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RESEARCH ARTICLE

Tang et al: Thyroid cancer burden worldwide

Global, regional, and national trends in thyroid cancer burden (1990–2021): Insights from the GBD 2021 study

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ABSTRACT

The global incidence of thyroid cancer (TC) has been steadily increasing and is now recognized as one of the most prevalent endocrine malignancies. This study provides

a comprehensive evaluation of the prevalence, incidence, mortality, and disability-adjusted life years (DALYs) associated with TC from 1990 to 2021. Data for this study were sourced from the 2021 Global Burden of Disease, Injuries, and Risk Factors Study (GBD). To quantify temporal patterns and assess trends in age-standardized TC metrics—namely, age-standardized prevalence rate (ASPR), age-standardized incidence rate (ASIR), age-standardized death rate (ASDR), and DALYs—estimated annual percentage changes (EAPCs) were calculated. The analysis was stratified by sex, 20 age groups, 21 GBD regions, 204 countries/territories, and five Socio-demographic Index (SDI) quintiles. Statistical analyses and plotting were conducted using R statistical software version 4.4.2 and Joinpoint software. The study found that the global burden of thyroid cancer remains substantial, with a significant increase in the total number of cases. In 2021, regions with high SDI reported the highest ASPR, showing an upward trend compared to 1990; however, this trend began to decline significantly after 2009. Conversely, regions with low and low-middle SDI exhibited noticeable increases in ASPR, ASIR, ASDR, and DALYs. The highest prevalence and incidence were observed in the 55-59 age group, followed by a gradual decline. The majority of affected individuals were women. A high body mass index (BMI) was identified as the primary risk factor for TC, and both prevalence and incidence are expected to continue rising through 2040.

Keywords: Thyroid cancer; GBD database; risk factors; burden prediction.

INTRODUCTION

The incidence of TC continues to rise globally and is the tenth most common cancer worldwide in 2020, with more women affected(1). The most common types of TC are papillary carcinoma (accounting for 84%, predominantly affecting women(2)), follicular carcinoma (4%, more prevalent in iodine-deficient regions), and anaplastic carcinoma (the most aggressive and with a poor prognosis(3)). Most well-differentiated TC are asymptomatic and are often incidentally detected during routine physical exams or imaging studies. However, they may present with compressive symptoms, including hoarseness, dysphagia, and dyspnea.

Epidemiological studies related to TC have yielded the following findings: Wen-Qi Bao and colleagues, observed a continuous increase in the global incidence of TC and identified high body mass index (BMI) as a significant risk factor for the disease(4). The overall incidence rate in the United States between 2000 and 2019 was approximately 13.22 cases per 100,000 individuals(5), Asia accounts for over 50% of global TC cases, with Southeast Asia and East Asia being particularly affected(6), the incidence and mortality rates in Eastern Europe are significantly higher than in Western Europe(1). Epidemiological studies have consistently highlighted the persistent disparities in disease prevalence and incidence across geographic regions and different quintiles of the SDI. These variations significantly influence the global burden of various diseases. However, to date, no comprehensive analysis has been conducted using the latest GBD 2021 data to assess the worldwide burden of TC.

To address this knowledge gap, we aim to provide an updated assessment of global, regional, and national trends in TC prevalence, incidence, deaths, and DALYs from 1990 to 2021. Our analysis stratifies by sex, age, and SDI to identify the populations most affected by TC. Additionally, we incorporate the analysis of risk factors to inform targeted prevention and treatment strategies.

MATERIALS AND METHODS

Data collection

The GBD 2021 study provides a comprehensive evaluation of health losses due to 371 diseases, injuries, and disabilities, as well as 88 risk factors, across 204 countries and regions. This study utilized(7) the most up-to-date epidemiological data and improved standardized methodologies, stratifying the data by country, age, year of occurrence, and sex(8). Detailed information on the study design and methodology of the GBD research has been extensively described in the existing GBD literature(9).

This study collected data on the number and rates of prevalence, incidence, deaths, and DALYs, along with SDI, and population data across different age groups, from 21 GBD regions globally. These regions are classified based on socio-economic similarities and geographic proximity, including the Andean Latin America,

Australasia, North Africa and the Middle East, Oceania, Eastern Sub-Saharan Africa, Southeast Asia, Eastern Europe, East Asia, High-income North America, High-income Asia-Pacific, the Caribbean, etc.

Estimation framework

Incidence and prevalence rates were calculated using the DisMod-MR 2.1 (Disease Model – Bayesian Meta-Regression) tool. Mortality estimates are derived using the CODEm framework, which integrates vital registration and verbal autopsy data that are rigorously adjusted before analysis to ensure accuracy. CODEm enhances estimate precision by integrating multiple models. The method takes into account the differences in study design and methodology across multiple data sources to ensure the consistency and accuracy of the estimates. To calculate DALYs due to TC, two components are summed: years lived with disability reflecting the impact of surviving TC, and years of life lost due to premature mortality.

SDI

In GBD 2021, countries/regions are classified into five tiers based on SDI, which is quantified using fertility rates, education levels, and per capita income: high SDI (>0.81), high-middle SDI (0.71 < SDI ≤ 0.81), middle SDI (0.61 < SDI ≤ 0.71), low-middle SDI (0.46 < SDI ≤ 0.61), and low SDI (SDI ≤ 0.46). The SDI ranges from 0 to 1, with higher values indicating higher levels of development(10).

Risk factors

We focused on the risk factor of high body-mass index (BMI) identified in the GBD 2021 study. The DALYs and mortality data for TC influenced by this factor were examined and stratified by region to reveal geographic variations in its impact.

To quantify the impact of risk factors, we used advanced methods like DisMod-MR 2.1 and spatiotemporal Gaussian process regression to model exposure distributions across populations and regions(11). Subsequently, based on epidemiological evidence, we established the theoretical minimum risk exposure level (TMREL) for each risk factor, representing the optimal exposure level that minimizes the risk of TC(12). By integrating exposure data, relative risk estimates, and TMREL values, we calculated the population attributable fractions (PAFs) for each risk factor.

These PAFs were stratified by region, age, sex, and year to quantify the potential reduction in TC burden if the exposure level of a given risk factor were reduced to its TMREL. We multiplied PAFs by DALYs to derive burden estimates for each risk factor, revealing their potential impact on TC outcomes and providing a foundation for future intervention strategies.

Statistical analysis

EAPC regression model

To assess the trends in ASR of TC prevalence, incidence, deaths, and DALYs, this study utilized the EAPC. The ASR is calculated per 100,000 individuals using the following formula:

$$ASR = \frac{\sum_{i=1}^{A} a_i \, \omega_i}{\sum_{i=1}^{A} \omega_i} \times 100{,}000$$

In the formula, a_i represents the age-specific rate for a given age group, ω_i denotes the number of individuals in the standard population corresponding to that age group, and A indicates the number of age groups.

The calculation of EAPC is based on a regression model that describes the change pattern of ASR over a specific period of time. The formula(12) used is: $Y = \alpha + \beta X + e$. Where Y is the natural logarithm of ASR, X is the calendar year, α is the intercept, β is the slope or trend, and e is the error term. The formula for calculating EAPC is: $100 \times [\exp(\beta) - 1]$. 95% *CI* of EAPC was calculated using a linear regression model. If both the EAPC and the lower bound of its 95% CI are positive, ASR is considered to exhibit an upward trend; if both are negative, ASR shows a downward trend; if neither condition holds, ASR is regarded as stable. The Spearman correlation coefficient is used to assess the relationship between SDI and ASR.

Joinpoint regression model

This study used the Joinpoint regression model to analyze trends in ASPR from 1990 to 2021, calculating the Annual Percentage Change (APC) and Average Annual Percentage Change (AAPC). It identifies inflection points in disease burden trends

and assesses their significance(13). If the 95% *CI* of APC includes 0, the change is not significant; if APC > 0 and the *CI* does not include 0, ASPR increases annually; if APC < 0, ASPR decreases annually. In the absence of inflection points, AAPC reflects a singular trend.

BAPC model

This study applied the Bayesian Age-Period-Cohort (BAPC) model, using a second-order random walk to smooth priors for age, period, and cohort effects. The model employs the Integrated Nested Laplace Approximation (INLA) method to estimate the marginal posterior distribution and predict future trends in burden(14, 15).

