

Obesity-driven thyroid cancer burden in middle-aged and older populations: temporal trends and projected trajectories based on the Global Burden of Disease study

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ABSTRACT

Introduction: High body mass index (BMI) in middle-aged and older individuals (≥ 40 years) is a leading risk factor for thyroid cancer-related morbidity and mortality; however, the quantifiable impact of elevated BMI on disability-adjusted life years (DALYs) and mortality in ageing populations remains underexplored. This study comprehensively evaluated the global burden of thyroid cancer attributable to elevated BMI by integrating past epidemiological trends, demographic variability and risk attribution models, and provided relevant projected trajectories using data from the Global Burden of Disease (GBD) study.

Methods: We analysed mortality, DALYs, years of life lost (YLLs) and years lived with disability (YLDs). Temporal trends in disease burden from 1990 to 2021 were examined using linear regression models. Cluster analysis was used to assess region-specific burdens across GBD study regions. Finally, projections of future disease burden from 2022 to 2050 were generated using autoregressive integrated moving average and exponential smoothing models.

Results: In 2021, high BMI contributed to 5255 thyroid cancer-related deaths (age-standardised mortality rate: 0.06 per 100 000) and 144 955 DALYs (age-standardised rate: 1.68 per 100 000); women and low-middle Socio-demographic Index regions were identified as high-risk subgroups. Projections indicate continued increases in mortality and overall disease burden through 2050.

Conclusion: Substantial geographical heterogeneity in thyroid cancer burden was observed across GBD regions. Interventions targeting high-risk demographic groups and regions should be prioritised to reduce this growing disease burden.

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New knowledge added by this study

- This is the first study to confirm the quantifiable impact of elevated body mass index (BMI) on disability-adjusted life years and mortality in ageing demographic groups.
- This study comprehensively evaluated the global disease burden of thyroid cancer attributable to elevated BMI by integrating epidemiological trends, demographic variability, and risk attribution models from 1990 to 2021.

Implications for clinical practice or policy

- The Hong Kong Government could propose sex- and age-specific prevention strategies, metabolic risk mitigation, and early detection protocols to address the increasing public health threat posed by obesity-driven thyroid cancer.
- The Hong Kong Government could prioritise interventions in high-risk demographic groups and regions to reduce this growing disease burden.

由肥胖引致的中年及長者人口甲狀腺癌疾病負擔：根據《全球疾病負擔研究》數據分析趨勢及推算發展走向

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引言：在40歲或以上的中年及較年長人士中，身體質量指數偏高是導致甲狀腺癌相關患病及死亡的主要風險因素之一。然而，身體質量指數偏高對長者的傷殘調整生命年及死亡率所造成的實際影響仍未有充分研究。本研究使用《全球疾病負擔研究》數據，分析過去的流行病學趨勢、人口變化及風險歸因模型，並推算將來的發展走向，全面評估全球因身體質量指數升高而引致的甲狀腺癌疾病負擔。

方法：本研究分析了死亡人數、傷殘調整生命年、壽命損失年數及傷殘生存年數。我們利用線性迴歸模型分析1990至2021年間疾病負擔的變化趨勢，並透過群集分析比較《全球疾病負擔研究》各地區的情況。最後，我們採用自迴歸整合移動平均模型及指數平滑模型，推算2022至2050年間的疾病負擔趨勢。

結果：在2021年，高身體質量指數與5255宗甲狀腺癌相關死亡有關（年齡標準化死亡率：每10萬人0.06宗），並導致144 955個傷殘調整生命年（年齡標準化比率：每10萬人1.68）。女性及社會人口發展指數屬中低水平的地區被識別為高風險群組。推算結果顯示死亡率及整體疾病負擔將持續上升至2050年。

結論：不同《全球疾病負擔研究》地區之間的甲狀腺癌疾病負擔存在明顯地域差異。應優先針對高風險人口群組及地區推行相關措施，以減輕不斷上升的疾病負擔。

Introduction

Thyroid cancer is one of the most common endocrine malignancies,¹ and its global incidence has steadily increased in recent decades.² This rise is primarily attributed to an increased incidence of papillary thyroid carcinoma.³ Patients with papillary thyroid carcinoma generally have a favourable prognosis; with appropriate treatment, the 5-year survival rate exceeds 98.3%.⁴ Most known or suspected risk factors for thyroid cancer, such as age, sex, race or ethnicity, and family history, are non-modifiable.⁵

However, changes in other factors, including obesity, cancer detection, iodine intake and ionising radiation, may influence the observed incidence, mortality and disability-adjusted life years (DALYs) of thyroid cancer over time. It is well documented that elevated body mass index (BMI) influences cancer development across multiple malignancies.^{6,7} We speculate that these aggregated trends do not accurately reflect the true disease burden in populations with high BMI, particularly among middle-aged and older adults, because existing studies address only the heterogeneity of thyroid cancer incidence across regions.^{8,9} To address this gap, we used data from the Global Burden of Disease (GBD) 2021 study to systematically analyse the burden of thyroid cancer among middle-aged and

older adults with high BMI from 1990 to 2021, and to project the future burden from 2022 through 2050. This analysis will assist policymakers in assessing thyroid cancer burden, evaluating the progress in targeted therapies, allocating resources, and formulating evidence-based policies.

