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Original Article

Disparities in the global burden of tracheal, bronchus, and lung cancer from 1990 to 2019

Chenran Wang[1], Zheng Wu[1], Yongjie Xu[1], Yadi Zheng[1], Zilin Luo[1], Wei Cao[1], Fei Wang[1], Xuesi Dong[1], Chao Qin[1], Liang Zhao[1], Changfa Xia[1], Fengwei Tan[2], Wanqing Chen[1], Ni Li[1,3], Jie He[2]

[1] *Office of Cancer Screening, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China;*
[2] *Department of Thoracic Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China;*
[3] *Chinese Academy of Medical Sciences Key Laboratory for National Cancer Big Data Analysis and Implementation, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China.*

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ABSTRACT

Background: Tracheal, bronchus, and lung (TBL) cancer imposes a high disease burden globally, and its pattern varies greatly across regions and countries. This study aimed to explore the global burden and temporal trends of TBL cancer from 1990 to 2019.

Methods: Data on incidence, mortality, and disability-adjusted life years (DALYs) metrics (number, crude rate, and age-standardized rates), and the attributable risk fraction of DALY of TBL cancer from 1990 to 2019 in 21 Global Burden of Disease (GBD) regions, four World Bank income regions, 204 countries and territories, and the globe were obtained from the up-to-date GBD 2019 study. We applied estimated annual percentage changes (EAPCs) to the age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and age-standardized DALY rate (ASDR) to quantify the temporal trends of the TBL cancer burden from 1990–2019. Associations of EAPC of age-standardized rates with universal health coverage (UHC) index at the national level were evaluated with Pearson correlation analysis.

Results: Globally, approximately 2,260,000 new TBL cancer cases, 2,042,600 deaths, and 45,858,000 DALYs were reported in 2019. Combination of all modifiable risk factors, behavioral, environmental, and metabolic risk factors accounted for 79.1%, 66.4%, 33.3%, and 7.9% of global lung cancer DALYs, respectively. The overall ASIR (EAPC: −0.1 [95% confidence interval [CI]: −0.2, −0.1]), ASMR (EAPC: −0.3 [95% CI: −0.4, −0.3]), and ASDR (EAPC: −0.7 [95% CI: −0.7, −0.6]) decreased from 1990 to 2019. The highest mortality rate of TBL cancer occurred in the >85-year-old age group for both sexes among high-income countries (HICs) and upper-middle-income countries (UMCs), and in males aged 80–84 years and females aged >85 years in lower middle-income countries (LMCs). HICs experienced the largest declines in ASIR (−12.6%), ASMR (−20.3%), and ASDR (−27.8%) of TBL cancer between 1990 and 2019, while UMCs had the highest increases in ASIR (16.7%) and ASMR (8.0%) over the period. Eleven (52.4%), 14 (66.7%), and 15 (71.4%) regions of the 21 GBD regions experienced descending trends in ASIR, ASMR, and ASDR of TBL cancer between 1990 and 2019, respectively, with the greatest mean decrease per year (EAPC: −1.7 [95% CI: −2.0, −1.5] for ASIR, −1.9 [95% CI: −2.2, −1.7] for ASMR, and −2.2 [95% CI: −2.5, −2.0] for ASDR) being observed in eastern Europe. The ASIR, ASMR, and ASDR of TBL cancer were deemed to be in decreasing trends in 85, 91, and 104 countries and territories, with the largest decrease

Correspondence to: Ni Li, Office of Cancer Screening, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China.
E-mail address: nli@cicams.ac.cn

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in Bahrain (EAPC: −3.0 [95% CI: −3.3, −2.7] for ASIR, −3.0 [95% CI: −3.3, −2.6] for ASMR, and −3.4 [95% CI: −3.8, −3.1] for ASDR). ASIR (r=0.524), ASMR (r=0.411), and ASDR (r=0.353) of TBL cancer were positively associated with UHC index at the national level in 2019.

Conclusions: The TBL cancer burden shows a downward trend at the global level but varies greatly across regions and countries. A decreasing trend in the TBL cancer burden was observed in the most of the 21 GBD regions and 204 countries from 1990 to 2019. UMCs had the highest burden of TBL cancer and showed the largest increases in ASIR and ASMR.

Introduction

Tracheal, bronchus, and lung (TBL) cancer is the leading contributor to cancer-related burden worldwide, with an estimated 2.3 million newly diagnosed cases and 2.04 million deaths in 2019.[1] Globally, TBL cancer death cases and disability-adjusted life years (DALY) are estimated to account for approximately 20.4% and 18.3% of total cancer-related deaths and DALYs, respectively, ranking first for cancer burden in most regions.[2,3] Global efforts to further mitigate the TBL cancer burden were urgently required.

Over the past 30 years, the age-standardized rates of incidence, mortality, and DALY for TBL cancer have decreased globally, while the rates vary considerably across regions and countries.[2] Multiple variables, including the distribution of risk factor exposure, genetic predisposition, coverage of health gain, and demographic transition, contribute to geographical disparities in TBL cancer burden patterns.[4,5] For example, no significant improvements in TBL cancer outcomes were observed in Montenegro, Turkey, and Indonesia, which had a high prevalence of cigarette smoking.[6] However, the incidence of lung cancer has decreased in some developed countries such as the United States, the United Kingdom, Singapore, and New Zealand, which could be mainly attributed to the successful implementation of tobacco cessation campaigns.[7,8] Additionally, since low socioeconomic status may contribute to the risk of lung cancer incidence and lead to a poor survival, the disparities in TBL cancer burden across regions at varying economic levels should be tracked to identify different population-based interventions to effectively prevent TBL cancer loss.[9,10]

Even though many countries have made concerted efforts to reduce the TBL cancer burden through risk prevention programs, improved screening strategies, and accessible treatment options. Considering the severity of the demographic challenges and the cumulative effects of risk factor exposure, TBL cancer is projected to remain a serious health threat if there are not timely interventions. Prior to interventions must come knowledge; the Global Burden of Disease (GBD) study offers clinicians, researchers, and policymakers powerful resources to understand the changing health challenges faced by the global population. The updated GBD 2019 study provides the most comprehensive and comparable data on global health from 1990 to 2019.[2,3,6] In the present study, we aimed to provide an overview of the current status and temporal trends of TBL cancer burden at the global, regional, and national levels based on the most updated data from the GBD 2019 study. Furthermore, we also explored the association between the TBL cancer burden and effective health service coverage at the national level. Our study may help to provide a roadmap to understanding where the TBL cancer burden is high, which is critical to putting forward recommendations for public health policies and tailored interventions to mitigate the TBL cancer burden.