All analyses and visualizations were performed using the WHO's Health Equity Assessment Toolkit and R statistical software (version 4.4.2), with the Joinpoint software used to analyze trends in ASR. All statistical tests were two-sided, with $P < 0.05$ considered statistically significant.

Ethical statement

As this study utilized publicly available data that did not contain any confidential or personally identifiable patient information, the ethics committee granted an exemption for this study. Informed consent was not required for this study.

RESULTS

Global level

In 2021, the global burden of TC remained substantial, with a total of 1,987,148.5 cases (95%UI: 1776275.3-2198245.2), marking an astonishing increase of 193.7% compared to 1990. Not only did the absolute number of cases rise significantly, but the ASPR also increased from 14.9 cases per 100,000 people in 1990 (95%UI: 14.1–16.0) to 23.1 cases per 100,000 people in 2021 (95%UI: 20.7–25.6). The EAPC for ASPR was 1.58 (95%*CI*: 1.44~ 1.73). In 2021, the number of new TC cases reached 249,538 (95%UI: 223,290.3–274,638.2), representing an astonishing increase of 177.6% compared to 1990. The ASIR showed an increase from 2.1 cases per 100,000 people in 1990 (95%UI: 2.0–2.2) to 2.9 cases per 100,000 people in 2021

(95%UI: 2.6–3.2). The EAPC for ASIR was 1.25 (95%*CI*: 1.14~ 1.37). In 2021, the number of TC deaths was 44,798.5 (95%UI: 39,924.7–48,541.0), with the EAPC_ASDR was -0.24 (95%*CI*: -0.27~ -0.21). The total DALYs for TC in 2021 reached 1,246,484.8 (95%UI: 1,094,415.6–1,375,852.5), with DALY rate at 14.6 (95%UI: 12.8–16.1). The EAPC for DALYs was -0.14 (95%*CI*: -0.17~ -0.11) (Fig. 1A, Table 1).

Five SDI stratification levels

Regarding disease prevalence, in 2021, regions with a high SDI exhibited the highest ASPR, reaching 38.2 cases per 100,000 population (95% UI: 36.3–40.4). This was followed by high-middle SDI regions. Both values exceeded the global ASPR (Table 1). Regarding incidence, in 2021, regions with a high SDI exhibited the highest ASIR, reaching 4.5 cases (95% UI: 4.3–4.7). This was followed by high-middle SDI regions (Table 1). Nevertheless, compared to 1990, the increase in the ASPR and ASIR in high SDI and high-middle SDI regions was the slowest among all regions in 2021. Taking 2009 as the node, it showed an upward trend before and then a significant downward trend. This pattern markedly differs from the trends observed globally and in other SDI regions (Fig. 1A). In terms of deaths and DALYs rates, 2021 data show higher rates in low SDI, middle SDI, and low-middle SDI regions, whereas high SDI and high-middle SDI regions exhibit lower rates. This pattern contrasts sharply with the burden of prevalence and incidence. Compared to 1990, low-middle SDI and middle SDI regions show an increasing trend in both mortality and DALYs, while high SDI and high-middle SDI regions demonstrate a significant decline, with the rate of decrease surpassing the global decline in mortality (Table 1, Figure 1A). The visualizations clearly illustrate that high SDI and high-middle SDI regions display a trend in ASDR that is completely opposite to that of other regions (Figure 1A).

Regional levels

Regarding prevalence, compared to 1990, Central Europe is the only region globally that showed a decreasing trend in 2021, with an EAPC of -0.33 (95% *CI*: -0.52 ~ -0.14). The top two regions with the highest ASPR in 2021 were High-income

North America and Australasia. Regarding incidence, compared to 1990, Central Europe is the only region globally to show a decreasing trend. The regions with the highest ASIR in 2021 were High-income North America, Australasia, and High-income Asia Pacific, while the fastest-growing regions in terms of incidence were North Africa and the Middle East, Australasia, and Andean Latin America. Regarding mortality and DALYs, in 2021, the regions with the highest mortality rates were Andean Latin America, Eastern Sub-Saharan Africa, and Southeast Asia. Compared to 1990, South Asia and Southern Sub-Saharan Africa exhibited the most pronounced upward trends in mortality, whereas Central Europe and Western Europe showed the most significant declines (Table 1, Figure 1A, Figure 2).

Regarding changes in case numbers, the regions with the most significant increases in disease prevalence are Cape Verde, Saudi Arabia, Qatar, the United Arab Emirates, Equatorial Guinea, Iran, Ecuador and Belize, with case growth rates exceeding 300% in all of these regions. Regarding changes in incidence, the regions with the most significant increases are Saudi Arabia, Cape Verde, Qatar, the United Arab Emirates, and Iran, while the regions with the most notable decreases are Poland, Croatia, and Hungary. Regarding changes in mortality, the regions with the most significant increases in death rates are Cape Verde, Qatar, Iran, Ecuador, and the United Arab Emirates, while the regions with the most notable decreases in mortality are Hungary and Poland. The regions with the most significant increases of DALYs are Cape Verde, Qatar, the United Arab Emirates, Saudi Arabia, Iran, and Ecuador, while the most notable decreases are observed in Hungary, Poland, Croatia, and the Czech Republic (Figure 3).

The hierarchical clustering analysis reveals that regions such as Australasia, low-middle SDI, North Africa and the Middle East, South Asia, and Southern Sub-Saharan Africa are grouped into Cluster 1. In these regions, both the EAPC_incidence and the EAPC_DALYs are predominantly positive, indicating an increase in both disease incidence and burden. Regions such as Western Europe, Central Asia, Western Sub-Saharan Africa, Southern Latin America, High-income Asia Pacific, and Eastern Sub-Saharan Africa are grouped into Cluster 2. In these

regions, both the EAPC_incidence and the EAPC_DALYs are predominantly negative, suggesting that these regions may be in a transitional phase of disease burden control. Central Europe is classified into Cluster 3, where both the EAPC_incidence and EAPC_DALYs are negative, indicating that health improvements in this region are likely attributable to effective disease prevention measures (Figure 4).

Sex patterns and age

In 2021, the global prevalence rate for women was 31.33 per 100,000 (95% UI: 27.56-36.85), while for men it was 14.79 per 100,000 (95% UI: 12.96-16.44). The incidence rate for women was 3.83 per 100,000 (95% UI: 3.36-4.49), and for men, it was 1.98 per 100,000 (95% UI: 1.72-2.19). The DALYs rate for women was 16.7 per 100,000 (95% UI: 14.09-19.59), while for men it was 12.34 per 100,000 (95% UI: 10.34-13.77). The burden of disease and incidence among the middle-aged and early elderly populations show an upward trend with increasing age, peaking at 55-59 years for both prevalence and incidence, followed by a decline. In terms of prevalence, women reach their peak at 60-64 years, while men peak at 55-59 years; regarding incidence, women peak at 70-74 years, and men at 75-79 years, with a secondary peak at 55-59 years (Fig. 5). The incidence of TC increased year by year, with the largest increase from 2003 to 2009, and then the growth rate gradually stabilized (Figure 1A, Figure 1B).

Risk factors

This study identified High-BMI as a major risk factor by matching global data. The regions with the highest ASDR attributable to High-BMI are North Africa and the Middle East (17.4%), The regions with the greatest impact of High-BMI on DALYs are High-income North America (17.4%). At the SDI stratification level, the impact of High-BMI on deaths and DALYs is greater in High SDI and High-middle SDI regions (Figure 6).

Future projections of global TC burden

The global prevalence of TC is projected to rise from 24.06 per 100,000 in 2021 (95% UI: 24.03-24.10) to approximately 26.12 per 100,000 in 2040 (95% UI: 11.30-40.95). Among men, the rate is expected to increase to 16.51 per 100,000 (95%

UI: 4.38-28.65), while among women, it will rise from 32.60 per 100,000 (95% UI: 32.55-32.66) to 35.34 per 100,000 (95% UI: 15.24-55.44) (Fig. 7A). The incidence of TC is projected to rise to 3.34 (95% UI: 1.46-5.23). Among men, the rate is expected to increase to 2.20 per 100,000 (95% UI: 0.58-3.83), while among women, it will rise from 3.93 per 100,000 (95% UI: 3.91-3.94) to 4.40 per 100,000 (95% UI: 1.94-6.86) (Figure 7B). The age-standardized DALYs rate will decline from 14.53 (95% UI: 14.51-14.56) to approximately 14.12 per 100,000 in 2040 (95% UI: 8.61-19.64). Among men, the rate will decrease from 12.27 per 100,000 (95% UI: 12.24-12.31) to 11.88 per 100,000 (95% UI: 6.52-17.24), while among women, it will drop from 16.70 per 100,000 (95% UI: 16.67-16.74) to 16.15 per 100,000 (95% UI: 9.36-22.95) (Figure 7C).

