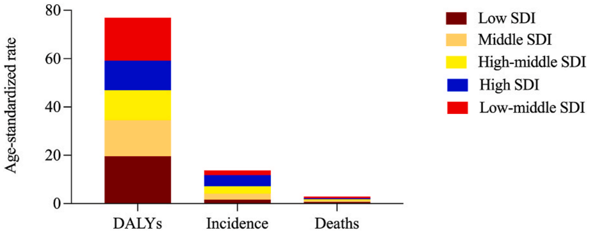

Fig. 3. Age-standardized incidence, death rates, and DALY rates by SDI region in 2019 (%).

with Western Sub-Saharan Africa having the lowest. As for age-standardized DALYs rate, Eastern Sub-Saharan Africa had the highest rates while Western Sub-Saharan Africa had the lowest (Table 1 and Fig. 4).

3.1.3. *National level*

This study found that age-standardized incidence rates of a certain disease varied across different countries. Rates ranged from 2/100,000 to 6/100,000 in various countries including Canada, Cuba, Spain, and Italy. Iceland had the highest incidence rates, ranging from 8/100,000 to 10/100,000. The incidence rate in other countries was relatively low, between 0 and 2/100,000 (Fig. 5).

3.1.4. *Age level*

The incidence of thyroid cancer DALYs was found to be higher in the >95 age group in areas with high SDI, while the 75–89 age group showed a higher rate in low SDI areas (Fig. 6A). Additionally, the rate of thyroid cancer DALYs was observed to be highest among women in the 70–74 age group and among men in the 85–89 age group (Fig. 6B and C).

In the 21 disease-burden regions, the age-standardized DALYs rate was higher in developed regions for those aged 95 years and above, with Eastern Europe showing a particularly significant impact (Fig. 7A–C). Thyroid cancer age-standardized DALYs rate was highest among women aged 70–74 and among men aged 95 years and above.

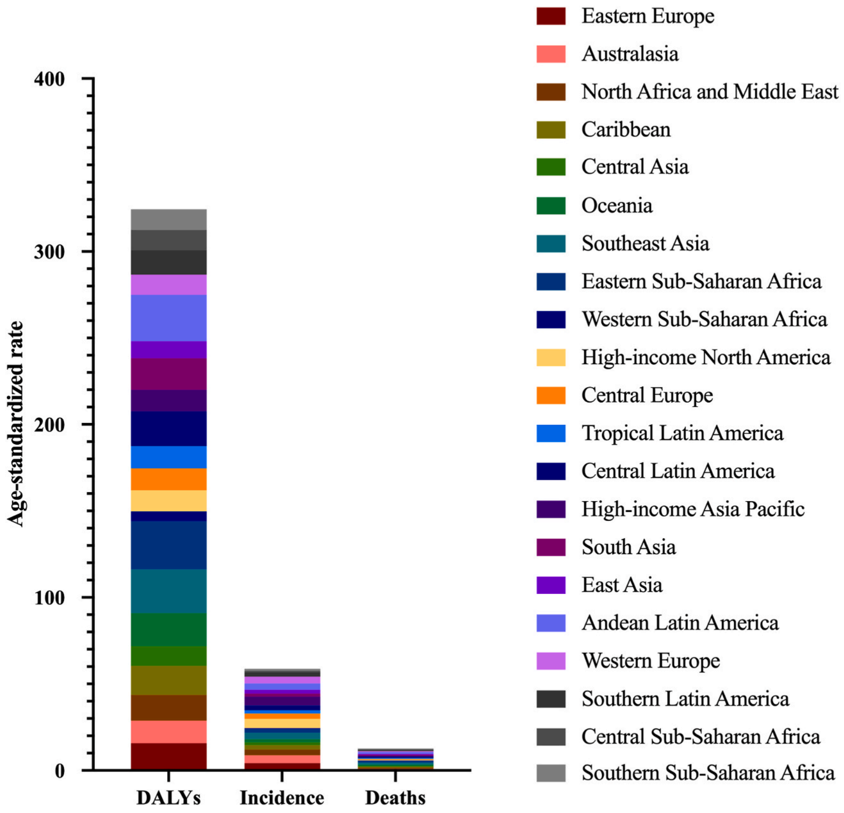

Fig. 4. Age-standardized incidence, death, and DALY rates in 21 disease burden areas in 2019 (%).