Methods

GBD overview

The GBD provides an important tool for policymakers and health practitioners worldwide to obtain an overview of the health status. The most up-to-date GBD 2019 study provided comprehensive assessments of the incidence, prevalence, mortality, DALY, and health life expectancy of 369 diseases and injuries in 204 countries and territories from 1990 to 2019. Accessible data from the original epidemiological surveys, national vital registration and statistics, disease surveillance systems, and high-quality pooled studies were collected globally for the GBD estimation process. Standard and unified modelling methodologies were applied to ensure that the estimates were globally comparative and regionally and nationally representative. The Bayesian meta-regression tool *DisMod-MR* was applied to estimate the incidence and prevalence of nonfatal diseases; cause-specific mortality and risk factor exposure were analyzed using the Cause of Death Ensemble Model and spatiotemporal Gaussian process regression. The 2019 GBD study conforms to the Guidelines for Accurate and Transparent Health Estimate Reporting statement.[2]

Data sources

Incidence, death, and DALY metrics

Data in this study are publicly available via the Global Health Data Exchange (GHDx) of the GBD 2019 study (https://vizhub.healthdata.org/).[11] Indicators of incidence, death, and DALY were obtained to describe the TBL cancer (diagnosis codes were C33, C34-C34.92, Z12.2, Z80.1-Z80.2, and Z85.1-Z85.20, according to the International Classification of Diseases, Tenth Revision [ICD-10]) burden. We extracted age- and sex-specific incidence, mortality, and DALY metrics (number, crude rate, and age-standardized rates) of TBL cancer in 21 GBD regions, four World Bank income regions, 204 countries and territories, and the globe from 1990 to 2019. Age-standardized rates of incidence, mortality, and DALY were calculated based on the GBD global population age standard.[3] Furthermore, to quantify the modifiable risk-attributable burden of TBL cancer, we extracted the attributable fraction of TBL cancer DALY for all risk factors combined, and behavioral, environmental/occupational, and metabolic risk clusters across regions in 2019.

Universal health coverage index

We collected data on the universal health coverage (UHC) index in 204 countries and territories. UHC is defined that all people have access to high-quality health services without financial hardship.[12] To monitor the effective coverage of health systems at the population level across settings, the GBD 2019 study offered a new measurement framework mapping 23 effective coverage indicators on five health service domains (i.e., promotion, prevention, treatment, rehabilitation, and palliation); the UHC index by country was measured on the scale of 1 to 100. The UHC values of 204 countries and territories were provided in Supplementary Table 1.

Socio-demographic index

The socio-demographic index (SDI) is a composite indicator that unites a location's lag distributed income per capita, educational attainment for the population aged >15 years, and the total fertility rate in <25-year-old females. It is positively associated with the level of a country's development status, which is relevant to health outcomes. SDI values ranged from 0 to 1, and the reference SDI quintile was defined as low (<0.455), low-middle (0.455≤SDI<0.608), middle (0.608≤SDI<0.690), high-middle (0.690≤SDI<0.805), and high (0.805≤SDI≤1) levels.[13] The SDI values of 204 countries and territories were provided in Supplementary Table 1.

Statistical analysis

We applied the estimated annual percentage changes (EAPCs) of the age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and age-standardized DALY rate (ASDR) to explore temporal trends in the TBL cancer burden across countries, regions, and globally from 1990 to 2019. A linear regression was fitted with the natural logarithm of ASIR, ASMR, and ASDR, that is, $y = \alpha + \beta x + \varepsilon$, where y is ln (age-standardized rate), x is the calendar year, and ε is the error term. EAPC was defined as $100 \times (\exp(\beta)\text{-}1)$. The positive values of EAPC and the lower boundary of 95% confidence interval (CI) indicated an upward trend of age-standardized rates over the time interval, while the negative values of EAPC and the upper boundary of 95% CI indicated an opposite downward trend.

The correlation coefficient (r) of ASIR, ASMR, and ASDR with the UHC index in 204 countries and territories in 2019 was sequentially calculated using Pearson correlation analysis to detect the potential association between the two indicators. A polynomial curve was fitted with ASIR, ASMR, and ASDR on the y-axis and the UHC index on the x-axis, with the SDI quintile represented as the index variable. All statistical analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA).

Results

Global burden of TBL cancer

Global patterns in 2019

Globally, there were approximately 2,260,000 (95% uncertainty interval [UI]: 2,067,300, 2,451,800) cases newly diagnosed with TBL cancer in 2019. The incidence rate of TBL cancer was 29.2 (95% UI: 26.7, 31.7) per 100,000 population, and 39.2 (95% UI: 35.4, 43.2) per 100,000 in males and 19.1 (95% UI: 17.1, 21.1) per 100,000 in females. The numbers of deaths and DALY of TBL cancer were 2,042,600 (95% UI: 1,879,200, 2,193,300) and 45,858,000 (95% UI: 42,297,400, 49,339,900), respectively. The DALY rate due to TBL cancer was 592.7 (95% UI: 546.7, 637.7) per 100,000 population, with 813.8 (95% UI: 737.5, 893.6) per 100,000 population in males and 370.2 (95% UI: 337.1, 407.2) per 100,000 population in females (Table 1). The age-specific incidence and mortality rates of TBL cancer increased with age and were the highest in the population aged >85 years in whole population and both sexes at the global level (Fig. 1A–F). The highest TBL cancer DALY rate occurred in the 70–74-year-old age group globally (Fig. 1G). Males (70–74-year-old age group) reached the peak of DALY rate earlier compared with females (75–79-year-old age group) globally (Fig. 1H–I). The combination of all modifiable risk factors, and behavioral, environmental, and metabolic risk factors accounted for 79.1%, 66.4%, 33.3%, and 7.9% of global TBL cancer DALYs, respectively, with the attributable fractions being higher in males than in females (Fig. 2).

Temporal trends from 1990 to 2019

The global ASIR (EAPC: −0.1 [95% CI: −0.2, −0.1]), ASMR (EAPC: −0.3 [95% CI: −0.4, −0.3]), and ASDR (EAPC: −0.7 [95% CI: −0.7, −0.6]) of TBL cancer showed decreasing trends from 1990 to 2019. The ASIR and ASMR in females increased by a mean of 0.6% (95% CI: 0.5%, 0.7%) and 0.4% (95% CI: 0.3%, 0.5%) per year from 1990 to 2019, while the decrease trends of ASIR, ASMR and ASDR were observed in males, and the EAPC was −0.5% (95% CI: −0.5%, −0.4%), −0.7% (95% CI: −0.7%, −0.6%), and −1.0% (95% CI: −1.0%, −0.9%) in males over the same period globally, respectively (Table 2).

Regional burden of TBL cancer

Income-classified regional patterns in 2019

Upper middle-income countries (UMCs) experienced the highest cases of incidence (1,108,800), death (1,028,700), and DALY (23,670,700) due to TBL cancer in 2019, accounting for approximately 49.1%, 33.7%, and 51.6% of TBL cancer-related incidents, deaths, and DALY globally, respectively. The rates of incidence, mortality, and DALY for TBL cancer were highest in high-income countries (HICs) and lowest in low-income countries (LICs). Among the four income-classified regions, the age-specific incidence rate increased with age and peaked at ages of 80–84 years in whole population and females in HICs (Fig. 1A and C). The highest mortality rate of TBL cancer occurred in the >85-year-old age group for general population among HICs and UMCs, and in males aged 80–84 years and females aged >85 years in lower middle-income countries (LMCs) (Fig. 1D–F). The summit onset age of TBL cancer DALY rate was 70–74 years across all regions. The age-specific rates of incidence, mortality, and DALY of TBL cancer were consistently higher in males than in females in all income-classified regions (Fig. 1B, C, E, F, H and I).

Temporal trends from 1990 to 2019 in income-classified regions

HICs saw the largest declines in ASIR (−12.6%), ASMR (−20.3%), and ASDR (−27.8%) of TBL cancer from 1990 to 2019, while UMCs saw the highest increases in ASIR (16.7%) and ASMR (8.0%) (Supplementary Table 2).