DISCUSSION

TC burden analysis

Advances in diagnostic technology may be contributing to the increase in the global TC burden. Additionally, increased public awareness of health and the widespread use of general health check-ups have significantly improved the detection rates of TC, which could be another major reason behind the rise in epidemiological data(16). Although the ASPR and ASIR of TC have shown an increasing trend, both the mortality rate and DALYs rate exhibit a negative growth trend. This contrasting outcome further underscores the effectiveness of improved screening coverage and the enhanced diagnostic and therapeutic skills of healthcare professionals.

Compared to 1990 data, the increase in ASPR and ASIR in High and High-middle SDI regions in 2021 was relatively small, while ASDR and DALY rates showed a negative growth trend. This phenomenon may be attributed to the strong early diagnostic capabilities and medical resources in these regions, which are sufficient to improve patients' quality of life(17). In other regions, the higher mortality and DALY rates may be due to the lack of effective screening and diagnostic technologies, leading to patients being diagnosed only at advanced stages, which undoubtedly increases the difficulty of treatment(1, 18).

Margherita Pizzato and her team have indicated that the epidemiological pattern of high incidence and low mortality of TC is largely attributed to the overdiagnosis effect(19). A previous study found that, between 1988 and 2007, over 500,000 individuals in 12 high-income countries may have been overdiagnosed with TC(20). Overdiagnosis and the resulting overtreatment have placed a significant burden on healthcare systems, and this issue has garnered increasing attention in recent years. International guidelines have undergone substantial revisions, with clear recommendations to avoid TC screening in asymptomatic individuals(21).

In 2021, advanced medical equipment and screening practices in North America and the Asia-Pacific region improved early diagnosis rates of thyroid cancer, positioning their epidemiological data among the global leaders. However, compared to 1990, the growth rate in these regions ranks in the middle to lower range globally, with both mortality and DALY rates showing a downward trend(2, 22). Regions such as the Andes, Latin America, and South Asia have seen relative increases in prevalence, morbidity, mortality, and DALYs, and increases in early warning screening and job stress may be contributing to increases in prevalence and morbidity. The inability to improve treatment and care capacity at the same time could explain the increase in disability rates(4). In addition, the high altitude of the region (an average of 2,358 meters) is also considered to have a potential association with the high incidence of TC(23).

Multiple studies have found that the number of female patients is higher(5, 24). Estrogen promotes the proliferation, migration and invasion of TC cells through its receptors, and promotes the progression of TC by influencing the tumor microenvironment(25). Women typically undergo significant hormonal fluctuations during puberty, pregnancy, and menopause, which may increase the instability of thyroid cells. Additionally, women tend to undergo more frequent health screenings during these periods, which is one of the reasons why the detection rate is higher in women(26). The expression levels or mutation frequencies of TC-related genes, such as BRAF and RAS, are higher in females(27). The X chromosome may play a role in susceptibility to TC, with the presence of two X chromosomes in females potentially

influencing the regulation of specific tumor suppressor genes(28). Although the incidence of TC is lower in males, it typically presents with a higher degree of malignancy and is more likely to metastasize to lymph nodes and distant organs, which warrants heightened attention(29). Both the prevalence and incidence rates in both males and females show a positive correlation with age. Individuals aged 55 and older should be more vigilant about disease screening. It is worth considering that global aging will also contribute to this phenomenon(30). The overall prevalence exhibits an inverted U-shape, with a more pronounced increase in prevalence observed among middle-aged individuals compared to the elderly. This trend may, in part, be attributed to overdiagnosis(31).

Elevated BMI is an independent risk factor for various chronic metabolic diseases and cancers. It is recognized as the second most common and modifiable carcinogenic factor, following smoking(32). Studies have shown that obesity-related factors, including mild chronic inflammation, changes in cytokine levels, insulin resistance, oxidative stress, etc., have an impact on the progression of TC(33). In fact, the onset of TC is strongly influenced by a combination of factors(34), including lifestyle(35), environmental factors, such as radiation exposure (the aftermath of the Chernobyl disaster(36) and occupational radiation exposure(37)) and iodine intake(38) (both excess(39) and deficiency(40)). Additionally, a family history of TC(41) and personal medical history(42) are also important factors. With the continuous advancement in the study of the etiology of TC, an increasing number of potential pathogenic factors have been proposed, including other endocrine disorders(43), cytokines(44), smoking(45) and alcohol consumption(46), dietary habits(47), psychological stress, and environmental pollution(48). These factors may affect the epigenetic state of the organism, altering gene expression and influencing the progression of the disease(49). This underscores the importance of a multifaceted approach to analyzing the interactions among various factors while continuously refining preventive and therapeutic strategies to enhance disease management and optimize patient care.

The COVID-19 pandemic may have influenced the burden trends of TC observed in our study. The pathogenesis of COVID-19 involves the induction of

autoimmune responses and cytokine storms, and the thyroid, as an endocrine organ vulnerable to autoimmune attack, experiences a complex and bidirectional interaction with the virus(50). A study in the United Arab Emirates found a significant increase in poor prognostic markers and aggressive subtypes of papillary thyroid carcinoma (PTC) in patients undergoing thyroidectomy post-pandemic, highlighting the need for ongoing updating of thyroid cancer prevention and management strategies(51).

This study has several limitations, including differences in the quality and availability of data from various sources, as well as uncertainties introduced by assumptions and modeling techniques inherent in the GBD approach. Nevertheless, this result is still the best estimate based on current evidence.

CONCLUSION

The burden of TC remains significant and is steadily increasing, with notable disparities across regions, countries, and different levels of the SDI. Improving health systems, reducing socioeconomic polarization, and strengthening early screening and prevention are critical, as are raising public awareness of the disease and avoiding overtreatment.

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Data availability statement: The data that support the findings of this study are openly available in 2021 GBD database at https://vizhub.healthdata.org/gbd-results/.

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TABLES AND FIGURES WITH LEGENDS

Table 1. Trends in TC burden: prevalence, incidence, deaths, and DALYs (1990–2021).

	location	1990		2021		EAPC_95% CI
		Number	ASR	Number	ASR	
Prevalence	**Global**	**676648.8 (636788.9-727722.8)**	**14.9 (14.1-16)**	**1987148.5 (1776275.3-2198245.2)**	**23.1 (20.7-25.6)**	**1.58 (1.44 to 1.73)**
	Low SDI	21971.9 (17309-27986.9)	6.2 (4.9-7.9)	92787.3 (71789.9-126590)	11.1 (8.7-14.9)	1.87 (1.76 to 1.99)
	Low-middle SDI	56029.2 (47678.1-71121.3)	6.3 (5.3-7.9)	251682.8 (206843.3-308118.1)	14 (11.5-16.9)	2.67 (2.64 to 2.7)
	Middle SDI	122505.4 (108257.6-142672.6)	8.6 (7.7-10.1)	594136.2 (493696.7-673492)	21 (17.5-23.8)	3.03 (2.95 to 3.12)
	High-middle SDI	186568 (174097.6-198522.8)	17.6 (16.4-18.7)	448569.8 (401405.4-510752.5)	25.2 (22.6-28.8)	1.4 (1.22 to 1.58)
	High SDI	288686.4 (280129.1-297109)	28.5 (27.6-29.3)	598370 (566881.9-629719.5)	38.2 (36.3-40.4)	1.23 (0.93 to 1.53)
	Andean Latin America	2640.4 (2211.1-3138.8)	9.8 (8.1-11.5)	18047.3 (13837.2-22793)	28.1 (21.6-35.6)	3.55 (3.34 to 3.77)
	Australasia	4599.9 (4076.9-5210.9)	20.6 (18.3-23.3)	16211.2 (13090.8-19620.8)	38.9 (31.4-47.6)	2.87 (2.29 to 3.47)
	Caribbean	3118.1 (2873.6-3378.8)	10.6 (9.8-11.5)	9357.3 (8102.5-10834.1)	17.8 (15.4-20.6)	1.86 (1.69 to 2.04)
	Central Asia	6945.8 (6347.8-7593.4)	12.7 (11.6-13.9)	13021.3 (11400.3-14782.4)	13.4 (11.7-15.2)	0.16 (-0.61 to 0.93)
	Central Europe	34174.4 (32484.3-36024.9)	23.6 (22.4-24.8)	37892.2 (34073.8-41467.7)	21.9 (19.7-24)	-0.33 (-0.52 to -0.14)
	Central Latin America	11472.2 (11049.9-11916.4)	10.2 (9.8-10.6)	58071 (51803-65647.6)	21.8 (19.4-24.6)	2.39 (2.28 to 2.5)
	Central Sub-Saharan Africa	870.5 (619-1301.5)	2.6 (1.8-3.9)	3432 (2194.6-5420.7)	4 (2.5-6.3)	1.42 (1.14 to 1.7)
	East Asia	95529.4 (76898.9-113229.6)	8.5 (6.9-10.1)	411402.4 (334530-513557.1)	20.5 (16.8-25.6)	3.16 (3 to 3.33)
	Eastern Europe	50163.3 (47847.6-52997.6)	18.9 (18.1-20)	75906.4 (68504.6-84343.5)	25.9 (23.3-28.8)	1.47 (0.97 to 1.97)
	Eastern Sub-Saharan Africa	12047 (9301.5-15328.6)	9.4 (7.3-12)	48137 (34449.7-73226.7)	15.4 (11.2-23.1)	1.47 (1.29 to 1.66)
	High-income Asia Pacific	55344.6 (51670.9-60632.8)	26.9 (25.1-29.6)	110959.1 (98931.9-129334.7)	37.1 (33.2-43.8)	1.42 (0.91 to 1.93)