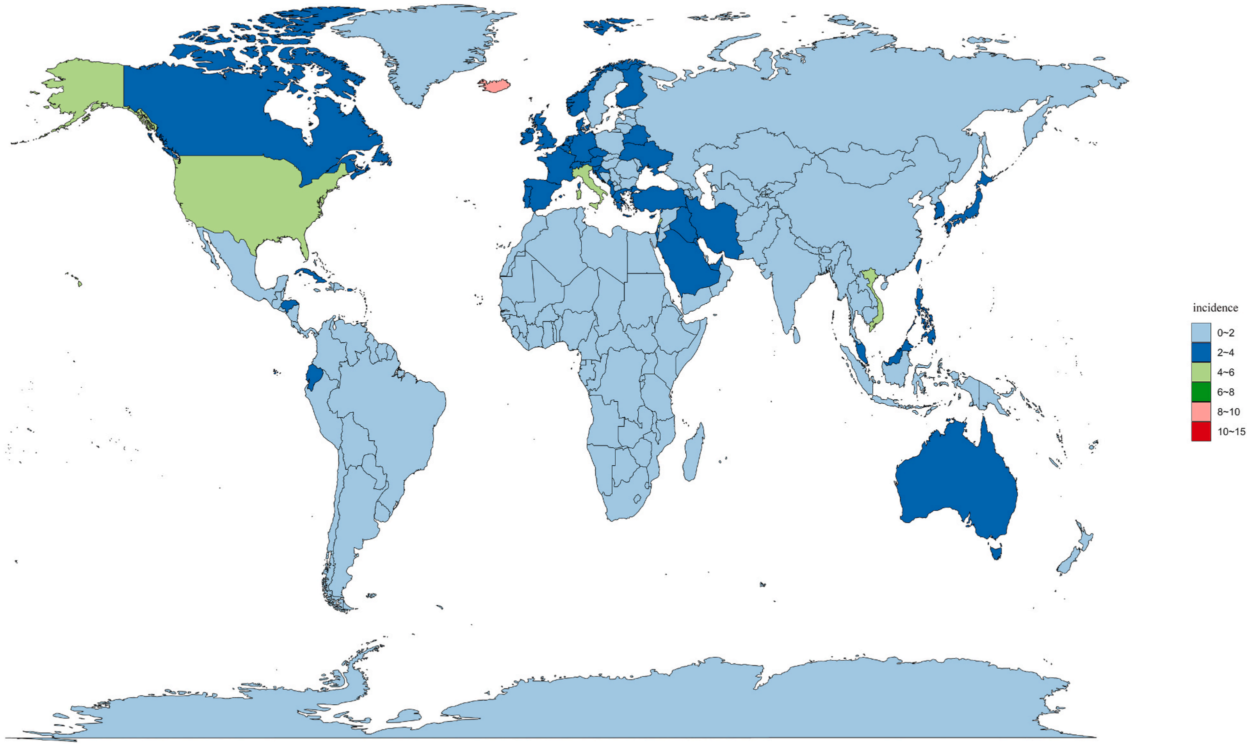

Fig. 5. Global distribution of age-standardized incidence rates of thyroid cancer in 2019.

3.1.5. *Risk factor analysis*

The main risk factors for thyroid cancer are linked to health risks, with obesity being the most significant influencing factor. The impact of obesity on thyroid cancer is more pronounced in developed countries, particularly in the high-income northern United States where the disease burden is greater (Fig. 8).