Methods

Overview

The GBD 2021 study conducted a comprehensive assessment of health loss across 204 countries and territories, encompassing 369 diseases, injuries and impairments, as well as 88 risk factors, using updated epidemiological data and refined standardisation methodologies.¹⁰ The GBD database employs sophisticated methods to address missing data and adjust for confounding factors. Detailed descriptions of the GBD study design and analytical approaches have been extensively documented.¹⁰ Data used in the present study were obtained from the GBD 2021 database (<https://ghdx.healthdata.org/gbd-2021>), which contains no personally identifiable information.

Socio-demographic Index

The Socio-demographic Index (SDI) quantifies regional development status using aggregated measures of fertility rate, per capita income and educational attainment, scaled from 0 (least developed) to 1 (most developed). Within the GBD 2021 framework, countries were classified into five SDI tiers: high (>0.81), high-middle (0.70-0.81), middle (0.61-0.69), low-middle (0.46-0.60), and low (<0.46).¹⁰

Time series analysis

A time series comprises systematically recorded data points indexed at uniform temporal intervals (daily, monthly or yearly), enabling the identification of temporal patterns and trends. To forecast thyroid cancer burden metrics, we implemented autoregressive integrated moving average (ARIMA) models, which incorporate systematic evaluation of autoregressive, moving average and differencing parameters to optimise predictive accuracy.¹¹

Study data

In this study, the burden of thyroid cancer associated with high BMI among populations aged <40 years was assumed to be negligible. Consequently, individuals aged ≥40 years were stratified into 12 age-groups.

Statistical analyses

The statistical analysis evaluated global deaths, DALYs, years of life lost (YLLs), years lived with disability (YLDs), and age-standardised rates for

high-BMI-related thyroid cancer in middle-aged and older populations (2021), stratified by age, sex, SDI, region and country. Temporal trends (1990-2021) were analysed globally and across subgroups using linear regression models to estimate annual percentage changes.¹² Decomposition analysis using the Das Gupta method (modified by Cheng et al [2020])^{13,14} isolated the effects of population ageing, population growth and epidemiological changes on variations in disease burden. The ARIMA and exponential smoothing models were used to project future disease burden (2022-2050). All analyses were performed using R software (version 4.0.2) for database management, computation and validation.

Results

Disease burden of thyroid cancer attributable to high body mass index in middle-aged and older populations

Globally, high-BMI-associated thyroid cancer among

middle-aged and older populations caused 5255 deaths (95% uncertainty interval [95% UI]=3914-6653), with an age-standardised mortality rate of 0.06 per 100 000 (95% UI=0.05-0.08) [Table 1]. The number of attributable DALYs totalled 144 955 (95% UI=109 230-184 747), corresponding to an age-standardised DALY rate of 1.68 per 100 000 (95% UI=1.26-2.14) [Table 2]. Specifically, the number of YLDs reached 15 968 (95% UI=10 370-23 793; age-standardised rate: 0.18 per 100 000 [95% UI=0.12-0.28]) [Table 3], whereas YLLs constituted 128 986 (95% UI=96 149-162 365; age-standardised rate: 1.50 per 100 000 [95% UI=1.12-1.88]) [Table 4]. Age-standardised mortality, DALY, and YLL rates for high-BMI-related thyroid cancer increased with age, whereas YLD rates peaked in the 70-74 years age-group before declining. Non-linear age-specific patterns were observed for absolute case counts: deaths and DALYs peaked in the 55-59 years age-group (Table 2), YLDs in the 55-59 years age-group (Table 3), and YLLs in the 65-69 years age-group

TABLE 1. Age-standardised mortality rates and mortality counts for thyroid cancer attributable to high body mass index, with trends from 1990 to 2021*