	High-income North America	100673.1 (97445.8-103313)	32.1 (31.1-32.9)	237732 (226609-247666.5)	45.5 (43.6-47.3)	1.23 (1.05 to 1.42)
	North Africa and Middle East	31166 (25920.4-41990)	13 (10.8-17.4)	183491.2 (151632.4-216130.2)	30.7 (25.4-36)	3.16 (2.99 to 3.33)
	Oceania	308.3 (199-418.5)	6.8 (4.5-9.3)	960.2 (576-1382.1)	8.6 (5.2-12.3)	0.59 (0.48 to 0.7)
	South Asia	53580.2 (43818.6-70783.2)	5.9 (4.9-7.8)	282509.1 (227052.9-343508.3)	15.3 (12.3-18.5)	3.24 (3.16 to 3.33)
	Southeast Asia	45506 (36198.2-51840.3)	12.7 (10.3-14.5)	206164.7 (161849.8-244210.6)	26.9 (21.1-31.8)	2.33 (2.23 to 2.43)
	Southern Latin America	6690 (5949.1-7523.9)	14.1 (12.6-15.9)	15500.3 (13535.1-17754.5)	19.7 (17.1-22.6)	1.21 (1 to 1.42)
	Southern Sub-Saharan Africa	2655.2 (2243.8-3153)	6.9 (5.8-8.2)	8000.6 (6622.7-9541.6)	10.7 (8.9-12.7)	1.8 (1.54 to 2.05)
	Tropical Latin America	9237.1 (8742.4-9743.8)	7.8 (7.4-8.2)	33082.7 (31066.3-34983.6)	12.6 (11.8-13.3)	1.32 (1.13 to 1.51)
	Western Europe	148253.3 (140945-155876.6)	31.1 (29.5-32.7)	211123.9 (193366-229245.3)	32.7 (29.9-35.5)	0.51 (0.09 to 0.94)
	Western Sub-Saharan Africa	1674 (1212.8-2106)	1.2 (0.9-1.5)	6146.3 (4496.6-8323.4)	1.8 (1.3-2.3)	1.09 (1 to 1.18)
Incidence	**Global**	**89885.5 (84681.3-96998.8)**	**2.1 (2-2.2)**	**249538 (223290.3-274638.2)**	**2.9 (2.6-3.2)**	**1.25 (1.14 to 1.37)**
	Low SDI	3431.3 (2759.4-4295.6)	1.1 (0.9-1.4)	12358.4 (9598.7-16514.5)	1.7 (1.3-2.2)	1.23 (1.12 to 1.34)
	Low-middle SDI	8233.9 (7035-10302.4)	1 (0.9-1.3)	33464 (27896.3-40292.7)	2 (1.7-2.3)	2.09 (2.07 to 2.12)
	Middle SDI	17155.2 (15282.6-19997.3)	1.4 (1.2-1.6)	75356.9 (62756-84674.8)	2.7 (2.3-3)	2.37 (2.28 to 2.46)
	High-middle SDI	24410.6 (22753.3-25919.8)	2.3 (2.2-2.5)	55158.1 (49518.3-62489)	3.1 (2.8-3.5)	1.05 (0.89 to 1.21)
	High SDI	36533.2 (35292-37708.3)	3.5 (3.4-3.7)	72995.8 (68514-76746.9)	4.5 (4.3-4.7)	1.01 (0.75 to 1.28)
	Andean Latin America	422.2 (354-495.4)	1.8 (1.5-2.1)	2424 (1907.2-3044.3)	3.9 (3.1-4.8)	2.6 (2.44 to 2.77)
	Australasia	585.9 (522.4-660.1)	2.6 (2.3-2.9)	1949.1 (1569.7-2343.2)	4.6 (3.7-5.5)	2.61 (2.06 to 3.16)
	Caribbean	442.8 (410.8-479.3)	1.6 (1.5-1.7)	1244.9 (1085.7-1427.4)	2.4 (2.1-2.7)	1.5 (1.32 to 1.69)
	Central Asia	914 (840.8-996.1)	1.7	1630.9	1.7 (1.5-2)	0.01 (-0.73