4. Age-period-cohort (APC) model and Bayesian APC model analysis of global thyroid cancer incidence

The study revealed that the risk of thyroid cancer is directly proportional to age, with the highest age effect observed in individuals aged 95 years or older, and the lowest in the age group of 0–14 years. The study also reported the highest and lowest values of age effect to be 18.86 (95 % CI 17.26–20.60) and 0.09 (95 % CI 0.08–0.10), respectively (Fig. 9A) . The impact of age was found to be most significant among females aged 95 years and above, with a value of 13.43 (95 % CI 12.09–14.92). Conversely, the lowest impact was observed in the age group of 0–14 years, with a value of 0.07 (95 % CI 0.06–0.07) (Fig. 9B). The study found that the age effect in men was most pronounced in the age group of 95 years and older, with a value of 4.58 (95 % CI 4.02–5.23), while it was lowest in the age group of 0–14 years, with a value of 0.02 (95 % CI 0.02–0.02). Additionally, the research revealed that females had a higher risk of thyroid cancer compared to males (Fig. 9C). In addition to the effect of age on disease incidence, the results of the period effect showed that the risk of thyroid cancer increased and decreased over time. The incidence period effect was highest in 2010–2014 and lowest in 1990–1994, at 1.13 (95 % CI 1.12–1.15) and 0.85 (95 % CI 0.83–0.86), respectively (Fig. 9A) . Females were highest in 2010–2014 and lowest in 1990–1994, with 1.08 (95 % CI 1.07–1.10) and 0.86 (95 % CI 0.84–0.88), respectively (Fig. 9B) . Between 1990 and 1994, males had the lowest risk of morbidity with a rate ratio (RR) of 0.81 (95 % CI 0.79–0.82). However, between 2015 and 2019, males had the highest risk of morbidity with a RR of 1.29 (95 % CI 1.27–1.31) (Fig. 9C) . In the period between 1990 and 2004, the RR was less than 0, indicating a relatively low risk of morbidity. However, in the period between 2005 and 2019, the RR was greater than 0, indicating a relatively higher risk of morbidity (Fig. 9A).

The results of the cohort effect analysis revealed a low incidence risk with a Cohort RR < 0 before and a relatively high incidence risk with Cohort RR > 0 after 1950. The incidence of thyroid cancer increased over time, with the highest cohort effect value observed in the period 2005–2009 and the lowest in the period 1895–1900. The maximum value of the cohort effect was 2.14 (95 % CI 1.90–2.41), while the minimum value was 0.47 (95 % CI 0.33–0.68) (Fig. 9A). The study found that the highest female cohort effect values were observed during the 2005–2009 period (1.86, 95 % CI 1.60–2.19) and the lowest were during the 1895–1900 period (0.56, 95 % CI 0.37–0.86) (Fig. 9B). Similarly, the highest male cohort effect values were observed during the 2005–2009 period (3.07, 95 % CI 2.69–3.49) and the lowest were during the 1895–1900 period (0.30, 95 % CI 0.17–0.53). For individuals born after 1895, females experienced a rise in incidence followed by a gradual decline, and then up. while males displayed a consistent increase over time (Fig. 9B and C). According to the projections, the incidence of thyroid cancer in both women and men is expected to rise globally