GBD regions patterns in 2019

A nearly 30-fold difference in the incidence rate of TBL cancer persisted among the 21 GBD regions, from 2.7 per 100,000 in eastern sub-Saharan Africa to 80.6 per 100,000 in the high-income Asia Pacific. Central Europe experienced the highest mortality (71.2 per 100,000) and DALY rates (1665.5 per 100,000) of TBL cancer, followed by high-income North America (63.2 per 100,000 for mortality rate and 1280.2 per 100,000 for DALY rate) (Table 1).

Modifiable risk factors had the greatest impact on TBL cancer DALY in central Europe, with the attributable fraction (85.1%) being far above that at the global level (79.1%) (Supplementary Table 3). The highest proportions of TBL cancer DALYs attributable to behavioral, environmental, and metabolic risk factors were observed in Central Europe, Eastern Sub-Saharan Africa, and high-income North America, respectively (Supplementary Tables 3–6). All three risk clusters accounted for higher proportions of TBL cancer DALYs in males than in females in the 21 GBD regions except for metabolic risk in Southern Sub-Saharan Africa (Fig. 2).

Temporal trends from 1990 to 2019 in GBD regions

A total of 52.4% (11 regions), 66.7% (14 regions), and 71.4% (15 regions) of the 21 GBD regions experienced descending trends in the ASIR, ASMR, and ASDR of TBL cancer between 1990 and 2019, respectively. The trends in ASIR, ASMR, and ASDR of TBL cancer showed heterogeneity across 21 GBD regions. The greatest mean decrease per year was observed in Eastern Europe (EAPC: −1.7 [95% CI: −2.0, −1.5] for ASIR, −1.9 [95% CI: −2.2, −1.7] for ASMR, and −2.2 [95% CI: −2.5, −2.0] for ASDR), and the incidence, mortality and DALY remained stable in eastern Sub-Saharan Africa (Table 2).

National burden of TBL cancer

National patterns in 2019

For 204 countries and territories, the absolute number of incident and death cases, and DALY of TBL cancer in China (0.83 million incident cases, 0.76 million death cases, and 17.13 million DALYs) accounted for 36.9%, 37.1%, and 37.4% of cases in the globe (2.26 million incident cases, 2.04 million death cases, and 45.86 million DALYs) in 2019, respectively (Table 1 and Supplementary Fig. 1 A–C). ASIR, ASMR, and ASDR varied considerably across the world, with the highest rates in Greenland, followed by Monaco and Montenegro in 2019 (Supplementary Table 7).

Populations with the highest age-specific incidence rate and DALY for TBL cancer were older in China (>85 years for incidence and 75–79

Table 1
Incidence, death, and DALY of TBL cancer globally in 2019 based on GBD study.

Regions	Incidence		Death		DALY	
	Cases (thousands) (95% UI)	Crude rate per 100,000 population (95% UI)	Cases (thousands) (95% UI)	Crude rate per 100,000 population (95% UI)	Number (thousands) (95% UI)	Crude rate per 100,000 population (95% UI)
China	832.9 (700.3, 981.6)	58.6 (49.2, 69.0)	757.2 (638.7, 887.8)	53.2 (44.9, 62.4)	17,128.6 (14,340.5, 20,231.3)	1204.2 (1008.2, 1422.4)
Global						
Both	2260.0 (2067.3, 2451.8)	29.2 (26.7, 31.7)	2042.6 (1879.2, 2193.3)	26.4 (24.3, 28.4)	45,858.0 (42,297.4, 49,339.9)	592.7 (546.7, 637.7)
Male	1522.8 (1373.8, 1676.7)	39.2 (35.4, 43.2)	1386.1 (1260.2, 1513.8)	35.7 (32.5, 39.0)	31,582.3 (28,622.1, 34,681.7)	813.8 (737.5, 893.6)
Female	737.2 (658.0, 814.0)	19.1 (17.1, 21.1)	656.5 (590.2, 719.0)	17.0 (15.3, 18.6)	14,275.7 (13,000.1, 15,704.8)	370.2 (337.1, 407.2)
GBD Regions						
Andean Latin America	6.0 (4.8, 7.3)	9.4 (7.6, 11.5)	6.2 (5.0, 7.6)	9.8 (7.9, 12.0)	139.0 (110.7, 171.9)	218.6 (174.1, 270.4)
Australasia	15.3 (12.5, 18.7)	52.7 (43.1, 64.2)	12.0 (11.1, 12.8)	41.4 (38.1, 43.9)	237.4 (222.7, 250.0)	816.8 (766.3, 860.1)
Caribbean	11.5 (9.8, 13.5)	24.4 (20.8, 28.6)	11.2 (9.6, 13.1)	23.8 (20.4, 27.8)	254.1 (216.0, 298.9)	538.8 (457.9, 633.8)
Central Asia	14.3 (13.0, 15.9)	15.3 (13.9, 17.0)	14.0 (12.7, 15.5)	15.0 (13.5, 16.5)	387.5 (349.2, 429.8)	414.3 (373.3, 459.5)
Central Europe	84.0 (74.2, 94.8)	73.6 (64.9, 83.0)	81.3 (71.4, 92.2)	71.2 (62.5, 80.7)	1902.4 (1667.4, 2173.2)	1665.5 (1459.8, 1902.6)
Central Latin America	27.2 (23.2, 31.8)	10.9 (9.3, 12.7)	27.3 (23.3, 31.9)	10.9 (9.3, 12.7)	620.5 (525.1, 734.9)	248.2 (210.0, 293.9)
Central Sub-Saharan Africa	6.8 (4.4, 11.7)	5.2 (3.4, 8.9)	6.9 (4.5, 11.7)	5.2 (3.4, 8.9)	195.5 (126.1, 339.5)	148.6 (95.8, 258.1)
East Asia	854.6 (721.0, 1002.0)	58.1 (49.0, 68.1)	778.4 (658.1, 907.3)	52.9 (44.7, 61.6)	17,614.1 (14,810.3, 20,721.5)	1196.4 (1006.0, 1407.5)
Eastern Europe	86.3 (76.6, 97.0)	41.1 (36.5, 46.2)	78.7 (69.6, 88.0)	37.5 (33.1, 41.9)	1980.2 (1746.4, 2218.1)	943.1 (831.7, 1056.4)
Eastern Sub-Saharan Africa	10.9 (9.2, 13.3)	2.7 (2.2, 3.2)	11.5 (9.6, 13.9)	2.8 (2.3, 3.4)	298.3 (248.0, 365.7)	72.5 (60.2, 88.8)
High-income Asia Pacific	150.9 (126.7, 173.1)	80.6 (67.6, 92.4)	111.0 (96.1, 119.3)	59.3 (51.3, 63.7)	1830.1 (1655.0, 1933.6)	977.2 (883.6, 1032.4)
High-income North America	285.2 (250.1, 325.2)	78.2 (68.6, 89.2)	230.3 (216.0, 239.4)	63.2 (59.3, 65.7)	4667.0 (4458.3, 4821.3)	1280.2 (1222.9, 1322.5)
North Africa and Middle East	71.7 (63.4, 81.1)	11.8 (10.4, 13.3)	72.5 (64.1, 81.9)	11.9 (10.5, 13.5)	1870.0 (1648.8, 2118.4)	307.2 (270.9, 348.0)
Oceania	1.5 (1.1, 2.1)	11.2 (8.4, 15.8)	1.5 (1.1, 2.1)	11.2 (8.5, 15.9)	41.9 (31.3, 59.7)	315.8 (235.6, 449.6)
South Asia	117.2 (100.1, 133.9)	6.5 (5.5, 7.4)	119.6 (101.2, 137.4)	6.6 (5.6, 7.6)	3089.9 (2617.4, 3550.9)	171.2 (145.0, 196.7)
Southeast Asia	132.5 (111.0, 153.6)	19.7 (16.5, 22.8)	134.6 (112.8, 155.9)	20.0 (16.7, 23.1)	3429.7 (2859.9, 3965.3)	509.0 (424.5, 588.5)
Southern Latin America	19.7 (15.7, 24.5)	29.5 (23.4, 36.7)	19.6 (18.5, 20.6)	29.4 (27.7, 30.9)	442.1 (418.3, 465.3)	662.2 (626.7, 697.1)
Southern Sub-Saharan Africa	10.3 (9.3, 11.5)	13.1 (11.9, 14.6)	10.5 (9.5, 11.6)	13.3 (12.1, 14.8)	271.2 (244.5, 304.1)	345.1 (311.1, 387.0)
Tropical Latin America	37.3 (35.0, 39.1)	16.7 (15.7, 17.5)	37.9 (35.4, 39.8)	16.9 (15.9, 17.8)	887.6 (843.8, 929.4)	397.0 (377.4, 415.7)
Western Europe	300.7 (263.2, 341.1)	68.9 (60.3, 78.2)	260.8 (244.0, 270.4)	59.8 (55.9, 62.0)	5272.9 (5026.0, 5452.4)	1208.5 (1151.9, 1249.7)
Western Sub-Saharan Africa	16.2 (13.6, 18.9)	3.5 (3.0, 4.1)	16.9 (14.2, 19.9)	3.7 (3.1, 4.4)	426.7 (354.2, 511.7)	93.5 (77.6, 112.1)
Income-classified regions						
High income	828.4 (746.9, 903.0)	69.1 (62.3, 75.3)	688.9 (638.3, 717.9)	57.5 (53.2, 59.9)	13,691.3 (13,012.1, 14,167.1)	1142.0 (1085.3, 1181.7)
Upper middle income	1108.8 (966.4, 1256.6)	41.9 (36.5, 47.5)	1028.7 (903.5, 1161.6)	38.9 (34.1, 43.9)	23,670.7 (20,785.2, 26,849.4)	894.2 (785.2, 1014.3)
Lower middle income	288.5 (252.8, 319.3)	9.1 (8.0, 10.0)	289.9 (253.5, 321.3)	9.1 (8.0, 10.1)	7571.6 (6626.3, 8388.7)	238.1 (208.4, 263.8)
Low income	33.4 (26.6, 41.5)	4.7 (3.8, 5.9)	34.3 (27.5, 42.4)	4.9 (3.9, 6.0)	902.3 (713.9, 1142.3)	127.6 (101.0, 161.6)