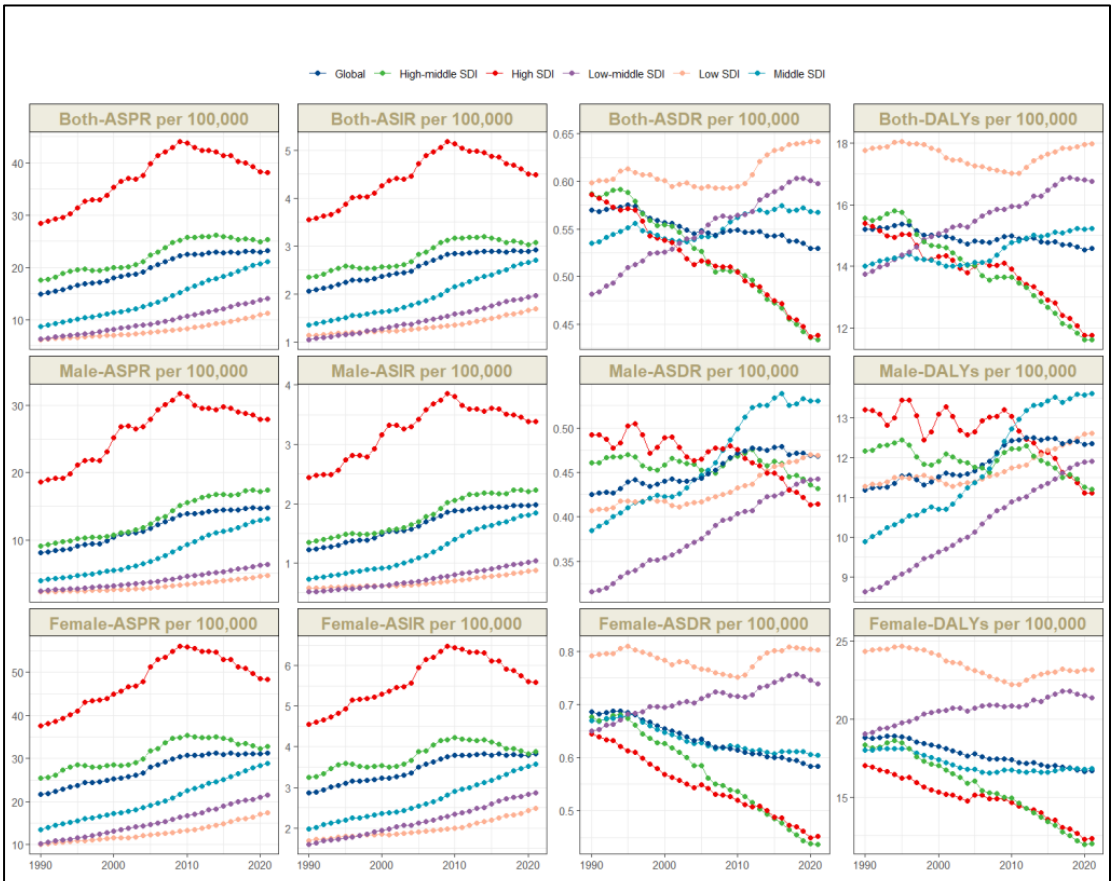
			(1.6-1.9)	(1432.2-1845.3)		to 0.75)
	Central Europe	4654.9 (4428.6-4883.6)	3.2 (3-3.4)	4876.2 (4406.6-5323.5)	2.7 (2.4-2.9)	-0.65 (-0.86 to -0.45)
	Central Latin America	1712.2 (1651.2-1775.4)	1.7 (1.7-1.8)	7752.6 (6907.4-8701.4)	3 (2.6-3.3)	1.66 (1.52 to 1.8)
	Central Sub-Saharan Africa	153.7 (111.5-225.9)	0.6 (0.4-0.8)	495.7 (319.2-770.7)	0.7 (0.4-1.1)	0.63 (0.42 to 0.83)
	East Asia	13203.4 (10809.5-15460.8)	1.3 (1.1-1.5)	50885.2 (41562-63161.9)	2.5 (2.1-3.1)	2.43 (2.26 to 2.6)
	Eastern Europe	6467.8 (6164.2-6831)	2.4 (2.3-2.6)	9617 (8698.1-10650.3)	3.2 (2.9-3.5)	1.27 (0.8 to 1.75)
	Eastern Sub-Saharan Africa	1908.4 (1516.6-2387.8)	1.8 (1.5-2.2)	6384.4 (4629.9-9478.7)	2.4 (1.8-3.5)	0.76 (0.6 to 0.92)
	High-income Asia Pacific	6950.1 (6496.3-7654.3)	3.4 (3.2-3.8)	14277.6 (12630.3-16476.5)	4.4 (3.9-5.2)	1.15 (0.68 to 1.61)
	High-income North America	12130.3 (11695.2-12450)	3.8 (3.7-3.9)	28289.1 (26782.7-29536)	5.3 (5.1-5.5)	1.15 (0.97 to 1.33)
	North Africa and Middle East	3792 (3150.6-5143.1)	1.7 (1.4-2.3)	21222.4 (17602-24974.6)	3.7 (3.1-4.3)	2.89 (2.72 to 3.06)
	Oceania	44.6 (29.9-60.2)	1.2 (0.8-1.6)	131.1 (80.2-185.4)	1.4 (0.9-1.9)	0.33 (0.24 to 0.42)
	South Asia	7853.1 (6476.2-10284.5)	1 (0.8-1.3)	37335.6 (30262.7-44931.4)	2.1 (1.7-2.6)	2.54 (2.46 to 2.62)
	Southeast Asia	6440.6 (5205.8-7276.5)	2 (1.7-2.3)	26559 (20898.8-31183.5)	3.6 (2.9-4.2)	1.82 (1.74 to 1.9)
	Southern Latin America	1000.1 (896.4-1118.9)	2.1 (1.9-2.4)	2046.9 (1787.2-2334)	2.5 (2.2-2.9)	0.7 (0.48 to 0.92)
	Southern Sub-Saharan Africa	376.9 (317.8-447.9)	1.1 (0.9-1.3)	1116.8 (934.8-1315.9)	1.6 (1.3-1.9)	1.54 (1.3 to 1.79)
	Tropical Latin America	1371.6 (1299.4-1443.4)	1.3 (1.2-1.3)	4491.1 (4197.7-4757.9)	1.7 (1.6-1.8)	0.76 (0.6 to 0.91)
	Western Europe	19206.5 (18291.7-20159.2)	3.9 (3.7-4.1)	26004.5 (23787.6-28201.5)	3.8 (3.5-4.2)	0.28 (-0.1 to 0.67)
	Western Sub-Saharan Africa	254.3 (186.2-312.4)	0.2 (0.2-0.3)	803.8 (597.7-1068.9)	0.3 (0.2-0.3)	0.52 (0.45 to 0.58)
Deaths	**Global**	**21893 (20437.5-24108.1)**	**0.6 (0.5-0.6)**	**44798.5 (39924.7-48541)**	**0.5 (0.5-0.6)**	**-0.24 (-0.27 to -0.21)**
	Low SDI	1454.5 (1199.2-1778.3)	0.6 (0.5-0.7)	3392.4 (2687.9-4328.7)	0.6 (0.5-0.8)	0.19 (0.11 to 0.28)
	Low-middle SDI	3015.5 (2624-3757.1)	0.5 (0.4-0.6)	8531.2 (7410.5-9771.6)	0.6 (0.5-0.7)	0.74 (0.71 to 0.78)
	Middle SDI	5275.6 (4815.1-6144.8)	0.5 (0.5-0.6)	14666.5 (12466.8-16170.9)	0.6 (0.5-0.6)	0.21 (0.16 to 0.26)

High-middle SDI	5609.4 (5200.9-5934.9)	0.6 (0.5-0.6)	8436.7 (7553.5-9304.5)	0.4 (0.4-0.5)	-1.03 (-1.09 to -0.97)
High SDI	6504.9 (6098.3-6798.4)	0.6 (0.5-0.6)	9730.2 (8465.5-10437.2)	0.4 (0.4-0.5)	-0.91 (-0.96 to -0.86)
Andean Latin America	182.3 (153.4-211.5)	0.9 (0.8-1)	641.2 (507.9-794.5)	1.1 (0.9-1.4)	0.66 (0.54 to 0.77)
Australasia	97.6 (87.2-109.1)	0.4 (0.4-0.5)	199.1 (161.3-237.4)	0.4 (0.3-0.4)	0.14 (-0.13 to 0.41)
Caribbean	142.5 (131.7-156)	0.6 (0.5-0.6)	321.3 (280.7-367.5)	0.6 (0.5-0.7)	0.42 (0.2 to 0.65)
Central Asia	253.3 (235.5-274.3)	0.5 (0.5-0.6)	339.3 (301.7-378.5)	0.4 (0.4-0.5)	-0.81 (-1.43 to -0.18)
Central Europe	1266.4 (1213.2-1316.6)	0.9 (0.8-0.9)	985.7 (898-1064.6)	0.4 (0.4-0.5)	-2.37 (-2.65 to -2.1)
Central Latin America	635.6 (613.9-657.6)	0.8 (0.8-0.8)	1964.6 (1748.8-2165.4)	0.8 (0.7-0.9)	-0.07 (-0.26 to 0.11)
Central Sub-Saharan Africa	78.4 (57.7-112.8)	0.4 (0.3-0.5)	182.8 (118.4-284)	0.3 (0.2-0.6)	-0.11 (-0.23 to 0.01)
East Asia	3780.9 (3211.5-4380.1)	0.5 (0.4-0.6)	8063.8 (6456.3-9800.1)	0.4 (0.3-0.5)	-0.65 (-0.74 to -0.55)
Eastern Europe	1349.5 (1274-1423.5)	0.5 (0.5-0.5)	1650.5 (1508.2-1807.4)	0.5 (0.4-0.5)	-0.25 (-0.6 to 0.09)
Eastern Sub-Saharan Africa	838.7 (685.7-1015.1)	1 (0.8-1.2)	1800.9 (1337.6-2485.5)	1 (0.7-1.3)	-0.18 (-0.29 to -0.07)
High-income Asia Pacific	1235.9 (1126.1-1404.5)	0.6 (0.6-0.7)	2843.9 (2308.9-3185.8)	0.5 (0.4-0.6)	-0.82 (-0.98 to -0.65)
High-income North America	1391.8 (1285-1450.1)	0.4 (0.4-0.4)	2765.7 (2473-2948.9)	0.4 (0.4-0.4)	0.15 (0.06 to 0.23)
North Africa and Middle East	657.9 (546.1-936.5)	0.4 (0.3-0.6)	1935.2 (1676.1-2236.4)	0.4 (0.4-0.5)	0.64 (0.49 to 0.79)
Oceania	14.6 (10.3-19.3)	0.6 (0.4-0.7)	36.6 (23.3-50.4)	0.5 (0.4-0.7)	-0.13 (-0.16 to -0.1)
South Asia	2914.5 (2454.1-3700.4)	0.5 (0.4-0.6)	9323.8 (7794.2-10741.5)	0.6 (0.5-0.7)	0.92 (0.88 to 0.97)
Southeast Asia	2008.1 (1698.1-2303.1)	0.8 (0.7-1)	5642.9 (4564.6-6450.7)	0.9 (0.7-1)	0.32 (0.24 to 0.4)
Southern Latin America	359 (324.7-394.6)	0.8 (0.7-0.9)	485.2 (425.8-553.7)	0.6 (0.5-0.6)	-1.01 (-1.26 to -0.77)
Southern Sub-Saharan Africa	123.6 (102.4-148.3)	0.5 (0.4-0.6)	323.8 (264.5-372.4)	0.6 (0.5-0.7)	0.92 (0.65 to 1.18)
Tropical Latin America	509 (480-537.2)	0.6 (0.5-0.6)	1252.8 (1142-1332)	0.5 (0.5-0.5)	-0.6 (-0.69 to -0.5)
Western Europe	3951 (3667.4-4173.8)	0.7 (0.6-0.7)	3829.2 (3318.9-4190.8)	0.4 (0.3-0.4)	-1.7 (-1.77 to -1.64)
Western Sub-Saharan Africa	102.7 (77.8-122.8)	0.1 (0.1-0.1)	210.4 (165.3-263.6)	0.1 (0.1-0.1)	-0.51 (-0.59 to -0.43)