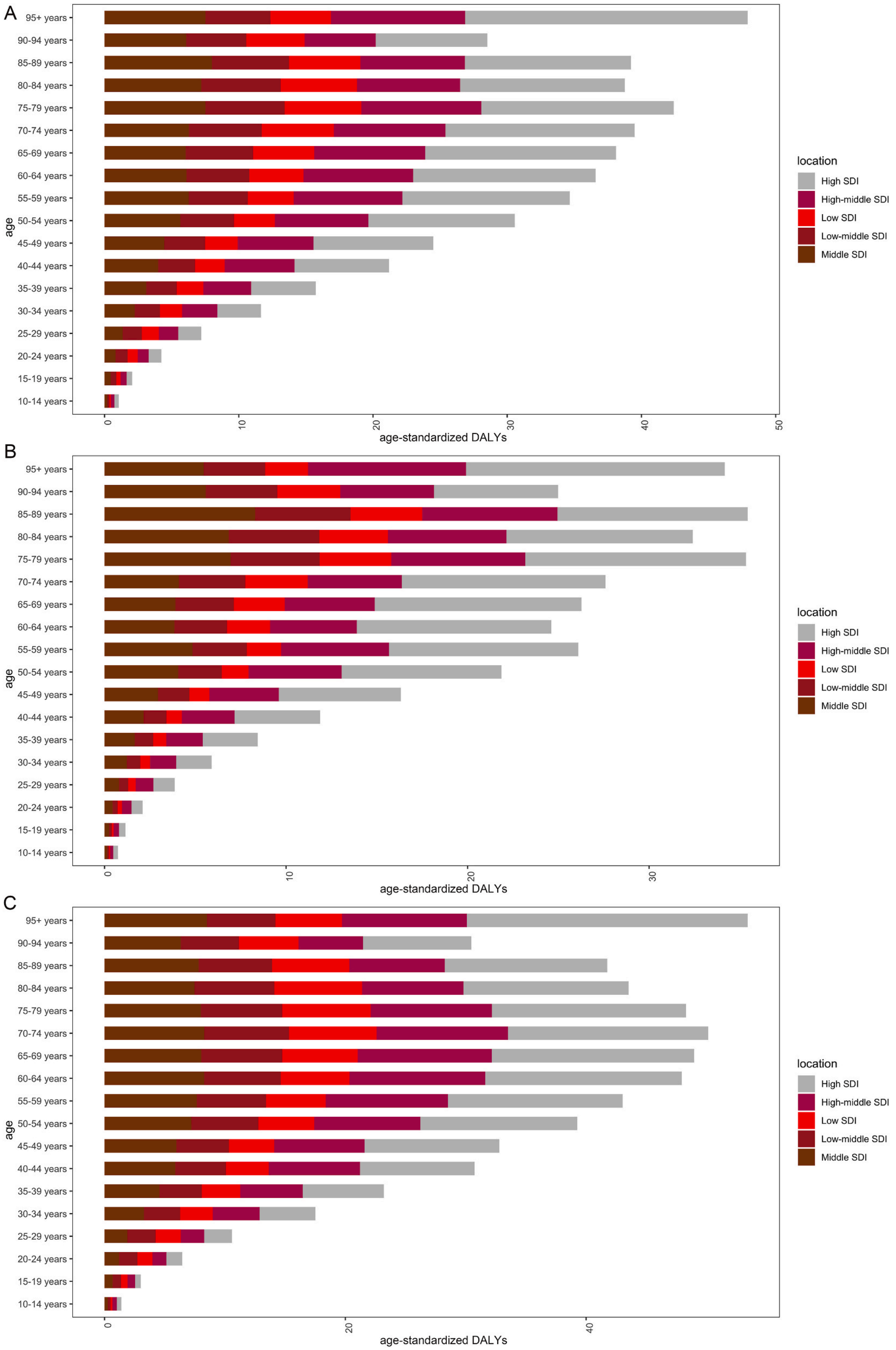

Fig. 6. Age-standardized DALY rates for different age groups in SDI regions in 2019 (A: both; B: males; C: females).

