Global, regional, and national burden of tracheal, bronchus, and lung cancer and its risk factors from 1990 to 2021: findings from the global burden of disease study 2021

Ziyu Kuang,[a,b] Jiaxi Wang,[a] Kexin Liu,[a,b] Jingyuan Wu,[a,b] Yuansha Ge,[a,b] Guanghui Zhu,[a] Luchang Cao,[a] Xinyi Ma,[a] and Jie Li[a,*]

[a]Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, 10053, China
[b]Graduate School, Beijing University of Chinese Medicine, Beijing, 10029, China

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Summary

Background Studies from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2021 can guide screening and prevention strategies for tracheal, bronchus, and lung (TBL) cancer. We aim to provide global, regional, and national estimates of the TBL cancer burden and its attributable risk from 1990 to 2021, including during the coronavirus disease 2019 (COVID-19) pandemic.

Methods Incidence, age-standardised incidence rate (ASIR), deaths, age-standardised mortality rate (ASMR), disability-adjusted life years (DALYs), age-standardised rate of DALYs (ASDR), and the burden due to risk factors associated with TBL cancer were analysed from 1990 to 2021. Trends in ASIR, ASMR, and ASDR of TBL cancer during the COVID-19 pandemic (2019–2021) were also determined. All statistical analyses were performed using Join-point software (version 4.9.1.0).

Findings Between 1990 and 2021, the global incidence, deaths, and DALYs of TBL cancer to varying degrees. However, the ASIR (Average Annual Percent Change [AAPC], −0.3 [−0.4 to −0.2]), ASMR (AAPC, −0.5 [−0.7 to −0.4]), and ASDR (AAPC, −0.9 [−1.0 to −0.7]) all showed a decreasing trend. However, the ASIR, ASMR, and ASDR of TBL cancer in males all showed a decreasing trend from 1990 to 2021. In contrast, the ASIR and ASMR of TBL cancer in females showed an increasing trend, while the ASDR showed a relatively stable trend. During the COVID-19 pandemic, the trends for ASIR, ASMR, and ASDR remained stable across both sexes combined, females, males, five socio-demographic index (SDI) quintiles, and the 21 GBD regions. In 2021, smoking was a major risk factor for TBL cancer DALYs, but the attributable ASDR for smoking decreased from 1990 to 2021 in both sexes combined, as well as individually for males and females. Conversely, the attributable ASDR for secondhand smoke, high fasting plasma glucose and occupational exposure factors increased primarily among females. Furthermore, the attributable ASDR for ambient particulate matter pollution, household air pollution from solid fuels, and low–fruit diets increased primarily in regions with lower SDI quintiles from 1990 to 2021.

Interpretation The burden attributable to TBL cancer has increased in some populations from 1990 to 2021, highlighting the importance of implementing targeted measures to mitigate this trend. No significant change in the burden of TBL cancer was observed during the COVID-19 pandemic; however, post-COVID-19 rates still require further observation.

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Keywords: Tracheal, bronchus, and lung cancer; Risk factors; Incidence; Mortality; Disability–adjusted life years

*Corresponding author. Guang'anmen Hospital of China Academy of Chinese Medical Sciences, 5 Beixiange Street, Xicheng District, Beijing, 100053, China.
E-mail address: qfm2020jieli@yeah.net (J. Li).

Research in context

Evidence before this study

We conducted a systematic search of the PubMed and EMBASE databases from inception to June 10, 2024, using the keywords "Lung cancer", "Tracheal cancer", "Bronchus cancer", "Incidence", "Mortality", and "Trend analysis". According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, a report by the GBD 2019 Respiratory Tract Cancers Collaborators indicated that despite the decline in age-standardised incidence and mortality rates, tracheal, bronchus, and lung (TBL) cancer remains the leading global cancer–related death. Given the significant impact of the COVID-19 pandemic on global public health, especially TBL cancer, which shares the same disease locus as the coronavirus disease 2019 (COVID-19), estimating epidemiologic trends in TBL cancers throughout the pandemic (2019–2021) is crucial.