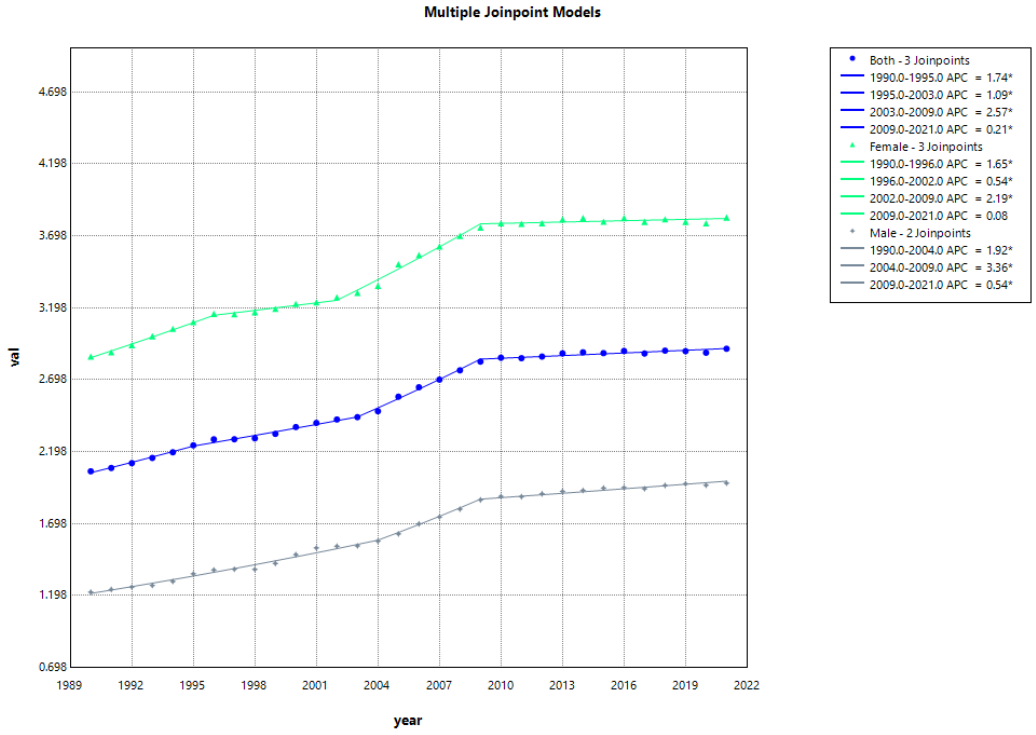
DALYs	**Global**	**646740.5 (599118.8-717357)**	**15.2 (14.2-16.8)**	**1246484.8 (1094415.6-1375852.5)**	**14.6 (12.8-16.1)**	**-0.14 (-0.17 to -0.11)**
	Low SDI	52661.5 (43472.1-63947.7)	17.8 (14.6-21.6)	120143.3 (93672.8-157131.4)	18 (14.2-23.1)	-0.05 (-0.12 to 0.02)
	Low-middle SDI	103647.8 (90342.8-129887.4)	13.8 (12-17.1)	269914.2 (229089.1-316826.3)	16.8 (14.3-19.4)	0.67 (0.63 to 0.7)
	Middle SDI	166177 (149966.3-190691.4)	14 (12.8-16.2)	416217.6 (350751-460888.7)	15.2 (12.8-16.8)	0.28 (0.22 to 0.34)
	High-middle SDI	158942.1 (146716.9-170152.9)	15.6 (14.4-16.6)	218961.3 (196634.7-244418.1)	11.6 (10.4-13)	-0.99 (-1.05 to -0.92)
	High SDI	164381.5 (155870.6-173717.9)	15.4 (14.6-16.3)	220135.9 (201450.2-237834.8)	11.8 (10.8-12.8)	-0.77 (-0.86 to -0.68)
	Andean Latin America	5273.8 (4419.1-6186.5)	23 (19.3-27)	16689.8 (13207.7-20766.9)	27.5 (21.7-34.3)	0.54 (0.43 to 0.65)
	Australasia	2544 (2273.1-2867.8)	11 (9.9-12.5)	5041.1 (4103.8-6033.3)	10.6 (8.7-12.8)	0.51 (0.21 to 0.82)
	Caribbean	4116.6 (3769-4556.3)	14.9 (13.7-16.5)	8690.2 (7532.9-10099.5)	16.3 (14.1-19)	0.46 (0.25 to 0.68)
	Central Asia	8144.5 (7568-8817.1)	15.9 (14.7-17.2)	10272.9 (9055.5-11543.5)	11.7 (10.3-13)	-1.19 (-1.81 to -0.57)
	Central Europe	34786.3 (33224.2-36474.4)	23.5 (22.4-24.6)	23433.7 (21250.4-25475.1)	11.6 (10.5-12.7)	-2.47 (-2.76 to -2.17)
	Central Latin America	18293.1 (17666.1-18920.9)	19.5 (18.9-20.2)	52186.9 (47013.3-58083.4)	20.4 (18.4-22.7)	0 (-0.2 to 0.2)
	Central Sub-Saharan Africa	2545.3 (1889.3-3609.5)	9.4 (6.9-13.7)	5956.3 (3862.9-9187.8)	8.9 (5.8-13.9)	-0.19 (-0.31 to -0.06)
	East Asia	116582.2 (98062.3-136720.9)	12.2 (10.4-14.2)	213609.2 (173066.2-262361.7)	10.3 (8.3-12.5)	-0.56 (-0.67 to -0.46)
	Eastern Europe	37930 (35923.3-40329.4)	13.9 (13.1-14.7)	42085.6 (38218.3-46388.2)	12.9 (11.7-14.1)	-0.29 (-0.68 to 0.11)
	Eastern Sub-Saharan Africa	31046 (25044.5-38047.3)	30.1 (24.5-36.7)	66490.9 (48520.2-94804.4)	27.8 (20.6-38.4)	-0.43 (-0.55 to -0.32)
	High-income Asia Pacific	30855.9 (28505.4-35131.3)	15.4 (14.1-17.5)	50783.2 (43704.3-57571.4)	11.8 (10.5-13.7)	-0.75 (-0.99 to -0.5)
	High-income	37316	11.2	70641.6	12 (11-13)	0.21 (0.11 to