DALY: Disability-adjusted life years; GBD: Global Burden of Disease; TBL: Tracheal, bronchus, and lung cancer; UI: Uncertainty interval.

Table 2
ASIR, ASMR, and ASDR (per 100,000) of TBL cancer in 1990 and 2019, and relative changes globally from 1990 to 2019 based on GBD 2019 study.

Regions	1990			2019			EAPC (%), 1990–2019		
	ASIR (95% UI)	ASMR (95% UI)	ASDR (95% UI)	ASIR (95% UI)	ASMR (95% UI)	ASDR (95% UI)	ASIR (95% CI)	ASMR (95% CI)	ASDR (95% CI)
China	30.2 (26.2, 34.3)	31.2 (27.1, 35.5)	760.7 (654.3, 875.4)	41.7 (35.2, 48.8)	38.7 (32.8, 45.0)	831.3 (699.1, 980.0)	1.3 (1.2, 1.5)	0.9 (0.7, 1.1)	0.4 (0.2, 0.6)
Global									
Both	28.4 (27.2, 29.7)	27.3 (26.0, 28.6)	658.0 (628.3, 690.8)	27.7 (25.3, 30.0)	25.2 (23.2, 27.0)	551.6 (509.0, 593.1)	−0.1 (−0.2, −0.1)	−0.3 (−0.4, −0.3)	−0.7 (−0.7, −0.6)
Male	46.2 (44.0, 48.8)	45.1 (42.8, 47.6)	1053.3 (997.1, 1117.7)	40.4 (36.6, 44.4)	37.4 (34.1, 40.7)	802.9 (727.6, 879.8)	−0.5 (−0.5, −0.4)	−0.7 (−0.7, −0.6)	−1.0 (−1.0, −0.9)
Female	13.8 (13.0, 14.5)	13.0 (12.2, 13.8)	311.8 (293.5, 331.7)	16.8 (15.0, 18.6)	15.0 (13.5, 16.4)	327.6 (298.5, 360.5)	0.6 (0.5, 0.7)	0.4 (0.3, 0.5)	0.1 (0, 0.2)
GBD Regions									
Andean Latin America	12.9 (11.3, 14.6)	13.8 (12.0, 15.6)	323.4 (280.4, 366.7)	10.8 (8.7, 13.2)	11.4 (9.2, 13.9)	245.1 (195.4, 303.0)	−0.6 (−0.8, −0.4)	−0.7 (−0.9, −0.4)	−1.0 (−1.2, −0.8)
Australasia	38.0 (36.7, 39.0)	33.5 (32.3, 34.3)	776.2 (755.5, 794.8)	30.7 (25.0, 37.5)	23.8 (22.1, 25.1)	500.9 (473.0, 526.3)	−0.7 (−0.8, −0.6)	−1.2 (−1.3, −1.1)	−1.6 (−1.7, −1.5)
Caribbean	21.9 (20.8, 23.2)	22.6 (21.3, 23.9)	519.3(492.8, 551.3)	22.2 (19.0, 26.0)	21.7 (18.6, 25.3)	489.1 (415.7, 575.1)	0.2 (0.1, 0.3)	0 (−0.1, 0.1)	−0.1 (−0.2, 0)
Central Asia	29.5 (28.6, 30.3)	29.1 (28.2, 29.9)	819.3 (795.4, 843.5)	18.9 (17.1, 20.8)	19.0 (17.3, 20.9)	473.7 (428.6, 523.6)	−1.5 (−1.7, −1.3)	−1.4 (−1.6, −1.2)	−2.0 (−2.2, −1.8)
Central Europe	39.6 (38.8, 40.2)	38.8 (38.0, 39.4)	1049.8 (1031.3, 1065.9)	40.0 (35.2, 45.2)	38.3 (33.6, 43.5)	946.0 (823.7, 1081.4)	0.1 (0, 0.2)	0 (−0.1, 0.1)	−0.4 (−0.5, −0.3)
Central Latin America	14.4 (13.8, 14.7)	15.1 (14.5, 15.5)	345.3 (335.5, 352.5)	11.7 (10.0, 13.6)	11.8 (10.1, 13.8)	259.9 (220.3, 307.2)	−1.0 (−1.1, −0.9)	−1.1 (−1.2, −1.0)	−1.2 (−1.3, −1.2)
Central Sub-Saharan Africa	14.6 (9.0, 27.8)	15.5 (9.9, 29.3)	381.2 (229.0, 735.2)	12.7 (8.4, 21.2)	13.5 (8.9, 22.3)	328.9 (212.8, 560.8)	−0.6 (−0.8, −0.4)	−0.6 (−0.8, −0.5)	−0.7 (−0.8, −0.5)
East Asia	30.0 (26.2, 34.0)	31.0 (27.1, 35.2)	756.8 (653.5, 869.6)	41.3 (35.0, 48.1)	38.4 (32.7, 44.6)	825.8 (696.9, 969.5)	1.3 (1.1, 1.5)	0.9 (0.7, 1.1)	0.4 (0.2, 0.6)
Eastern Europe	35.9 (34.9, 36.6)	34.1 (33.2, 34.7)	945.3 (915.1, 964.5)	25.0 (22.2, 28.1)	22.7 (20.1, 25.3)	588.5 (518.6, 658.3)	−1.7 (−2.0, −1.5)	−1.9 (−2.2, −1.7)	−2.2 (−2.5, −2.0)
Eastern Sub-Saharan Africa	6.8 (5.7, 8.2)	7.4 (6.1, 8.8)	172.0 (142.6, 209.1)	7.0 (6.0, 8.5)	7.6 (6.5, 9.2)	173.3 (145.5, 211.0)	0 (0, 0.1)	0.1 (0, 0.1)	0 (−0.1, 0)