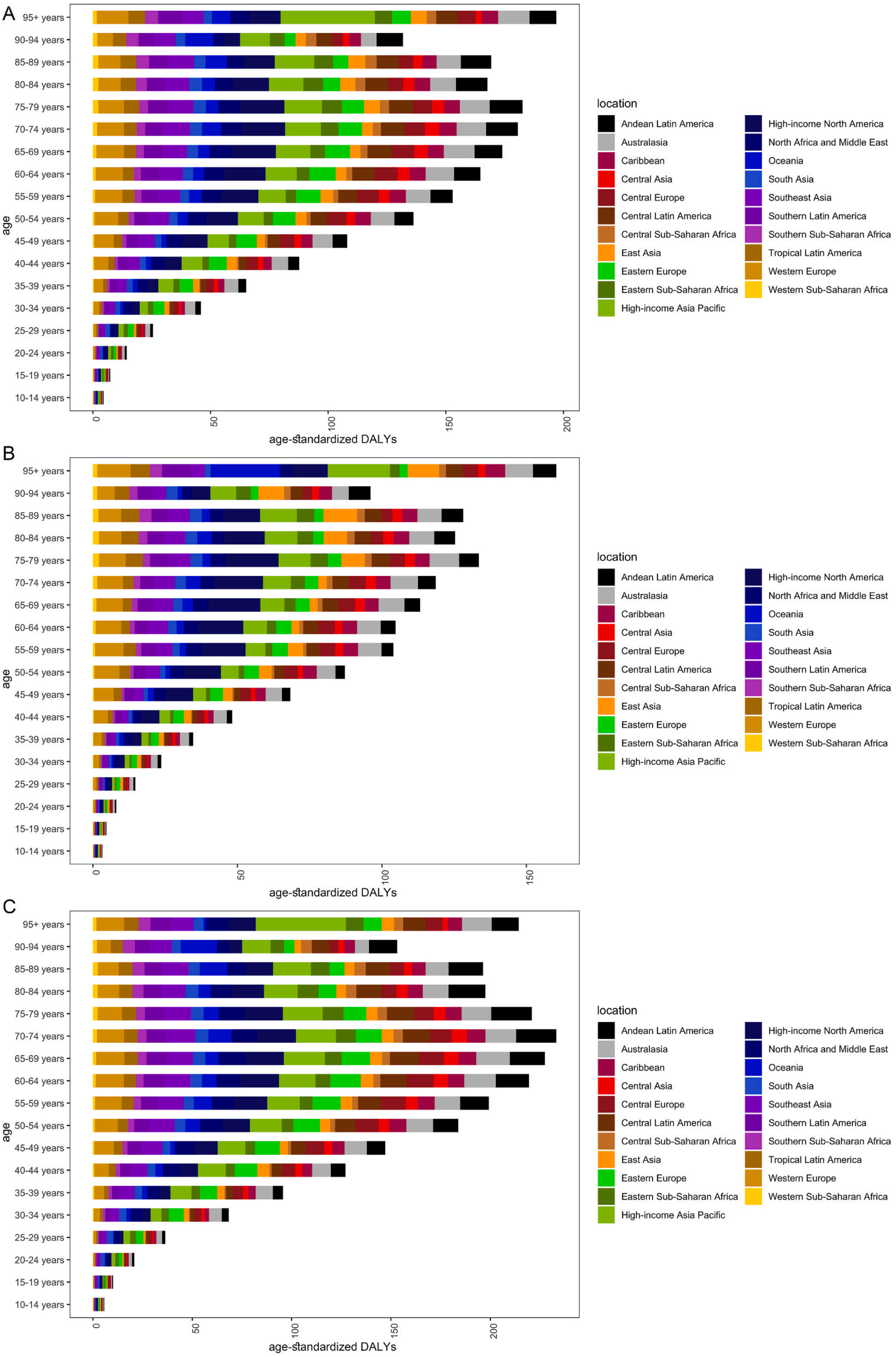

Fig. 7. Age-standardized DALY rates for different age groups in 21 disease-burden regions in 2019 (A: both; B: males; C: females).

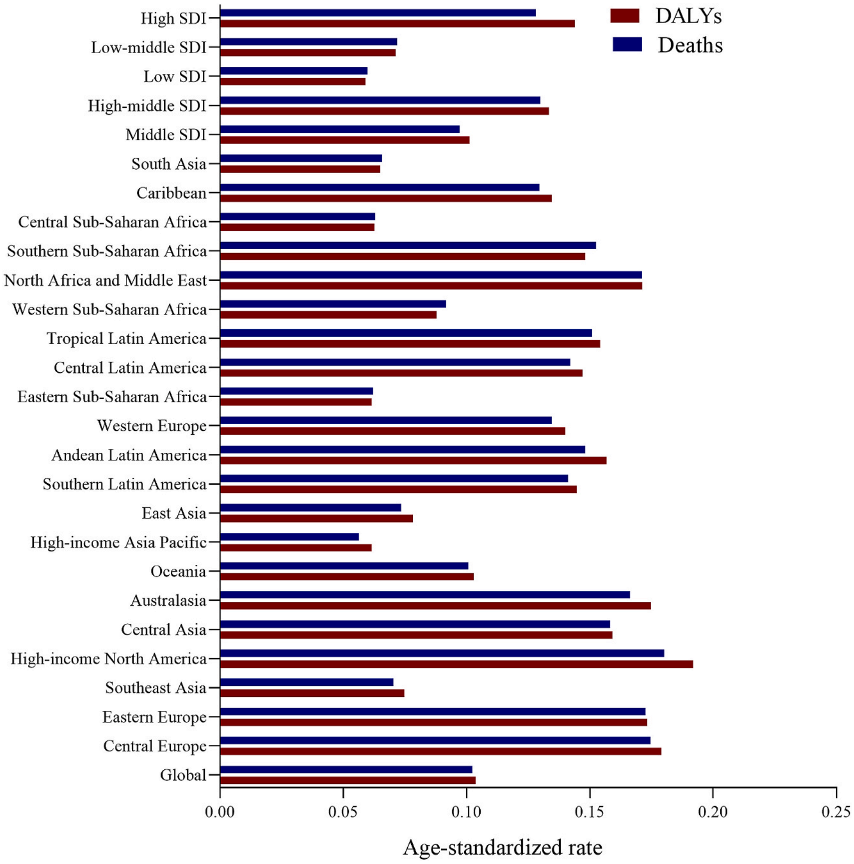

Fig. 8. Percentage of risk factors in 21 disease burden regions in 2019.

between 2019 and 2030 (Fig. 10A and B).