Added value of this study

This study extends the estimation of the age-standardised incidence rate (ASIR), age-standardised mortality rate (ASMR), and age-standardised disability-adjusted life years (DALYs) rate (ASDR) of TBL cancer. It includes data from 1990 to 2021 and from 2019 to 2021 (COVID-19 pandemic), examining trends across different sexes and regions globally, as well as DALYs attributable risk factors. The results aim to assist policymakers in identifying populations disproportionately burdened by TBL cancer and developing targeted strategies to reduce its impact.

Implications of all the available evidence

Over the past three decades, the global incidence for TBL cancer have risen, with particularly concerning increases in ASIR, ASMR, and ASDR determined in females. Addressing modifiable risk factors and enhancing the clinical effectiveness and cost-effectiveness of screening are crucial strategies for mitigating the burden of TBL cancer. Although no significant changes in the burden of TBL cancer were observed during the COVID-19 pandemic, ongoing monitoring of trends in the post-COVID-19 period is necessary.

Introduction

Although the burden of tracheal, bronchus, and lung (TBL) cancer varies by region, it remains the leading cause of cancer-related morbidity and mortality globally. According to the International Agency for Research on Cancer, there were an estimated 2,480,675 cases of TBL cancer in 2022, constituting 12.4% of all cancers worldwide. Additionally, 1,817,469 new deaths from TBL cancer were recorded, accounting for 18.7% of global cancer-related deaths, ranking first among all cancers in both new cases and deaths.[1] Regarding economic impact, TBL cancer incurred a cost of $3.9 trillion in 2017, ranking the highest among all cancers. In most countries, including China and the United States, TBL cancer represents the largest cancer-related financial burden.[2]

Concerning risk factors associated with TBL cancer, smoking is the most significant.[3,4] Despite a substantial decrease in smoking-related TBL cancer cases over recent decades due to effective tobacco control strategies, reports indicate an increase in TBL cancer cases among never-smokers.[5] Non-smoking risk factors include airborne particulate pollution, indoor solid fuels, occupational exposures (e.g., asbestos), and residential radon exposure, etc. However, the prevalence and impact of these risk factors vary widely across regions and populations.[6,7] Understanding the latest trends and burdens associated with these risk factors is crucial for reducing the overall burden of TBL cancer.

The coronavirus disease 2019 (COVID-19) pandemic has had a catastrophic impact on global healthcare systems, profoundly affecting the screening and management of TBL cancer cases.[8] A cross-sectional study across 54 countries revealed that during the pandemic, 88.2% of cancer centres faced significant challenges in providing care. These difficulties were attributed to overwhelmed healthcare systems, lack of protective equipment, reduced healthcare staff, and less access to medications.[9] Also, the increased mortality among patients with thoracic malignancies infected with COVID-19 may undermine recent advancements in TBL cancer survival.

In this study, we analysed data from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2021 to identify changes in the burden of TBL cancer and associated risk factors across sex, regional, and national levels between 1990 and 2021, to guide accurate screening and prevention. Moreover, we examined the TBL cancer data burden separately from 2019 to 2021 to assess the impact of the COVID-19 pandemic on these trends.

Methods

Overview

This study adheres to the GATHER checklist (https://www.who.int/publications/m/item/gather-checklist), and registered in the GBD 2021 Paper Proposal Form (https://uwhealthmetrics.co1.qualtrics.com/). GBD 2021 evaluates health risks associated with 371 diseases, injuries, and 88 risk factors.[10] Our study utilised secondary data from this collaborative endeavour, and we had no direct contact with participants. No patients were involved in the formulation of the research questions or outcome measures, or in the design and implementation of the study. Consequently, it is not feasible to delineate the methodologies employed to calculate uncertainty in the estimates.

This analysis included patients, from 1990 to 2021, with TBL cancer and of all ages. However, since GBD 2021 does not include data on the TBL cancer burden for individuals under 15 years old, our focus was primarily on those aged 15 years and over. Incidence, mortality, and disability-adjusted life-years (DALYs) for TBL cancer, along with their 95% uncertainty intervals (UIs), were sourced from GBD 2021. The GBD 2021 companion paper details the data input, processing, synthesis, and final model used to predict disease burden (Figure S1).[10] The estimates used in this study are publicly available through the GBD results tool (http://ghdx.healthdata.org/gbd-results-tool).