High-income Asia Pacific	30.6 (29.3, 31.4)	25.6 (24.3, 26.2)	545.4 (528.6, 555.2)	31.6 (27.0, 36.3)	22.2 (19.7, 23.6)	427.4 (395.7, 448.3)	0.1 (0, 0.3)	−0.6 (−0.8, −0.5)	−1.0 (−1.1, −0.9)
High-income North America	58.2 (56.6, 59.3)	49.1 (47.5, 50.0)	1188.7 (1164.0, 1207.1)	45.0 (39.5, 51.4)	35.9 (33.8, 37.3)	762.0 (729.6, 787.1)	−1.2 (−1.3, −1.0)	−1.3 (−1.4, −1.2)	−1.8 (−1.9, −1.7)
North Africa and Middle East	16.7 (14.1, 20.0)	17.5 (14.9, 21.0)	433.2 (363.4, 518.3)	16.8 (14.9, 19.0)	17.6 (15.6, 19.8)	406.7 (359.1, 459.5)	0.4 (0, 0.7)	0.3 (0, 0.7)	0.1 (−0.3, 0.4)
Oceania	19.4 (15.1, 27.6)	20.6 (16.0, 29.1)	490.5 (379.0, 700.8)	21.6 (16.6, 30.4)	22.9 (17.8, 32.0)	539.6 (407.6, 764.0)	0.4 (0.3, 0.4)	0.4 (0.3, 0.4)	0.3 (0.3, 0.4)
South Asia	7.6 (6.4, 8.7)	8.1 (6.9, 9.3)	191.6 (163.9, 221.6)	8.4 (7.1, 9.5)	8.8 (7.4, 10.1)	208.5 (176.7, 239.6)	0.2 (0.1, 0.3)	0.1 (0, 0.2)	0.2 (0.1, 0.3)
Southeast Asia	20.5 (18.6, 22.6)	21.6 (19.6, 23.7)	531.2 (482.7, 584.5)	22.0 (18.4, 25.4)	23.0 (19.3, 26.6)	532.9 (445.9, 615.8)	0 (0, 0.1)	0 (0, 0.1)	−0.2 (−0.3, −0.1)
Southern Latin America	29.2 (28.4, 30.0)	29.7 (28.8, 30.5)	753.5 (734.3, 773.3)	23.6 (18.8, 29.5)	23.5 (22.0, 24.6)	540.9 (512.1, 569.0)	−0.8 (−0.9, −0.8)	−0.9 (−0.9, −0.8)	−1.3 (−1.3, −1.2)
Southern Sub-Saharan Africa	19.9 (16.9, 25.5)	20.6 (17.4, 26.4)	523.1 (443.1, 662.3)	18.4 (16.7, 20.3)	19.2 (17.5, 21.2)	455.7 (411.9, 509.5)	−0.5 (−0.7, −0.2)	−0.4 (−0.7, −0.1)	−0.7 (−1.0, −0.4)
Tropical Latin America	17.1 (16.5, 17.6)	17.9 (17.2, 18.4)	431.6 (419.1, 442.9)	15.4 (14.5, 16.2)	15.8 (14.7, 16.6)	359.3 (341.0, 376.3)	−0.4 (−0.5, −0.3)	−0.4 (−0.5, −0.3)	−0.7 (−0.8, −0.6)
Western Europe	37.8 (37.0, 38.4)	35.2 (34.3, 35.7)	851.1 (836.4, 862.1)	34.5 (30.1, 39.4)	29.0 (27.4, 30.0)	654.0 (628.1, 675.5)	−0.3 (−0.3, −0.2)	−0.6 (−0.7, −0.6)	−0.9 (−0.9, −0.8)
Western Sub-Saharan Africa	7.7 (6.5, 9.2)	8.4 (7.0, 10.0)	191.6 (159.0, 229.9)	9.2 (7.7, 10.6)	10.0 (8.5, 11.6)	218.0 (183.1, 257.7)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.6 (0.6, 0.7)
Income-classified Regions									
High income countries	41.9 (40.8, 42.5)	37.4 (36.3, 37.9)	896.2 (880.1, 906.2)	36.6 (33.1, 39.9)	29.8 (28.0, 31.0)	646.7 (619.4, 667.6)	−0.5 (−0.6, −0.4)	−0.9 (−0.9, −0.8)	−1.2 (−1.3, −1.2)
Upper middle income countries	28.1 (25.8, 30.6)	28.6 (26.2, 31.1)	720.7 (657.6, 787.8)	32.8 (28.7, 37.1)	30.9 (27.2, 34.7)	684.1 (601.3, 775.0)	0.6 (0.5, 0.7)	0.3 (0.2, 0.4)	−0.2 (−0.3, −0.1)
Lower middle income countries	13.1 (12.2, 14.1)	13.4 (12.4, 14.5)	330.9 (307.3, 355.9)	12.2 (10.7, 13.5)	12.6 (11.0, 14.0)	301.5 (263.7, 334.1)	−0.4 (−0.5, −0.3)	−0.4 (−0.5, −0.3)	−0.5 (−0.6, −0.4)
Low income countries	10.9 (8.8, 13.8)	11.6 (9.4, 14.6)	280.6 (224.3, 358.8)	11.0 (8.8, 13.4)	11.6 (9.4, 14.1)	271.3 (216.5, 338.4)	0 (0, 0.1)	0 (0, 0.1)	−0.1 (−0.2, −0.1)

ASDR: Age-standardized DALY rate; ASIR: Age-standardized incidence rate; ASMR: Age-standardized mortality rate; CI: Confidence interval; DALY: Disability-adjusted life years; EAPC: Estimated annual percentage changes; GBD: Global Burden of Disease; TBL: Tracheal, bronchus, and lung cancer; UI: Uncertainty interval.