	1990		2021		1990-2021 Estimated annual percentage change [‡]
	No. of deaths [†]	Age-standardised death rate/100 000 population [†]	No. of deaths [†]	Age-standardised death rate/100 000 population [†]	
Global	2198 (1642-2818)	0.06 (0.04-0.07)	5255 (3914-6653)	0.06 (0.05-0.08)	0.89 (0.61-1.16)
Both	2198 (1642-2818)	0.06 (0.04-0.07)	5255 (3914-6653)	0.06 (0.05-0.08)	0.2 (0.17-0.24)
Female	1494 (1117-1923)	0.07 (0.05-0.09)	3225 (2329-4164)	0.07 (0.05-0.09)	-0.12 (-0.15 to -0.09)
Male	704 (515-901)	0.04 (0.03-0.05)	2029 (1510-2596)	0.05 (0.04-0.07)	0.89 (0.83-0.95)
High-middle SDI	666 (496-856)	0.07 (0.05-0.09)	1194 (882-1509)	0.06 (0.04-0.08)	-0.48 (-0.54 to -0.41)
High SDI	811 (612-1024)	0.07 (0.06-0.09)	1368 (977-1734)	0.06 (0.05-0.08)	-0.47 (-0.52 to -0.42)
Low-middle SDI	197 (142-264)	0.03 (0.02-0.04)	782 (584-1013)	0.05 (0.04-0.07)	1.8 (1.76-1.83)
Low SDI	86 (60-120)	0.04 (0.02-0.05)	256 (177-355)	0.05 (0.03-0.07)	0.92 (0.83-1.01)
Middle SDI	434 (321-567)	0.04 (0.03-0.06)	1649 (1201-2116)	0.06 (0.05-0.08)	1.18 (1.12-1.24)
40-44 years	65 (49-85)	0.02 (0.02-0.03)	137 (101-178)	0.03 (0.02-0.04)	0.5 (0.41-0.59)
45-49 years	90 (68-115)	0.04 (0.03-0.05)	206 (155-263)	0.04 (0.03-0.06)	0.33 (0.29-0.37)
50-54 years	157 (118-200)	0.07 (0.06-0.09)	341 (258-432)	0.08 (0.06-0.10)	0.15 (0.09-0.21)
55-59 years	217 (163-275)	0.12 (0.09-0.15)	489 (369-620)	0.12 (0.09-0.16)	0.21 (0.14-0.29)
60-64 years	278 (207-351)	0.17 (0.13-0.22)	561 (422-700)	0.18 (0.13-0.22)	0 (-0.08-0.07)
65-69 years	309 (231-396)	0.25 (0.19-0.32)	678 (508-851)	0.25 (0.18-0.31)	-0.14 (-0.19 to -0.09)
70-74 years	279 (208-358)	0.33 (0.25-0.42)	711 (527-898)	0.35 (0.26-0.44)	-0.08 (-0.15 to -0.01)
75-79 years	311 (230-399)	0.5 (0.37-0.65)	685 (510-875)	0.52 (0.39-0.66)	0.2 (0.15-0.25)
80-84 years	216 (153-279)	0.61 (0.43-0.79)	560 (390-722)	0.64 (0.44-0.82)	0.16 (0.08-0.24)
85-89 years	114 (77-148)	0.76 (0.51-0.98)	384 (252-502)	0.84 (0.55-1.10)	0.43 (0.35-0.51)
90-94 years	39 (25-51)	0.91 (0.6-1.2)	202 (125-268)	1.13 (0.70-1.50)	0.79 (0.73-0.85)
≥95 years	9 (6-13)	0.92 (0.57-1.23)	72 (42-99)	1.33 (0.78-1.81)	1.28 (1.17-1.38)

Abbreviations: GBD = Global Burden of Disease; SDI = Socio-demographic Index

* Totals may not equal the sum of subgroups due to independent GBD modelling

† 95% uncertainty intervals are shown in brackets

‡ 95% confidence intervals are shown in brackets

TABLE 2. Age-standardised disability-adjusted life year (DALY) rates and DALY counts for thyroid cancer attributable to high body mass index, with trends from 1990 to 2021*