5. Discussion

This study offers valuable insights into the causative factors of the disease, aiding in biomedical understanding and the development of interventions and treatments. Conducting epidemiological studies to establish the correlation between thyroid cancer and risk factors can provide evidence-based medical evidence to support clinical guideline recommendations. Additionally, analyzing regional variability will enable policymakers to assess the burden of thyroid cancer in specific areas, facilitating the rational and effective allocation of resources. This study aimed to analyze temporal trends of thyroid cancer incidence by region, country, age, sex, and risk factors. The APC model was utilized to analyze incidence data, while the BAPC model was used to predict thyroid cancer incidence trends in 2030. The findings of this study have implications for developing strategies in regions and countries where thyroid cancer is a common endocrine malignancy. Understanding the disease burden of thyroid cancer through GBD is crucial for effective management and prevention.

From 1990 to 2019, there was a global increase in the age-standardized incidence of thyroid cancer. However, during the same time period, there was a decrease in the age-standardized death and DALY rates for thyroid cancer. This decrease can likely be attributed to the improvement in diagnosis and management of DTC, MTC, and ATC in many countries, which has led to an overall improvement in the level of care [17,18]. However, The U.S. Preventive Services Task Force has identified thyroid cancer as one of the most overdiagnosed and overtreated cancers, and the potential harm of screening outweighs the benefits [19]. There is substantial evidence indicating that overdiagnosis of thyroid cancer (TC) is a major factor in the rising incidence of the disease [20,21]. Nonetheless, the screening, diagnosis, and treatment of papillary thyroid cancer are evolving to reflect the understanding that many cases of thyroid cancer are low-risk and do not warrant aggressive and immediate intervention. In fact, the rate at which thyroid cancer incidence is increasing has slowed down in recent years [20].

Overdiagnosis and overtreatment do not fully explain the increased burden of thyroid cancer. Studies have shown that the increased incidence of thyroid cancer may also stem from increasing risk factors [22]. Epidemiological evidence suggests that obesity is a risk factor for thyroid cancer and that the increased incidence of differentiated thyroid cancer (DTC) is pathologically linked to the spread of obesity [6,23]. Elevated body fat percentages are linked to an increased proportion of thyroid cancer DALYs. Furthermore, recent studies have shown a significant rise in thyroid cancer incidence, which may be attributed to lifestyle choices and environmental