North America	(34968.1-39721.4)	(10.5-12)	(65003.7-76456.6)		0.31)
North Africa and Middle East	21944.4 (18189.4-30745.7)	11 (9.1-15.5)	65316.2 (55454.2-76496.3)	12.7 (10.9-14.8)	0.76 (0.62 to 0.9)
Oceania	480.3 (324.9-641.5)	13.9 (9.8-18.5)	1173.6 (724.9-1641.6)	13.5 (8.6-18.6)	-0.1 (-0.14 to -0.06)
South Asia	105302.9 (88400.4-135793.4)	14.2 (12-18.2)	302256.8 (249827.8-356789.4)	18.2 (15.1-21.4)	0.85 (0.81 to 0.88)
Southeast Asia	62694.8 (51465.3-70374.5)	21.4 (17.9-24.3)	164547.4 (130332.7-189174.4)	23.6 (18.8-27)	0.27 (0.21 to 0.34)
Southern Latin America	9491.8 (8618.3-10469.6)	20.3 (18.4-22.3)	11959.8 (10465.3-13594.3)	14.3 (12.5-16.2)	-1.02 (-1.28 to -0.75)
Southern Sub-Saharan Africa	4035.3 (3398.8-4776.4)	12.4 (10.3-14.8)	10253.2 (8481-11926)	15.7 (12.8-18.1)	1 (0.72 to 1.27)
Tropical Latin America	15021.1 (14259-15822.7)	14.8 (14-15.6)	32680.5 (30547-34741.4)	12.7 (11.8-13.5)	-0.65 (-0.75 to -0.55)
Western Europe	94707.5 (89027.2-100543.1)	17.6 (16.6-18.8)	84464.5 (75823.1-92550.5)	10.5 (9.4-11.5)	-1.5 (-1.64 to -1.36)
Western Sub-Saharan Africa	3628.7 (2761.6-4379.4)	3.2 (2.4-3.8)	7951.2 (6109.3-10289)	2.8 (2.2-3.5)	-0.49 (-0.56 to -0.42)

△The 95% Uncertainty Interval (95% UI) refers to a range within which the model predicts there is a 95% probability that the true value lies. These uncertainty intervals are typically calculated by considering factors such as variability in data sources, statistical uncertainty, and changes in model parameters.



(A) Trends in thyroid cancer prevalence, incidence, deathes and DALYs from 1990 to 2021



(B) Age-standardized incidence rate Joinpoint regression time trend analysis

Figure 1. Trend chart of TC burden from 1990 to 2021

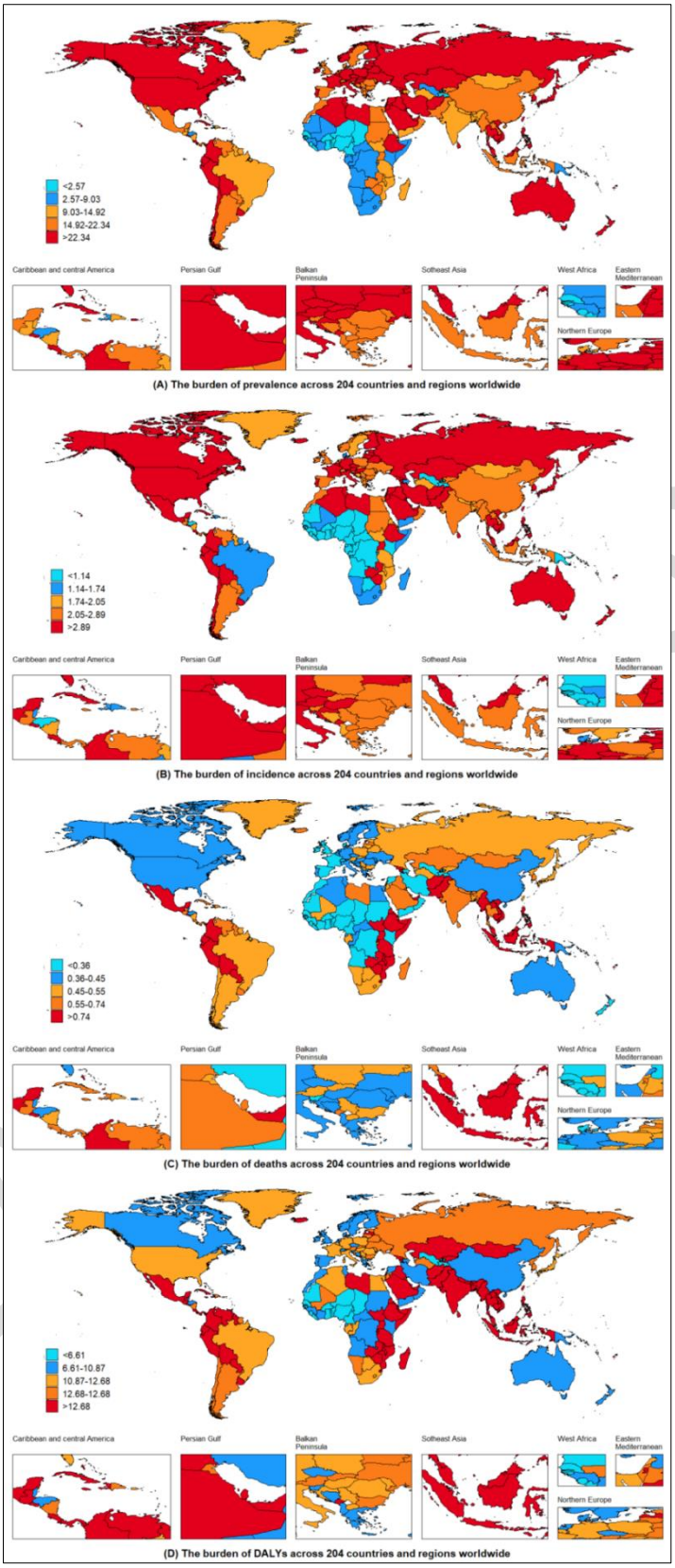


Figure 2. Global disease burden in 204 countries and regions.

△The legend in the four panels (A, B, C, D) of Figure 2 refers to EAPC of ASR (per 100,000).

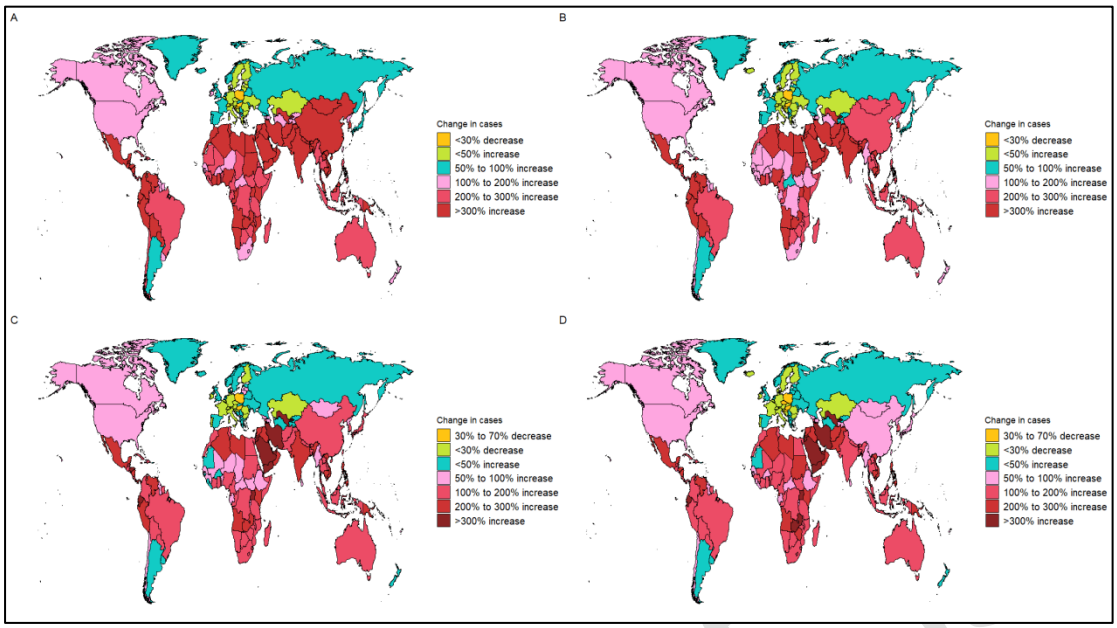


Figure 3. Change cases of TC in 204 countries and territories.