	1990		2021		1990-2021
	No. of DALYs†	Age-standardised DALY rate/100 000 population†	No. of DALYs†	Age-standardised DALY rate/100 000 population†	Estimated annual percentage change‡
Global	61 815 (46 571-79 116)	1.49 (1.12-1.9)	144 955 (109 230-184 747)	1.68 (1.26-2.14)	0.95 (0.75-1.15)
Both	61 815 (46 571-79 116)	1.49 (1.12-1.9)	144 955 (109 230-184 747)	1.68 (1.26-2.14)	0.38 (0.34-0.41)
Female	40 936 (31 059-52 907)	1.87 (1.42-2.41)	88 120 (64 992-114 469)	1.96 (1.44-2.55)	0.1 (0.06-0.13)
Male	20 879 (15 682-26 681)	1.06 (0.79-1.36)	56 835 (42 680-73 440)	1.38 (1.04-1.79)	0.93 (0.87-0.99)
High-middle SDI	18 467 (13 894-23 642)	1.81 (1.36-2.32)	31 264 (23 243-40 272)	1.63 (1.21-2.10)	-0.4 (-0.47 to -0.33)
High SDI	20 543 (15 669-25 939)	1.91 (1.46-2.41)	32 562 (24 816-41 098)	1.75 (1.32-2.20)	-0.2 (-0.28 to -0.12)
Low-middle SDI	6410 (4655-8632)	0.9 (0.65-1.21)	24 618 (18 601-32 274)	1.54 (1.16-2.02)	1.84 (1.81-1.88)
Low SDI	2975 (2067-4183)	1.06 (0.74-1.48)	8911 (6160-12 571)	1.38 (0.96-1.91)	0.76 (0.67-0.86)
Middle SDI	13 304 (9887-17 216)	1.15 (0.86-1.5)	47 448 (35 193-60 878)	1.71 (1.27-2.20)	1.28 (1.22-1.35)
40-44 years	3565 (2696-4621)	1.24 (0.94-1.61)	8031 (6061-10 515)	1.61 (1.21-2.10)	0.76 (0.69-0.84)
45-49 years	4371 (3333-5580)	1.88 (1.44-2.4)	10 672 (8113-13 885)	2.25 (1.71-2.93)	0.55 (0.5-0.61)
50-54 years	6604 (4932-8416)	3.11 (2.32-3.96)	15 149 (11 434-19 465)	3.40 (2.57-4.37)	0.34 (0.28-0.41)
55-59 years	7888 (5951-9995)	4.26 (3.21-5.4)	18 589 (14 083-23 742)	4.70 (3.56-6.00)	0.38 (0.31-0.44)
60-64 years	8609 (6450-10 842)	5.36 (4.02-6.75)	17 982 (13 706-22 678)	5.62 (4.28-7.09)	0.14 (0.07-0.2)
65-69 years	7986 (6017-10 257)	6.46 (4.87-8.3)	18 047 (13 603-22 832)	6.54 (4.93-8.28)	-0.03 (-0.08 to 0.03)
70-74 years	5883 (4407-7540)	6.95 (5.21-8.91)	15 411 (11 361-19 512)	7.49 (5.52-9.48)	0.01 (-0.06 to 0.09)
75-79 years	5171 (3883-6618)	8.4 (6.31-10.75)	11 653 (8695-14 928)	8.84 (6.59-11.32)	0.26 (0.21-0.31)
80-84 years	2787 (1979-3587)	7.88 (5.6-10.14)	7291 (5090-9420)	8.33 (5.81-10.76)	0.2 (0.12-0.27)
85-89 years	1168 (790-1515)	7.73 (5.23-10.03)	3947 (2591-5192)	8.63 (5.67-11.35)	0.45 (0.37-0.52)
90-94 years	343 (224-451)	8.01 (5.22-10.53)	1773 (1099-2367)	9.91 (6.15-13.23)	0.79 (0.73-0.85)
≥95 years	78 (48-104)	7.65 (4.7-10.2)	593 (347-806)	10.88 (6.36-14.79)	1.23 (1.12-1.33)

Abbreviations: GBD = Global Burden of Disease; SDI = Socio-demographic Index

* Totals may not equal the sum of subgroups due to independent GBD modelling

† 95% uncertainty intervals are shown in brackets

‡ 95% confidence intervals are shown in brackets

(Table 4). In 2021, female predominance was evident across all metrics. Females accounted for 61.37% of deaths, 60.79% of DALYs, 66.23% of YLDs, and 60.12% of YLLs. Geographically, middle-SDI regions had the highest absolute burden (1649 deaths; 47 448 DALYs), whereas high-middle SDI regions exhibited the highest age-standardised mortality (0.06 per 100 000) and DALY rates (1.63 per 100 000) [Tables 1 and 2].

Globally, substantial disparities in the burden of high-BMI-related thyroid cancer were observed across 50 GBD regions in 2021. Asia displayed the highest absolute burden, with 75 130 DALYs (95% UI=54 305-97 695), 2601 deaths (95% UI=1884-3397), 7596 YLDs (95% UI=4771-11 735), and 67 533 YLLs (95% UI=48 806-88 249), whereas Oceania reported the lowest values, with 163 DALYs (95% UI=102-238) and five deaths (95% UI=3-7). Age-standardised rates revealed regional

heterogeneity: Andean Latin America exhibited among the highest age-standardised rates for DALYs (4.26 per 100 000; 95% UI=3.03-5.89), deaths (0.16 per 100 000; 95% UI=0.12-0.23) and YLLs (3.98 per 100 000; 95% UI=2.80-5.48).

At the national level, China recorded the highest number of DALYs (23 684; 95% UI=16 056-32 507) and deaths (871; 95% UI=588-1177), followed by India (11 546-20 676 DALYs; 506 deaths). Fiji (Oceania) demonstrated the highest age-standardised DALY rate (6.07 per 100 000; 95% UI=3.76-8.98), exceeding that of Ecuador (South American, Andean region: 5.12 per 100 000; 95% UI=3.57-6.92). China also exhibited the highest global YLD (2871; 95% UI=1780-4650) and YLL (20814; 95% UI=13 923-28 116) counts, reflecting its disproportionate burden among ageing populations with elevated BMI (online supplementary Fig 1).