Definition

All estimates for this study are stratified by sex, age, location, and nation, covering the period from 1990 to 2021. The GBD database includes 21 GBD regions and 204 countries or regions, classified by quintiles of the socio-demographic index (SDI) (The regional division of SDI can be obtained from Institute for Health Metrics and Evaluation: https://ghdx.healthdata.org/search/site/SDI). The SDI is a composite measure of per capita income, total fertility rate (age <25 years), and average educational attainment (age ≥15 years), reflecting a country's overall social and economic development.[10]

Incidence, mortality and DALYs estimates

The first step involved estimating mortality using data from sources such as vital registration systems, cancer registries, and oral autopsies. In places where mortality data was unavailable, mortality-to-incidence ratio models (MIRs) were used to derive mortality estimates from incidence data. The codes for TBL cancer were obtained from the International Classification of Diseases (ICD)-9 and ICD-10 coding books (Table S1). Furthermore, to confirm that single-cause mortality estimates matched those predicted individually, these estimates were compared to whole-cause mortality estimates using CoDCorrect (Figure S1).[10]

Survival rates were modelled using MIRs estimate for each site, year, sex, and age. The annual prevalence of the population that did not survive beyond 10 years was categorised into four sequelae corresponding to disease stages: the diagnostic and treatment-naive phase, the control phase, the metastatic phase, and the terminal phase. Conversely, the annual prevalence of the population that survived longer than 10 years was divided into stages I to II. The disability weights associated with each of these four phases were multiplied by the incidence of sequelae to calculate the number of years of disability survival (YLDs). To determine the number of years lost in life (YLLs) associated with each type of cancer, the number of deaths was multiplied by age and the DALYs were calculated by summing the YLDs and YLLs.[10]

For the analysis of the all-age population, we used the age-standardised rate (ASR) per 100,000 population, given by GBD 2021, including age-standardised incidence rate (ASIR), age-standardised mortality rate (ASMR), and age-standardised DALYs rate (ASDR). For specific age groups (e.g., 15–19 years, 20–24 years, 25–29 years, up to 95+ years), we used crude rates as GBD 2021 provides only these for such groups. All data are available online from the GBD results tool (http://ghdx.healthdata.org/gbd-results-tool).

Risk factors: population attributable fraction estimation

For risk factors in GBD 2021, exposure data were modelled using spatiotemporal Gaussian process regression or DisMod–MR 2.1.[9] Quantitative relative risk estimates were generated for each risk–outcome pair. These estimates were then paired with corresponding exposure estimates to calculate a population–attributable fraction (PAF) for each risk–outcome pair. The PAF multiplied by the outcome rate was used to determine the years of attributable disability survival, years of life lost, and disability-adjusted life years. The specific calculation process can be found in previous studies.

The article identifies 16 risk factors associated with TBL cancer in GBD 2021, including ambient particulate matter pollution, a diet low in fruits, high fasting plasma glucose, household air pollution from solid fuels, occupational exposures (arsenic, asbestos, beryllium, cadmium, chromium, diesel engine exhaust, nickel, polycyclic aromatic hydrocarbons, and silica), as well as residential radon, secondhand smoke, and smoking. These risk factors were automatically matched by GBD 2021 when selecting TBL cancer. Detailed information on the definition of these risk factors and their relative risk for TBL cancer can be found in previous studies.[11]

Statistics

Joinpoint regression is a statistical method used to analyse trend changes in time series data by identifying "joinpoints", splitting the time series into multiple phases, and calculating the annual percent change (APC) for each segment. In this study, we used the Joinpoint software (version 4.9.1.0, https://surveillance.cancer.gov/joinpoint/) developed by the National Cancer Institute Division of Cancer Control & Population Sciences. The Monte Carlo permutation test, the default model optimisation method of the Joinpoint software, was used to select the optimal number of joinpoints. For our analysis, we used the number of connection points recommended by the software for analysis.

The rate trend was assessed using a joinpoint regression model (selecting the log-linear model: $\ln y = xb$) that calculated the APC with its 95% confidence interval (CI) to depict the trend over the delineated time frame. The mean annual percent change (AAPC) was then calculated based on the trend of the APC. An upward trend is indicated if both the AAPC estimate and its 95% CI upper and lower bounds are greater than 0.