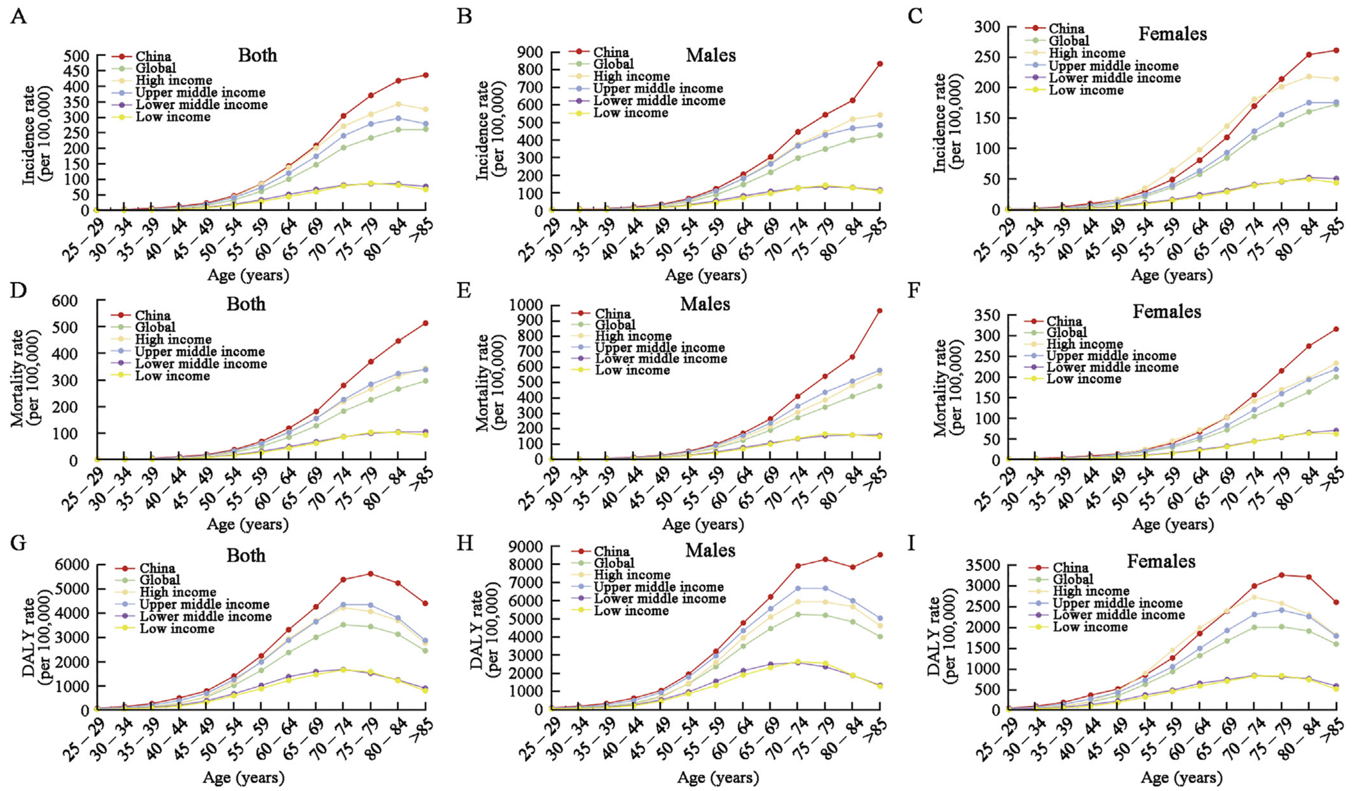

Fig. 1. Age-specific rates of incidence, mortality, and DALY for TBL cancer by sex globally in 2019. A–C: Age-specific incidence rates in the whole population (A), males (B), and females (C). D–F: Age-specific mortality rates in the whole population (D), males (E), and females (F). G–I: Age-specific DALY rates in the whole population (G), males (H), and females (I). DALY: Disability-adjusted life years; TBL: Tracheal, bronchus, and lung cancer.

years for DALY) than in HICs, LMCs, and LICs (Fig. 1A and G). Behavioral, environmental, and metabolic risk clusters accounted for 67.6%, 36.4%, and 6.5% of TBL cancer DALY in China in 2019, respectively, with the proportions being higher in males than in females (Fig. 2B–D). The highest attributable risk factor of lung cancer DALY in China was smoking (62.7%), followed by particulate matter pollution (27.5%), and occupational carcinogens (8.8%). China experienced higher proportions of TBL cancer DALY attributable to smoking, particulate matter pollution, and secondhand smoke than most GBD regions and the globe, whereas occupational carcinogens accounted for relatively lower proportions of TBL cancer DALY compared with other regions globally (Table 3, Supplementary Fig. 2).

Temporal trends from 1990 to 2019

Age-standardized rates of TBL cancer vary considerably across 204 countries and territories. The ASIR, ASMR, and ASDR of TBL cancer were deemed to decrease in 85, 91, and 104 countries and territories, with the largest decrease in Bahrain (EAPC: −3.0 [95% CI: −3.3, −2.7] for ASIR, −3.0 [95% CI: −3.3, −2.6] for ASMR, and −3.4 [95% CI: −3.8, −3.1] for ASDR) from 1990 to 2019 (Supplementary Table 8). Between 1990 and 2019, the ASIR, ASMR, and ASDR of TBL cancer in China increased by a mean of 1.3% (95% CI: 1.2%, 1.5%), 0.9% (95% CI: 0.7%, 1.1%), and 0.4% (95% CI: 0.2%, 0.6%) per year, respectively (Table 2).

Association between age-standardized rates and UHC

Potential positive associations were observed between ASIR (r=0.524, $P < 0.001$), ASMR (r=0.411, $P < 0.001$), and ASDR (r=0.353, $P < 0.001$) of TBL cancer and UHC index at the national level in 2019 (Fig. 3 A–C).

Discussion

Based on the most up-to-date and high-quality data from the GBD 2019 study, we conducted a comprehensive assessment of the global landscape, temporal trends, and regional and national discrepancies in the incidence, mortality, and DALY of TBL cancer. We also explored the association between TBL cancer burden and effective health service coverage at the national level. Our study showed that the global ASIR, ASMR, and ASDR for TBL cancer decreased between 1990 and 2019. Eastern Europe experienced the largest mean decrease per year in ASIR, ASMR, and ASDR of TBL cancer over the study period and Central Europe had the greatest behavioral risk-attributable DALY. Among four income regions, UMCs had the highest cases of incidence, death, and DALY for TBL cancer in 2019 and showed the largest increases in ASIR and ASMR from 1990 to 2019. Notably, we also observed a potentially positive association between the UHC index and the TBL cancer burden at the national level.