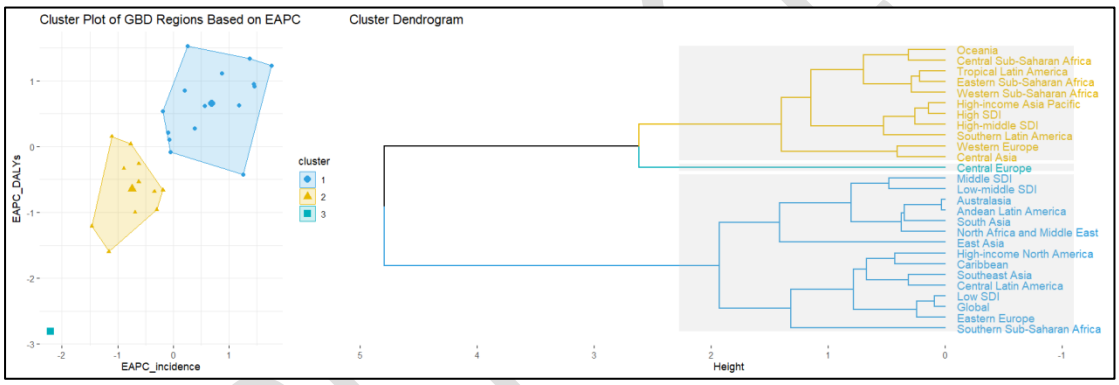


Figure 4. Hierarchical clustering analysis based on EAPC. The left panel represents a scatter plot based on EAPC clustering. The horizontal axis indicates the trend in incidence rates across different regions, while the vertical axis shows the trend in disease burden changes. Data points are grouped into three clusters, with points in the same cluster representing similar trends between 1990 and 2021. The right panel presents the corresponding hierarchical clustering dendrogram.

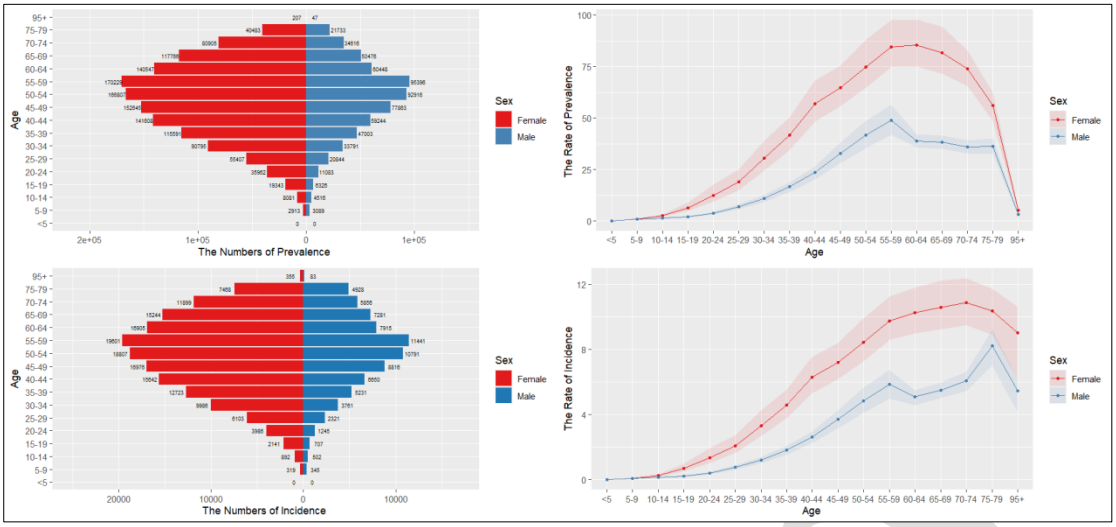


Figure 5. Trend chart of TC burden stratified by age and sex

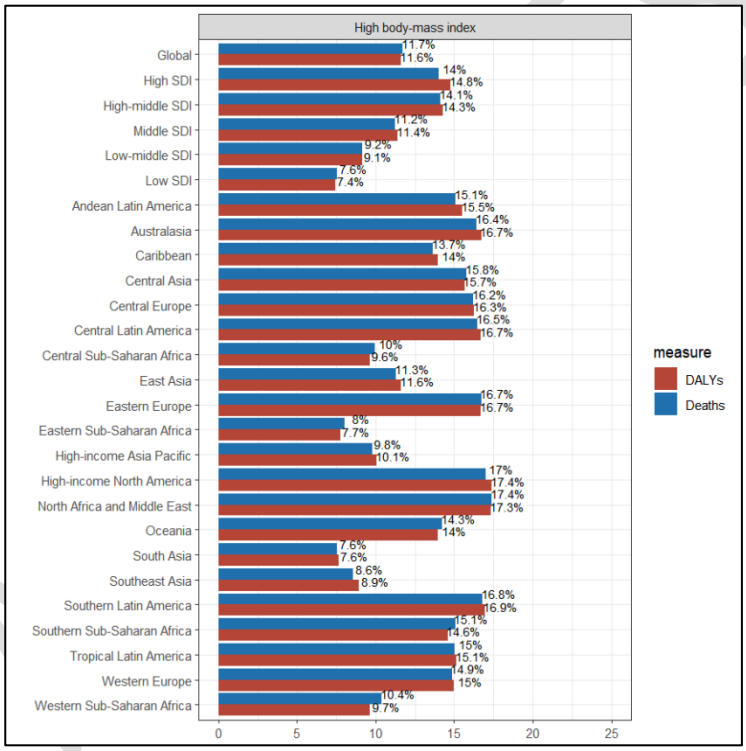


Figure 6. Illustrates the major risk factors influencing DALYs

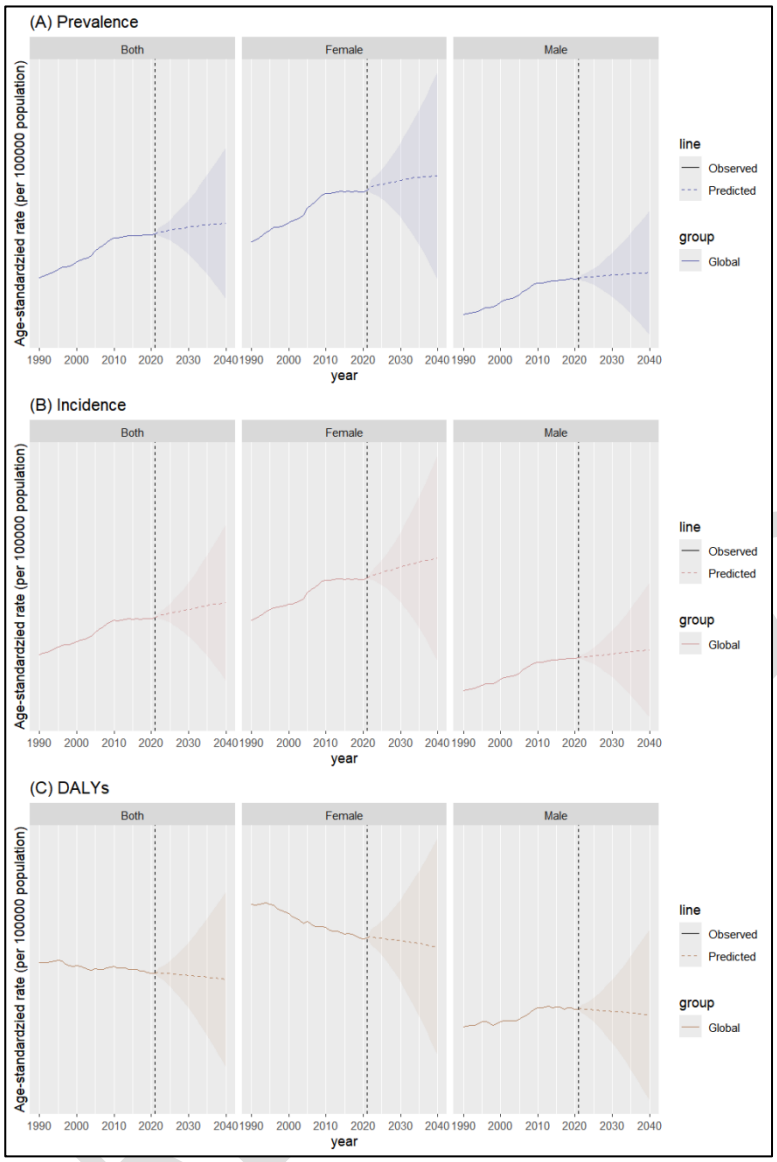


Figure 7. Future projections of the global burden of TC