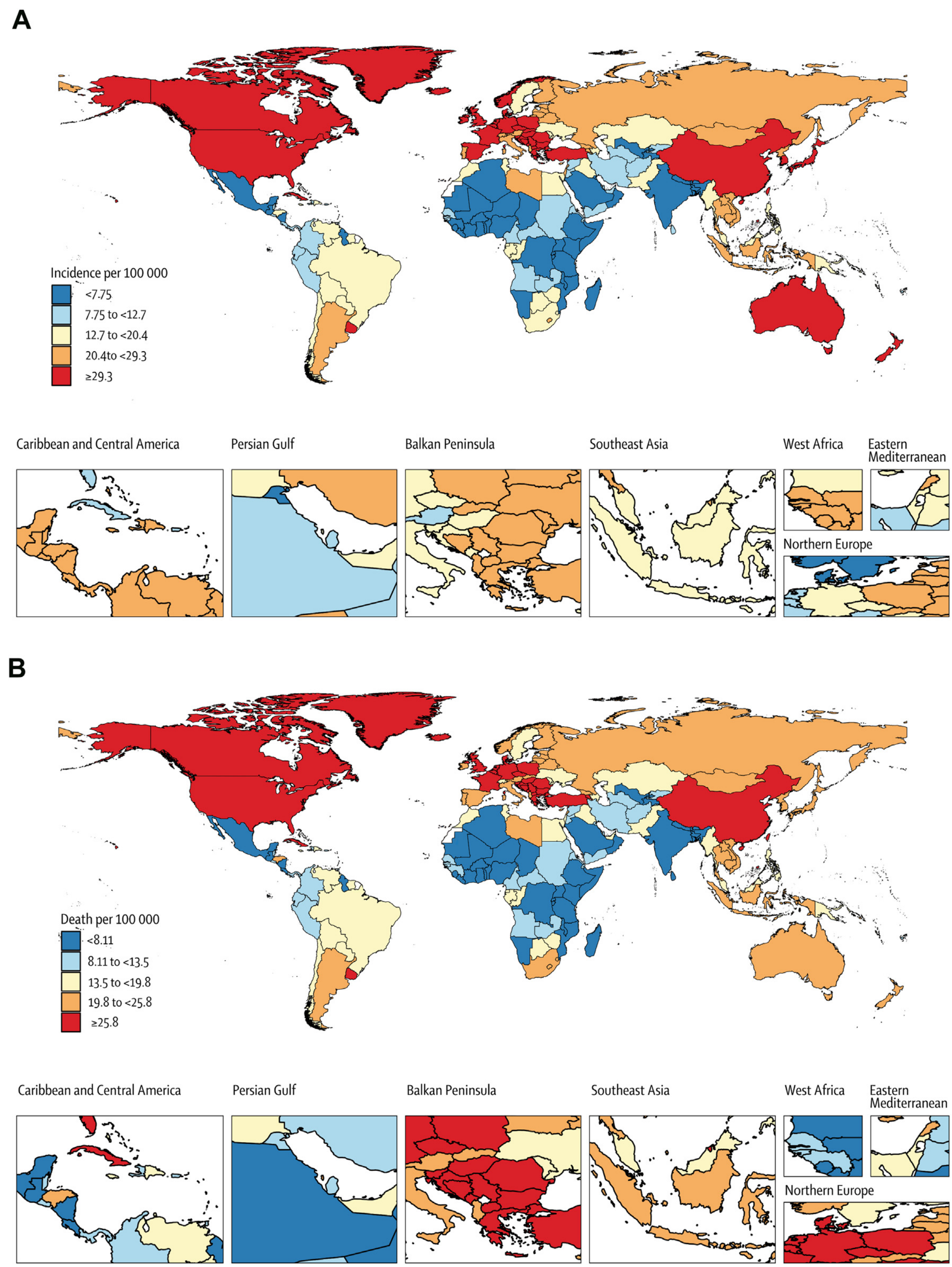

Fig. 1: Age-standardised incidence (A), mortality (B) and DALYs rate (C) of tracheal, bronchus, and lung cancer in both sexes combined in 204 countries around the world. DALYs, disability-adjusted life–years.