The TBL cancer burden varies considerably across regions and countries; geographic disparities indicate health inequity in access to early prevention and control of TBL cancer. To avoid the impact of age structures on TBL cancer burden variation, we applied age-standardized rates to explore and compare temporal trends over time and across areas. Notably, we found opposite trends in ASIR and ASMR of TBL cancer among UMCs compared with HICs and LMCs, which could be attributed to the discrepancies in epidemiological and demographic transitions, the application of screening and diagnostic techniques, and the availability of health resources among different income-classified regions. Income status is generally associated with the accessibility of health services: deprived patients with TBL cancer have less access to healthcare resources, which may lead to advanced-stage diagnoses and hamper timely therapeutic procedures.[14] Our correlation analysis, which showed a positive association between TBL cancer burden and the UHC index at

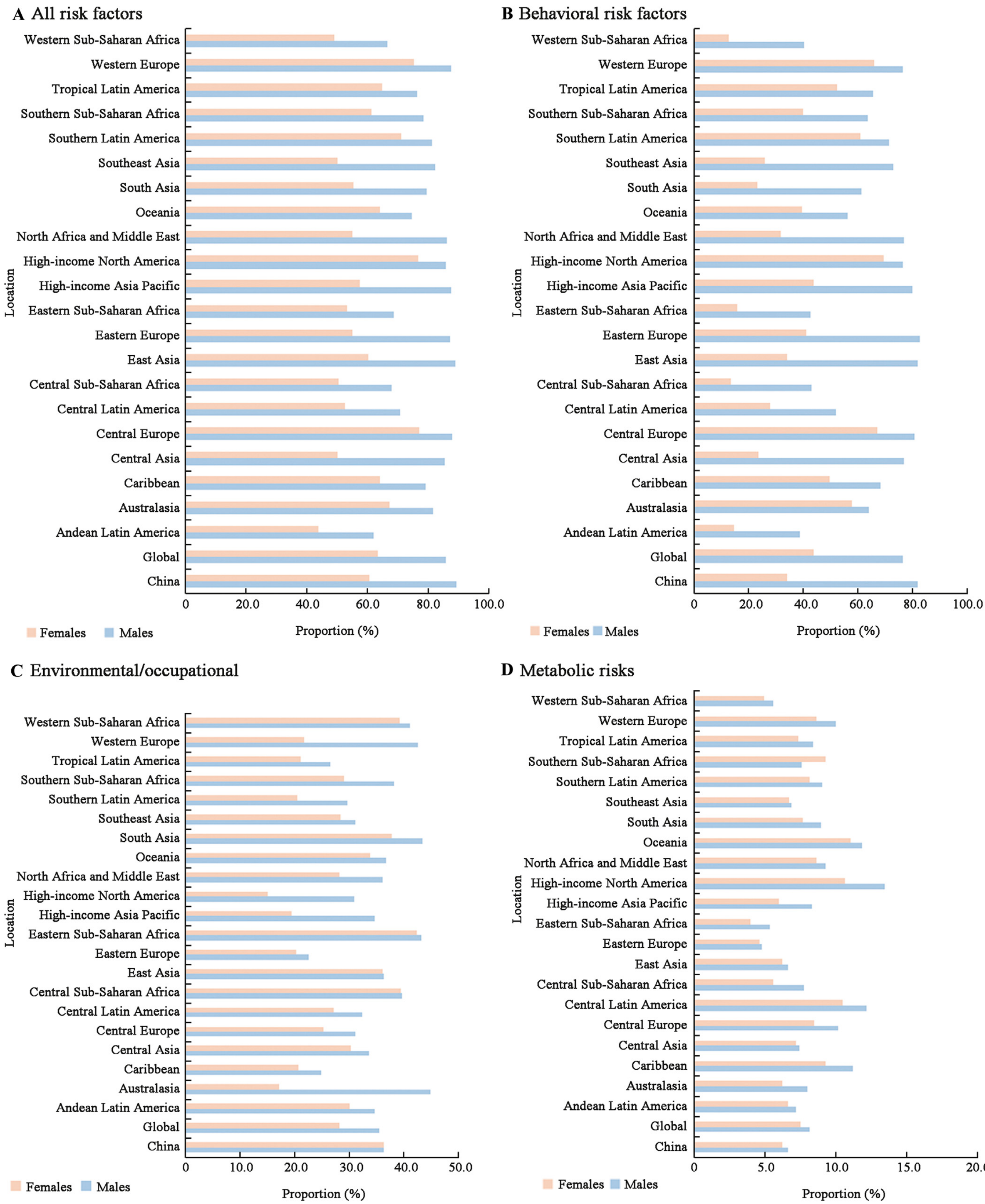

Fig. 2. Proportion of TBL cancer DALY attributable to combination of all risk factors (A), behavioral (B), environmental/occupational (C), and metabolic (D) risk factors by sex in 2019. DALY: Disability-adjusted life years; TBL: Tracheal, bronchus, and lung cancer.

Table 3
Proportion of TBL cancer DALY attributable to risk factors globally in 2019 (%).

Location	Smoking	Particulate matter pollution	Secondhand smoke	Occupational carcinogens	Diet low in fruits	Residential radon
Western Sub-Saharan Africa	27.0	33.7	2.9	6.3	4.6	4.6
Central Sub-Saharan Africa	31.0	31.3	1.8	8.8	5.0	3.8
East Asia	62.5	27.4	7.8	8.8	3.6	3.8
Eastern Europe	72.6	8.7	4.6	8.9	4.6	6.5
Oceania	47.8	27.6	5.3	9.1	4.8	3.2
Caribbean	59.2	13.9	4.2	9.4	2.6	1.9
Southeast Asia	53.9	20.9	5.2	10.1	4.2	2.0
Eastern Sub-Saharan Africa	30.0	34.0	2.0	10.3	4.7	3.9
South Asia	44.8	31.6	4.7	11.1	6.3	4.4
Central Asia	61.6	18.6	5.8	11.2	4.0	7.3
Central Europe	74.6	15.6	5.9	11.7	4.0	5.4
Central Latin America	38.6	16.7	2.8	11.8	3.2	5.2
Andean Latin America	24.1	19.8	1.7	12.4	3.2	4.1
Tropical Latin America	57.0	9.9	5.0	12.4	2.4	4.1
Global	62.4	19.5	5.8	13.0	3.8	4.1
North Africa and Middle East	64.0	21.6	6.7	13.0	1.8	3.7
Southern Sub-Saharan Africa	51.9	19.9	3.7	15.4	5.8	4.5
Southern Latin America	65.3	10.7	5.4	15.6	2.5	2.8
High-income North America	71.5	4.0	3.7	17.3	3.7	4.2
High-income Asia Pacific	67.1	11.7	3.8	18.9	4.2	2.5
Western Europe	70.9	7.8	4.2	26.0	3.4	5.7
Australasia	58.5	3.0	3.3	30.2	4.1	1.4
China	62.7	27.5	7.9	8.8	3.6	3.8

TBL: Tracheal, bronchus, and lung cancer; DALY: Disability-adjusted life years.