TABLE 3. Age-standardised years lived with disability (YLD) rates and YLD counts for thyroid cancer attributable to high body mass index, with trends from 1990 to 2021*

	1990		2021		1990-2021 Estimated annual percentage change‡
	No. of YLDs†	Age-standardised YLD rate/100 000 population†	No. of YLDs†	Age-standardised YLD rate/100 000 population†	
Global	4693 (3057-6940)	0.11 (0.07-0.16)	15 968 (10 370-23 793)	0.18 (0.12-0.28)	2.37 (2.19-2.56)
Both	4693 (3057-6940)	0.11 (0.07-0.16)	15 968 (10 370-23 793)	0.18 (0.12-0.28)	1.86 (1.72-1.99)
Female	3311 (2125-4933)	0.15 (0.1-0.22)	10 576 (6834-15 955)	0.24 (0.15-0.36)	1.65 (1.53-1.78)
Male	1382 (899-2013)	0.07 (0.04-0.09)	5393 (3556-7943)	0.13 (0.08-0.19)	2.33 (2.15-2.5)
High-middle SDI	1412 (916-2090)	0.13 (0.09-0.2)	3951 (2594-5932)	0.21 (0.14-0.32)	1.65 (1.49-1.81)
High SDI	2272 (1481-3296)	0.22 (0.14-0.32)	5615 (3694-8096)	0.34 (0.22-0.5)	1.7 (1.44-1.96)
Low-middle SDI	254 (161-382)	0.03 (0.02-0.05)	1575 (1005-2414)	0.09 (0.06-0.14)	3.5 (3.47-3.54)
Low SDI	92 (59-145)	0.03 (0.02-0.05)	451 (279-742)	0.06 (0.04-0.1)	2.23 (2.09-2.36)
Middle SDI	656 (424-970)	0.05 (0.03-0.07)	4362 (2793-6577)	0.15 (0.1-0.23)	3.73 (3.65-3.81)
40-44 years	434 (279-668)	0.15 (0.1-0.23)	1486 (952-2282)	0.30 (0.19-0.46)	2.23 (2.14-2.33)
45-49 years	493 (316-741)	0.21 (0.14-0.32)	1800 (1149-2676)	0.38 (0.24-0.57)	1.92 (1.71-2.13)
50-54 years	612 (386-900)	0.29 (0.18-0.42)	2120 (1374-3170)	0.48 (0.31-0.71)	1.77 (1.56-1.98)
55-59 years	635 (413-937)	0.34 (0.22-0.51)	2213 (1426-3312)	0.56 (0.36-0.84)	1.83 (1.65-2)
60-64 years	594 (389-860)	0.37 (0.24-0.54)	1798 (1183-2599)	0.56 (0.37-0.81)	1.6 (1.46-1.74)
65-69 years	482 (322-693)	0.39 (0.26-0.56)	1556 (1042-2285)	0.56 (0.38-0.83)	1.37 (1.24-1.5)
70-74 years	306 (205-440)	0.36 (0.24-0.52)	1206 (821-1743)	0.59 (0.4-0.85)	1.39 (1.27-1.52)
75-79 years	224 (147-320)	0.36 (0.24-0.52)	728 (494-1063)	0.55 (0.37-0.81)	1.47 (1.34-1.61)
80-84 years	89 (56-133)	0.25 (0.16-0.38)	320 (200-474)	0.37 (0.23-0.54)	1.36 (1.19-1.52)
85-89 years	36 (21-54)	0.24 (0.14-0.36)	157 (92-236)	0.34 (0.2-0.52)	1.36 (1.2-1.52)
90-94 years	7 (4-10)	0.16 (0.09-0.24)	37 (21-56)	0.21 (0.12-0.31)	0.99 (0.92-1.05)
≥95 years	2 (1-2)	0.15 (0.08-0.24)	13 (7-20)	0.24 (0.13-0.37)	1.55 (1.44-1.66)

Abbreviations: GBD = Global Burden of Disease; SDI = Socio-demographic Index

* Totals may not equal the sum of subgroups due to independent GBD modelling

† 95% uncertainty intervals are shown in brackets

‡ 95% confidence intervals are shown in brackets

Temporal trends in disease burden attributable to high body mass index–related thyroid cancer in middle-aged and older populations

From 1990 to 2021, the numbers of thyroid cancer–related deaths, DALYs, YLDs, and YLLs increased worldwide, reflecting a growing public health burden. Age-standardised rates for all metrics showed an overall increasing trend during this period, indicating persistent elevations in mortality and morbidity risk independent of population ageing. These findings suggest that the increasing disease burden cannot be attributed solely to demographic expansion, but may involve synergistic drivers such as environmental exposures or lifestyle changes (online supplementary Fig 2).

Sex-specific disparities were evident in temporal progression patterns; men displayed concurrent upward trends in age-standardised morbidity and

mortality rates, as well as case numbers, highlighting sex-dimorphic epidemiological mechanisms (online supplementary Fig 3).