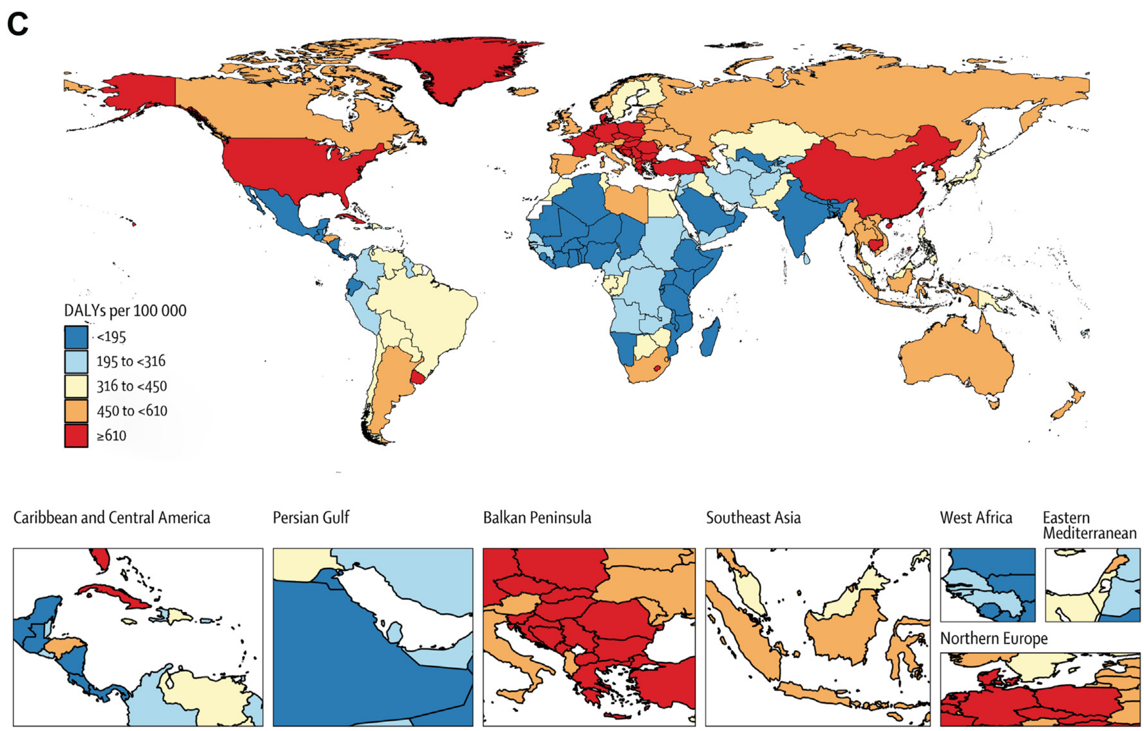

Fig. 1: (*continued*)

Conversely, a downward trend occurs if both the AAPC estimate and its upper and lower limits of 95% CI are less than 0. In this study, the R software package (version 4.2.3) and JD_GBDR (V2.22, Jingding Medical Technology Co., Ltd.) was used for the drawing of the figures.

Ethics

The institutional review board granted an exemption for this study, as it utilized publicly accessible data that contained no confidential or personally identifiable patient information.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Burden of tracheal, bronchus, and lung cancer in 2021

In 2021, the total incidence of TBL cancer was 2.3 million (95% UI, 2.1–2.5), with 1.5 million (1.3–1.7) cases in males and 0.8 million (0.7–0.9) in females. Total deaths were 2.0 million (1.8–2.2), with 1.3 million (1.2–1.5) in males and 0.7 million (0.6–0.8) in females. TBL cancer contributed 46.5 million (41.9–51.2) DALYs in 2021, with 31.4 million (27.5–35.6) DALYs in males and 15.1 million (13.6–16.7) in females (Table S2).