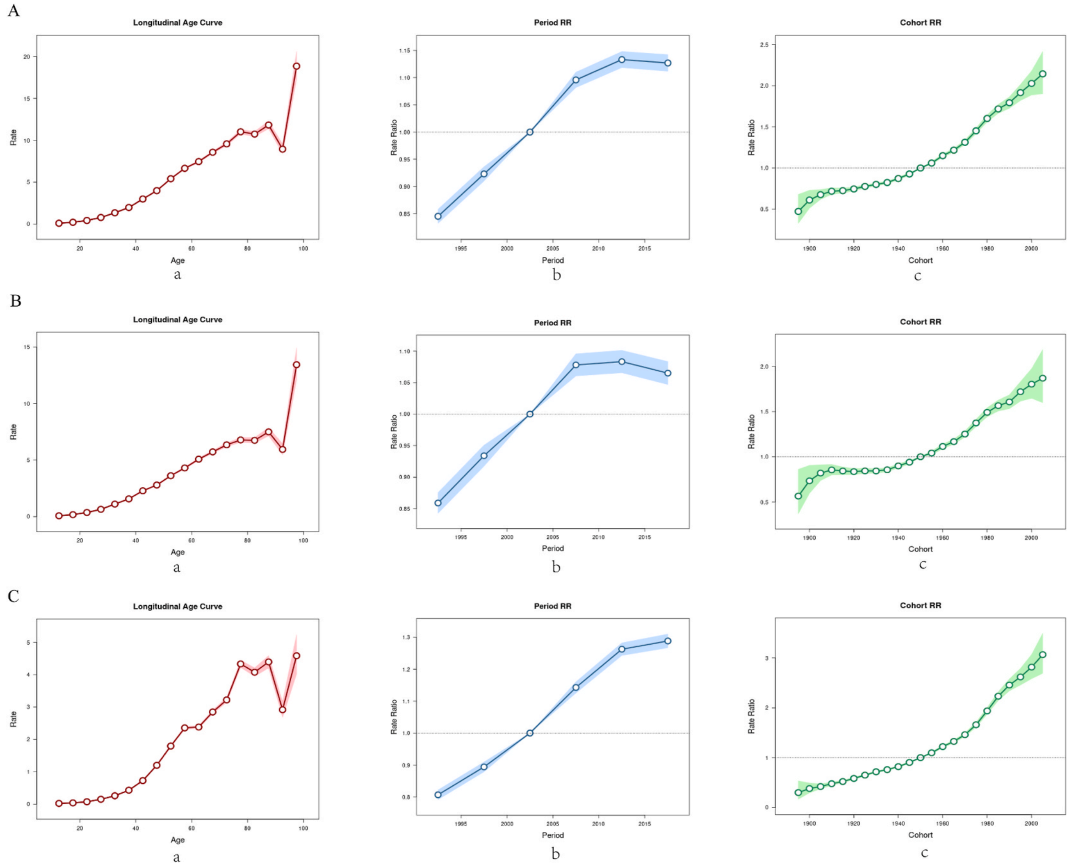

Fig. 9. Age-period-cohort effects for global thyroid cancer incidence, from 1990 to 2019 (A: both genders; B: females; C: males).

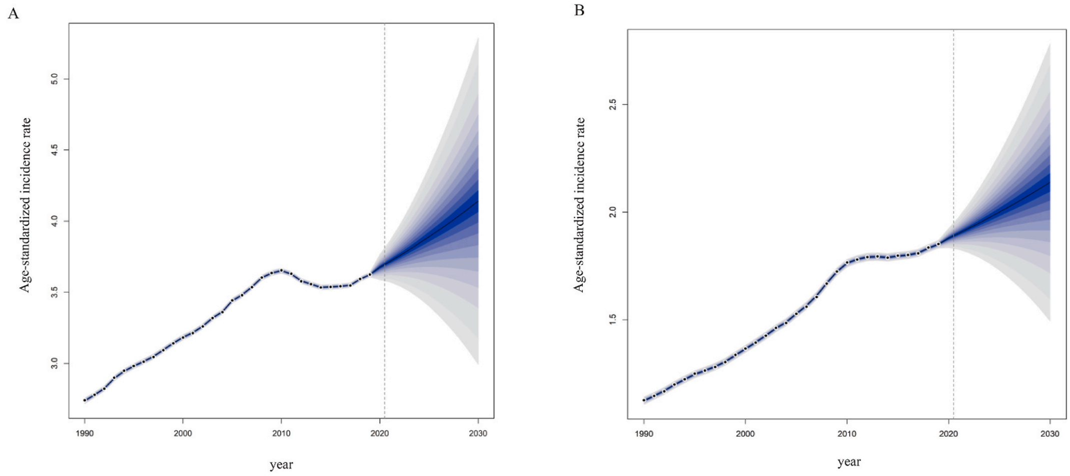

Fig. 10. Global thyroid cancer incidence projections, from 1990 to 2030 (A: females; B: males).

factors such as iodine intake and exposure to ionizing radiation [24].

Research has revealed that regions with a higher SDI have a greater likelihood of thyroid cancer occurrence, whereas areas with lower SDI have higher mortality rates and lower incidence of the disease. The American Cancer Society reported around 62,450 new cases of TC, with the United States being one of the countries with a high incidence of the disease [25]. According to previous research, thyroid cancer has been found to have a significant economic impact on patients in the United States, with survivors reporting higher rates of bankruptcy compared to other types of cancer [26]. Additionally, projections based on current trends suggest that thyroid cancer will become the fourth most prevalent cancer in the United States by 2030 [26]. The higher incidence of thyroid cancer in areas with high SDI may be attributed to better access to healthcare services and treatment due to higher levels of economic development. This allows for more tools for diagnosis and treatment, which in turn increases the incidence rate. Conversely, higher death rates from thyroid cancer in areas with lower SDI may be due to limitations in the level of medical care, including a lack of advanced medical services and accurate laboratory investigations [27]. The observed difference in thyroid diagnoses between genders may be attributed to the effects of female reproductive hormones. Studies have shown that estrogen can promote thyroid growth [25]. Additionally, sex differences may arise due to variations in reproductive activity and menopause, leading to earlier diagnosis and more frequent use of medical services by women. As a result, women are more likely to be diagnosed with thyroid disorders compared to men.