Age-stratified analysis revealed differential temporal patterns: middle-aged cohorts (40-44 years) showed relatively stable age-standardised rates in later decades despite increasing case counts, suggesting improved early detection or risk mitigation. Conversely, older populations (70-79 years) experienced concurrent increases in age-standardised morbidity metrics and absolute case counts, indicating that disease progression may be driven by ageing-related physiological vulnerabilities and prolonged exposure to risk factors (online supplementary Fig 4).

Geographical heterogeneity was observed across SDI regions. High- and high-middle-SDI regions achieved declining age-standardised rates despite increasing case numbers, likely reflecting

TABLE 4. Age-standardised years of life lost (YLL) rates and YLL counts for thyroid cancer attributable to high body mass index, with trends from 1990 to 2021*

	1990		2021		1990-2021
	No. of YLLs†	Age-standardised YLL rate/100 000 population†	No. of YLLs†	Age-standardised YLL rate/100 000 population†	Estimated annual percentage change‡
Global	57 121 (42 783-72 983)	1.38 (1.04-1.77)	128 986 (96 149-162 365)	1.50 (1.12-1.88)	0.8 (0.6-1.01)
Both	57 121 (42 783-72 983)	1.38 (1.04-1.77)	128 986 (96 149-162 365)	1.50 (1.12-1.88)	0.23 (0.19-0.26)
Female	37 624 (28 303-48 385)	1.72 (1.3-2.22)	77 544 (57 184-100 732)	1.72 (1.27-2.24)	-0.08 (-0.12 to -0.04)
Male	19 497 (14 368-24 946)	1 (0.73-1.27)	51 442 (38 389-66 316)	1.25 (0.94-1.62)	0.81 (0.76-0.87)
High-middle SDI	17 054 (12 649-21 863)	1.67 (1.24-2.15)	27 313 (20 287-34 512)	1.41 (1.05-1.79)	-0.63 (-0.7 to -0.56)
High SDI	18 271 (13 768-23 019)	1.69 (1.27-2.13)	26 948 (20 156-33 767)	1.40 (1.06-1.75)	-0.56 (-0.61 to -0.5)
Low-middle SDI	6156 (4464-8259)	0.87 (0.63-1.16)	23 042 (17 302-29 976)	1.45 (1.09-1.88)	1.76 (1.73-1.8)
Low SDI	2883 (2005-4037)	1.03 (0.72-1.44)	8460 (5805-11 836)	1.32 (0.91-1.83)	0.71 (0.62-0.8)
Middle SDI	12 648 (9367-16 378)	1.1 (0.81-1.43)	43 087 (31 933-54 929)	1.56 (1.14-1.99)	1.12 (1.06-1.18)
40-44 years	3131 (2324-4055)	1.09 (0.81-1.42)	6546 (4855-8525)	1.31 (0.97-1.7)	0.5 (0.41-0.58)
45-49 years	3877 (2908-4952)	1.67 (1.25-2.13)	8871 (6672-11 285)	1.87 (1.41-2.38)	0.32 (0.29-0.36)
50-54 years	5992 (4492-7645)	2.82 (2.11-3.6)	13 029 (9863-16 506)	2.93 (2.22-3.71)	0.15 (0.09-0.21)
55-59 years	7253 (5444-9210)	3.92 (2.94-4.97)	16 376 (12 351-20 777)	4.14 (3.12-5.25)	0.21 (0.14-0.29)
60-64 years	8015 (5963-10 112)	4.99 (3.71-6.3)	16 185 (12 198-20 218)	5.06 (3.81-6.32)	0 (-0.07 to 0.07)
65-69 years	7504 (5622-9625)	6.07 (4.55-7.79)	16 491 (12 359-20 677)	5.98 (4.48-7.5)	-0.14 (-0.19 to -0.08)
70-74 years	5578 (4152-7144)	6.59 (4.9-8.44)	14 205 (10 525-17 941)	6.90 (5.11-8.72)	-0.08 (-0.15 to -0.01)
75-79 years	4948 (3667-6358)	8.04 (5.96-10.33)	10 926 (8122-13 951)	8.28 (6.16-10.58)	0.19 (0.15-0.24)
80-84 years	2698 (1911-3476)	7.63 (5.4-9.83)	6971 (4850-8990)	7.96 (5.54-10.26)	0.15 (0.07-0.22)
85-89 years	1132 (768-1469)	7.49 (5.08-9.72)	3790 (2485-4959)	8.29 (5.44-10.85)	0.41 (0.34-0.49)
90-94 years	336 (220-441)	7.85 (5.13-10.3)	1736 (1077-2312)	9.71 (6.02-12.92)	0.79 (0.72-0.85)
≥95 years	76 (47-102)	7.5 (4.62-9.99)	580 (341-788)	10.64 (6.25-14.46)	1.22 (1.11-1.33)

Abbreviations: GBD = Global Burden of Disease; SDI = Socio-demographic Index

* Totals may not equal the sum of subgroups due to independent GBD modelling

† 95% uncertainty intervals are shown in brackets

‡ 95% confidence intervals are shown in brackets

advances in healthcare infrastructure and diagnostic precision. In contrast, low-middle- and low-SDI regions experienced parallel increases in age-standardised rates and absolute case counts, underscoring the compounding effects of limited healthcare access, delayed diagnosis, and unmitigated metabolic risk factors (online supplementary Fig 5).