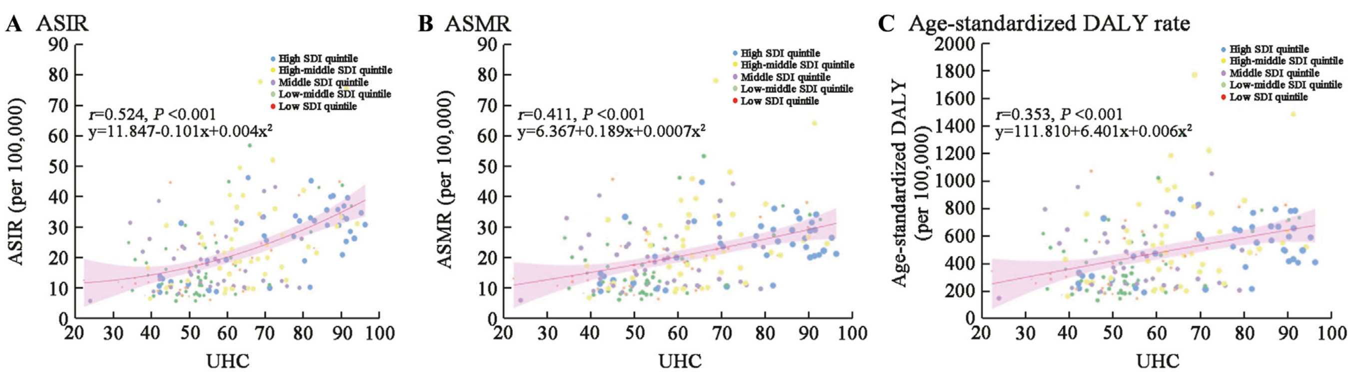

Fig. 3. Association between age-standardized rates of incidence (A), mortality (B), and DALY (C) for TBL cancer and universal health coverage index in 204 countries and territories in 2019. The SDI from 204 countries and territories globally is represented by circles, with a larger circle indicating a higher index. Circles with different colors represent the SDI quintiles (high, high-middle, middle, low-middle, and low). The *r* statistics and *P* values were calculated based on Pearson correlation analysis. The curve was then fitted using a polynomial model. ASIR: Age-standardized incidence rate; ASMR: Age-standardized mortality rate; DALY: Disability-adjusted life years; SDI: Socio-demographic index; TBL: Tracheal, bronchus, and lung cancer; UHC: Universal health coverage.

the national level, also confirmed this point. Additionally, deprivation is considered a contributor to the low adherence rate of lung cancer screening.[15] Hence, mitigating the income and education inequality, and strengthening the health resource support could provide a useful pathway for addressing the health inequality of cancer survival across countries.

The prevalence of behavioral, environmental, and metabolic risk factors associated with rapid economic development also contributed greatly to the high burden of global TBL cancer. According to the GBD 2019 estimates, the proportion of TBL cancer DALY in relation to modifiable risk factors was over 70% in most of the 21 GBD regions, of which the behavioral risk cluster accounted for the largest proportion. Tobacco use is the predominant specific risk factor for TBL cancer, with an estimated 65% of TBL cancer DALYs and 23.9% of total cancer DALYs attributable to smoking globally in 2019.[16] Our findings showed that smoking topped the list in TBL burden in all GBD regions, which indicated that there remain opportunities to reduce the TBL burden by enforcing tobacco control measures globally. The latest report on the global tobacco epidemic released in 2021 suggested that only two countries, Brazil and Turkey, adopted all WHO-recommended MPOWER (monitor, protect, offer, warn, enforce, raise) measures at the best practice level, whereas 49 countries had not yet adopted any MPOWER measure.[17,18] To achieve the Sustainable Development Goals' target to reduce premature mortality due to cancer and other non-communicable diseases by one-third by 2030, accelerating the pace of tobacco control is a crucial step for most countries.[19] Our analysis showed that the contribution of environmental exposure to TBL cancer was second only to behavioral risk factors, which is consistent with a previous report.[20] Environmental health risks are a great challenge worldwide, especially in regions of Asia and Africa, such as eastern Sub-Saharan Africa, South Asia, and western Sub-Saharan Africa. Hence, the development of effective risk exposure control is urgently needed for locations where the TBL cancer burden attributable to specific risk factors is high or on the rise.

Moreover, because TBL cancer is an age-related disease,[21] the rapid aging and population growth are key drivers of the rising TBL cancer burden in most countries. Age subgroup analyses also supported this, with the risk of morbidity and mortality for TBL cancer generally increasing with age, particularly in older age groups. Using a prediction model based on incident cases and population projections, Sang et al[22] estimated that lung cancer is predicted to account for 23.4% of all cancer cases in the two largest populated cities of Vietnam in 2025. In China, increases in TBL cancer deaths associated with adult population growth and aging between 1990 and 2019 were 96.4% and 72.2% of the absolute levels in 1990.[23] The *World Report on Ageing and Health,* released by World Health Organization in 2021, suggested that the proportion of the global population aged over 60 years is projected to be nearly double from 12% in 2015 to 22% in 2020.[24] Collaborative action to foster not just longer but healthier lives plays an important role in mitigating the TBL cancer burden.

Our study showed that over one-third of newly diagnosed TBL cancer cases and deaths worldwide occurred in China in 2019, and the TBL cancer burden has notably increased in the past 30 years. These findings support the critical role of reducing exposure to modifiable risk factors in the prevention and control of TBL cancer. Of note, China is going through a cancer spectrum transition, characterized by the increasing incidence of lung, breast, prostate, and colorectal cancers that commonly occur in developed countries.[25,26] Hence, early prevention and detection are urgently required to manage the TBL cancer burden in China. Low-dose computed tomography (LDCT) screening has been substantiated to be associated with a beneficial stage shift and reduced mortality of lung cancer.[27] The health authority of China implemented the population-based National Lung Cancer Screening program in urban areas in 2012, and the benefits of LDCT in reducing lung cancer mortality and all-cause cancer mortality have been observed among the Chinese population,[28] but there are potential risks of relatively low compliance rates and limited population coverage.[28-30] The early LDCT screening awareness, improved access to health care, and advanced therapy, such as mutation-targeted treatment for TBL cancer patients, should be additional steps to address the TBL cancer burden. In response to mitigating the preventable cancer burden proposed by the *Health China 2030 Plan*,[29] concerted efforts should be made to create an improved health system including TBL cancer risk reduction programs, advanced screening techniques, and subsequent treatment and management strategies in China.

From an epidemiological perspective, we conducted a comprehensive assessment of global, regional, and national patterns of TBL cancer burden from 1990 to 2019 based on the most updated GBD study. Our estimates were regionally and nationally comparable and the results were acceptable. The present study fills a gap in which actual data on TBL cancer burden were unavailable or scarce, which could inform policymakers of useful references to formulate prevention strategies and tailor interventions to mitigate the TBL cancer burden.

This study had several limitations. First, since clinical data were unavailable in the GBD study, we failed to provide an in-depth analysis of the vital characteristics and clinical variables of patients with TBL cancer. Second, we applied the EAPC of ASIR, ASMR, and ASDR to quantify the temporal trends of TBL cancer burden over the past 30 years, which may mask the variation over the short-term segment intervals. Third, due to inconsistencies in country coverage, data sources, and modelling methodologies between the GBD 2019 study and the Global Cancer Incidence, Mortality, and Prevalence (GLOBOCAN) 2020 study, data on the incidence and mortality of TBL cancer from the former were somewhat higher than those of GLOBOCAN 2020.[31] Thus, comparisons of estimates derived from different data sources should be interpreted with caution. Fourth, ecological bias could not be avoided in the interpretation of the association between the UHC index and TBL cancer burden at the national level. Furthermore, we could not measure the contribution of histological subtypes to the lung cancer burden based on the available data.

In summary, the TBL cancer burden shows a downward trend at the global level but varies greatly across regions and countries. A decreasing trend in the TBL cancer burden was observed in most of the 21 GBD regions from 1990 to 2019. UMCs had the highest burden of TBL cancer and showed the largest increases in ASIR and ASMR. The heterogeneity in the temporal trend and spatial distribution of TBL cancer burden over time and across areas underscores the need for taking targeted prevention and screening strategies for TBL cancer in different countries.

Funding

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pccm.2023.02.001.

Conflicts of interest

None.

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