The incidence and death rates of thyroid cancer vary based on the socio-demographic index (SDI) of different age groups, reflecting the disparities in medical care and income worldwide. While the age of onset for thyroid cancer patients is decreasing globally, the age of death from thyroid cancer is increasing. The highest incidence and death rates were observed in the >80 age group, which can be attributed to the aging population and the higher prevalence of thyroid cancer complications in older patients. According to research [28], a decrease in the proportion of deaths in other age groups may indicate improved levels of treatment. This suggests that we should focus on preventing and controlling thyroid cancer in the elderly. Additionally, it is important to note that the age of onset for thyroid cancer in women (65–79 years) is generally earlier than in men (75–89 years). Gender differences in biology and attitudes towards healthcare-seeking behavior may contribute to men being diagnosed with advanced stages of thyroid cancer, leading to earlier cause-specific deaths associated with the disease [19].

According to the APC model, the risk of thyroid cancer incidence increases with time and age. This may be due to the aging population of society, where the decline of physical functions and immunity, along with the long-term cumulative influence of external risk factors, lead to negative effects that become apparent and increase the risk of disease. Thyroid cancer risk is influenced by a combination of complex historical events and environmental factors which contribute to the period effect. Unhealthy lifestyle choices and exposure to harmful substances are the main causes of the increased period effect [29,30]. Additionally, the cohort effect indicates that the risk of thyroid cancer is higher among those born later. This could be attributed to over-screening for thyroid cancer and changes in dietary habits, including an increase in obesity, which has been linked to the rising incidence of thyroid cancer. The cohort effect suggests that individuals born later have a higher risk of developing thyroid cancer. This could be due to excessive screening for thyroid cancer and changes in dietary habits, including an increase in obesity. According to the BAPC prediction model, the incidence of thyroid cancer worldwide is expected to continue to rise until 2030. Comprehending the worldwide patterns and risk aspects of thyroid cancer can aid in the early identification of thyroid cancer risks, prompt interventions to efficiently alleviate the burden of thyroid cancer, and prioritize developing nations and older age groups [31,32].

This study utilized the GBD 2019 Burden of Disease database to examine the variability of thyroid cancer incidence, deaths, and DALYs by age and sex on a global scale and within 21 burdens of disease regions. By analyzing epidemiological trends, this study aims to gain a better understanding of the differences between regions, ultimately guiding future health actions. The analysis of trends in thyroid cancer and the prediction of future burden can provide insight into the future development of the disease and potential changes. This information can guide the formulation of tumor prevention and control policies, which are essential for creating effective medium- and long-term prevention and control plans.

6. Conclusion

According to our analysis, there is a global increase in the number and age-standardized incidence of thyroid cancer. This increase puts a greater strain on healthcare systems worldwide, particularly in countries with high SDI and among women. Fortunately, age-standardized death and age-standardized DALY rates for thyroid cancer have decreased, which could be attributed to advancements in treatment. Poorer lifestyles are associated with risk factors for thyroid cancer, highlighting the interdependence between economic development and the prevention and treatment of this disease. It is crucial to ensure a balanced development of health services across different regions and countries worldwide. Targeted programs and effective measures must be implemented to reduce the burden of thyroid cancer and curb its growing trend. Due to the concerning increase in thyroid cancer cases and the variation in incidence by sex and age, it is possible that estrogen and older age may contribute to a poorer prognosis. As a result, it is crucial to prioritize primary prevention efforts and investigate potential risk factors.

Ethical statement

The study was conducted after approval by the Shandong Second Provincial General Hospital Ethics Committee (XYK20210502). Use of the data was approved under a waiver of informed consent. The data accessed was de-identified (anonymized) and complied with the data protection and privacy regulations. No other approvals were required for data access.

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Data availability

Data associated with this study been deposited into a publicly available repository. The data presented in this study are available from the Global Burden of Disease Study 2019 (https://vizhub.healthdata.org/gbd-results/).

CRediT authorship contribution statement

Jingjing Chen: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Chong Wang:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Beibei Shao:** Methodology, Investigation, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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