Globally, thyroid cancer-related DALYs, deaths, YLDs, and YLLs among middle-aged and older populations with elevated BMI increased from 1990 to 2021. Population growth was the predominant driver of these increases, followed by epidemiological changes and population ageing.

High- and high-middle-SDI areas were primarily influenced by population growth and epidemiological shifts, with minimal contribution from ageing. Middle-SDI regions showed substantial contributions from all three factors—population growth, epidemiological changes, and ageing. In

low-middle- and low-SDI regions, population growth remained the dominant driver, although epidemiological changes and ageing also contributed (online supplementary Fig 6). Sex-specific decomposition revealed differing contribution patterns. Among women, population growth was the primary driver of the burden, with additional contributions from epidemiological changes and smaller effects from ageing. In contrast, men exhibited a dual-driver pattern in which population growth and epidemiological changes jointly accounted for most of the burden, while ageing played a lesser role (online supplementary Fig 7).

Predicted results for 2022 to 2050

The ARIMA model projections for 2022 to 2050 indicated that the numbers of deaths, DALYs, YLDs, and YLLs related to thyroid cancer are expected to increase in both sexes. Corresponding

age-standardised rates demonstrated relative stabilisation in women and an upward trend in men; these patterns were corroborated by exponential smoothing models (online supplementary Fig 8).

Discussion

Thyroid cancer is one of the most prevalent endocrine malignancies worldwide. Although the overall survival rate remains relatively high, its increasing incidence in many countries and regions, particularly in more developed nations, has become a growing public health concern.¹⁵ Globally, approximately 560 000 new cases of thyroid cancer are diagnosed annually, with a female-to-male incidence ratio of around 3:1.¹⁶⁻¹⁸ Concurrently, obesity has emerged as a major clinical and public health challenge, exhibiting rapid growth trends in both developed and developing countries. The impact of elevated BMI on cancer development has been well documented across multiple malignancies.⁷ However, the specific mechanisms underlying the association between elevated BMI and thyroid carcinogenesis remain poorly understood, constituting a critical knowledge gap that warrants further investigation.

According to the Global Burden of Disease Study 2021, thyroid cancer incidence rates have shown a sustained annual increase worldwide, with particularly pronounced rises among women in countries such as the United States and South Korea.¹⁹ This trend has been attributed to advances in early screening and diagnostic technologies. Furthermore, active surveillance has been recommended for the management of papillary microcarcinoma; these minimally invasive tumours frequently demonstrate favourable prognoses and indolent biological progression. This strategy effectively avoids overtreatment while reducing unnecessary surgical and therapeutic interventions.²⁰ In recent years, China has updated its clinical guidelines for thyroid nodule management, emphasising early screening protocols, standardisation of fine-needle aspiration biopsy, and personalised treatment planning.²¹ These revised strategies, particularly in the management of differentiated thyroid cancer, have further improved patient survival and quality of life.

The present study leveraged the GBD 2021 study database to evaluate thyroid cancer-related mortality, DALYs, YLDs, and YLLs among middle-aged and older individuals (≥ 40 years) with elevated BMI from 1990 to 2021. The results revealed an age-dependent increase in mortality burden, with DALYs and YLDs peaking in the 55-59-year age-group and YLLs reaching maximal levels in the 65-69-year age-group. Notably, populations aged ≥ 85 years displayed attenuated disease burden metrics in absolute counts, potentially reflecting diminished physiological reserves that mask the clinical

manifestations of malignancy, thereby contributing to diagnostic delays, therapeutic limitations, and exacerbated mortality. These findings underscore the critical interplay between ageing, metabolic risk, and healthcare accessibility in shaping thyroid cancer outcomes among high-BMI populations.