In 2021, the ASIR of TBL cancer for both sexes combined was 26.4 (95% UI, 23.9–29.1) per 100,000, with 37.9 (33.3–42.7) per 100,000 for males and 16.8 (14.9–18.6) per 100,000 for females. The ASMR of TBL cancer for both sexes combined was 23.5 (21.2–25.8) per 100,000, with 34.3 (30.3–38.6) per 100,000 for males and 14.5 (12.8–16.1) per 100,000 for females. The ASDR for both sexes combined was 533.0 (480.1–586.4) per 100,000, with 763.7 (668.6–862.7) per 100,000 for males and 328.8 (296.6–363.8) per 100,000 for females (Table S3 and Figure S2).

The regions with the highest ASIR, ASMR, and ASDR for TBL cancer for both sexes combined in 2021 were the high–middle SDI quintile and East Asia. Monaco had the highest ASIR, ASMR, and ASDR (Fig. 1 and Table S3).

The incidence and death number peaked at 70–74 years for both males and females, whilst DALYs peaked at 65–69 years. The highest age group for ASIR was 85–89 years for males and 90–94 years for females. ASMR peaked at 90–94 years for males and 95+ for females. ASDR peaked at 75–79 years for both males and females (Fig. 2).

The trend of tracheal, bronchus, and lung cancer burden from 1990 to 2021

From 1990 to 2021, the incidence number of TBL cancer increased from 1.1 million (95% UI, 1.1–1.2) to 2.3