This study confirmed persistent sex disparities in thyroid cancer burden, with the incidence and prevalence among women consistently exceeding those among men across all regions in both 1990 and 2021. These disparities likely arise from an interplay of biological and socio-cultural mechanisms. Central to this imbalance are hormonal drivers—particularly oestrogen fluctuations during the menopausal transition—which may promote thyroid cell proliferation and oncogenesis. In addition to these biological factors, sex-specific lifestyle patterns, such as chronic stress, dietary habits, and exposure to environmental pollutants, may further increase tumourigenic risk. Underlying both dimensions, socio-cultural determinants affecting healthcare access may introduce diagnostic ascertainment bias, potentially obscuring the true epidemiological landscape.¹⁷

Notably, our analysis revealed a progressive rise in the proportions of obesity-driven thyroid cancer mortality and DALY proportions from 1990 to 2021; men exhibited a substantially greater escalation in burden relative to women.²² These patterns align with global epidemiological shifts—47.1% and 27.5% increases in adult and childhood obesity prevalence, respectively, from 1980 to 2013.²³ Such trends likely contribute to the disproportionate increase in thyroid cancer burden among male populations. Mechanistically, prolonged obesity may synergise with age-related endocrine alterations through amplified metabolic dysregulation and chronic inflammation, thereby promoting thyroid carcinogenesis in ageing men.²⁴

Low-SDI regions display lower overall thyroid cancer incidence rates but significantly faster growth than high-SDI regions. In contrast, high-SDI regions show stable or marginally declining incidence trends, potentially attributable to advanced healthcare infrastructure and higher health literacy, which enable early diagnosis and optimised management. These disparities emphasise the critical role of socio-economic development in shaping the epidemiology of thyroid cancer. Prioritising SDI-stratified interventions tailored to regional healthcare capacity and risk profiles could enhance the precision and impact of burden-mitigation strategies.²⁵

Projections indicate escalating thyroid cancer mortality, DALYs, YLLs, and YLDs from 2022 to 2050, with progressive increases among men but stable rates among women, consistent with documented epidemiological trajectories.⁹ This rising burden in middle-aged and older populations with elevated

BMI likely reflects synergistic interactions involving demographic ageing, the proliferation of high-risk behaviours, and socio-economic transitions. These forecasts highlight the urgent need to integrate tertiary prevention strategies with early-stage interventions targeting metabolic risk mitigation and diagnostic optimisation.

This investigation is strengthened by its rigorous analysis of the obesity-driven thyroid cancer burden in ageing populations using the GBD 2021 study dataset (1990-2021), coupled with comprehensive male patient data to delineate sex-specific epidemiological trajectories. However, the findings are tempered by several methodological constraints. The lack of histopathological subtype classification, such as papillary, follicular, or anaplastic variants, limits prognostic granularity. Additionally, there was limited consideration of modifiable risk factors, including gradients of radiation exposure and fluctuations in dietary iodine intake, which may synergistically interact with metabolic risk. Furthermore, this study did not fully disentangle how therapeutic advances (eg, surgical techniques, radiotherapy protocols, and molecular-targeted agents) modulate longitudinal disease burden. Collectively, these gaps underscore the imperative for intervention-focused studies integrating molecular stratification and context-specific risk profiling to refine clinical management paradigms.

Obesity is associated with an increased risk of at least 13 cancers (eg, endometrial, oesophageal, renal, and pancreatic adenocarcinomas; hepatocellular carcinoma; gastric cancer; colorectal cancer; postmenopausal breast cancer; ovarian cancer; gallbladder cancer; and thyroid cancer). Its biological mechanisms are multifactorial, mainly involving chronic inflammation, hormonal dysregulation, and metabolic disturbances: (1) long-term systemic inflammation may impair tissue repair capacity and promote tumour development²⁶; (2) disruption of hormonal balance, as adipose tissue is a major source of aromatase activity that converts androgens to oestrogen, thereby increasing the risk of hormone-related malignancies²⁷; and (3) increased visceral and subcutaneous fat accumulation may promote metabolic abnormalities that contribute to the development of liver, endometrial, and other cancers.²⁸

Therefore, from a public health perspective, efforts should be strengthened to increase awareness of the association between obesity and cancer, promote health education, and encourage population-level weight control to reduce cancer incidence. From an individual perspective, effective weight management should be emphasised, including reducing the intake of high-fat and high-sugar foods, adopting a high-fibre, low-calorie diet,

increasing physical activity, and undergoing regular health screening (including monitoring body weight, waist circumference, blood glucose, lipid levels, and liver and kidney function) to reduce the risk of obesity-related tumours.

Conclusion

Significant geographical heterogeneity in thyroid cancer burden was observed across GBD regions. These findings underscore the urgent need for sex- and age-specific prevention strategies, metabolic risk mitigation, and early detection protocols to address the growing public health threat posed by obesity-driven thyroid cancer. Interventions targeting high-risk demographic groups and regions should be prioritised to reduce this increasing disease burden.

Author contributions

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All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Ethics approval

Detailed descriptions of the Global Burden of Disease (GBD) study design and analytical approaches have been extensively documented in existing GBD publications. The data used in this study were obtained from the GBD 2021 study database (<https://ghdx.healthdata.org/gbd-2021>), which contains no personally identifiable information. All original studies were reviewed and approved by the relevant ethics committees.

Supplementary material

The supplementary material was provided by the authors, and some information may not have been peer reviewed. Accepted supplementary material will be published as submitted by the

authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (<https://doi.org/10.12809/hkmj2513477>).

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