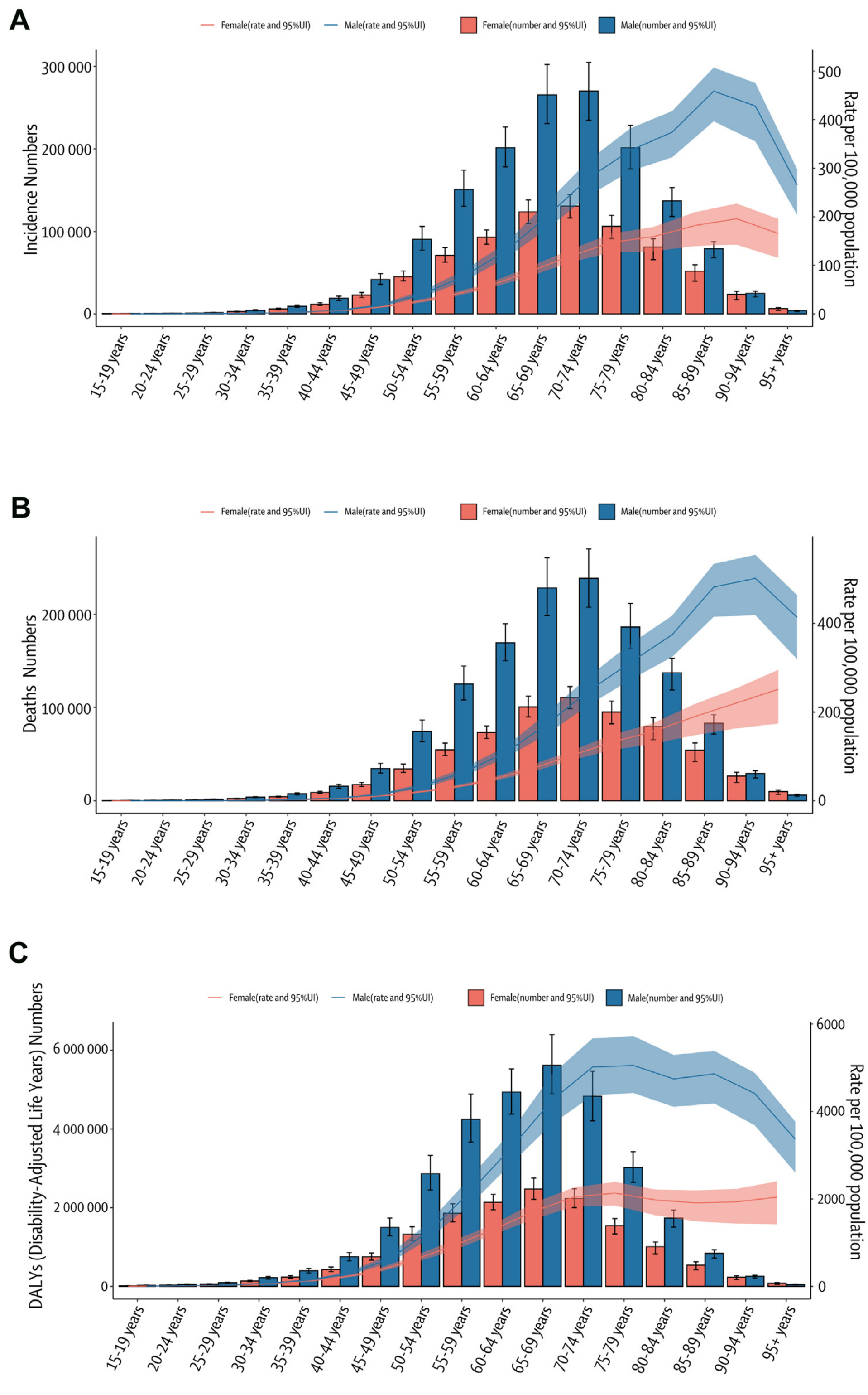

Fig. 2: The age-specific burden of tracheal, bronchus, and lung cancer, incidence and age-standardised incidence rate (A), deaths and age-standardised mortality rate (B), DALYs and age-standardised DALYs rate (C), in 2021. DALYs, disability-adjusted life–years; UI, uncertainty interval.

million (2.1–2.5), marking 101.5% (77.8–124.3) increase. The number of deaths due to TBL cancer increased by 86.7% (64.4–108.2), from 1.1 million (1.0–1.1) to 2.0 million (1.8–2.2). DALYs increased from 28.5 million (27.0–29.9) to 46.5 million (41.9–51.2), an increase of 63.5% (44.4–83.7).

During the COVID-19 pandemic (2019–2021), there was a slight increase in the incidence, deaths and DALYs associated with TBL cancer. The incidence rose from 2.2 million (95% UI, 2.0–2.4) to 2.3 million (2.1–2.5), an increase of 4.5% (–5.4 to 15.8). The number of deaths increased from 1.9 million (1.8–2.1) to 2.0 million (1.8–2.2), an increase of 4.3% (–5.4 to 15.4), and DALYs increased from 45.0 million (41.3–48.6) to 46.5 million (41.9–51.2), an increase of 3.5% (–6.9 to 15.5).

From 1990 to 2021, the overall global ASIR for TBL cancer has trended downward (AAPC, –0.3 [95% CI, –0.4 to –0.2]). However, the ASIR for TBL cancer specifically decreased in males (AAPC, –0.7 [–0.8 to –0.6]) and increased in females (AAPC, 0.6 [0.5–0.6]). Moreover, middle and low–middle SDI quintiles, east and south Asia, and western Sub–Saharan Africa showed an increasing trend in ASIR for males. Conversely, TBL cancer ASIR for females in all SDI quintiles and 15 GBD regions showed increasing trends (Table S4). Table S5 shows the change in ASIR of TBL cancer between 2019 and 2021 where the ASIR of both sexes combined (AAPC, –0.4 [–3.5 to 2.8]), females (AAPC, 0.3 [–4.0 to 4.8]), and males (AAPC, –0.6 [–3.3 to 2.1]) showed a flat trend. At the regional and national level, only three countries (Bahrain, Bangladesh, and Sudan) with both sexes combined showed an increasing trend in ASIR for TBL cancer, whilst other regions or countries showed a flat or decreasing trend (Table S5).

From 1990 to 2021, the ASMR of TBL cancer showed an overall decreasing trend for both sexes combined (AAPC, –0.5 [95% CI, –0.7 to –0.4]). Specifically, the ASMR for males decreased (AAPC, –0.9 [–1.0 to –0.8]) and increased for females (0.3 [0.2–0.3]). Moreover, the ASMR increased for males in low–middle SDI quintile, western Sub–Saharan Africa, and east Asia. In contrast, the ASMR for females showed increasing trends across the high-middle, middle, low-middle and low SDI quintiles and 14 GBD regions (Table S4). Table S5 demonstrates the changes in ASMR of TBL cancer during the COVID-19 pandemic. A flat trend in ASMR was observed during the study period for both sexes combined (AAPC, –0.5 [–2.8 to 1.9]), females (AAPC, 0.2 [–3.2 to 3.8]), males (AAPC, –0.8 [–2.8 to 1.3]). At the regional and national levels, only two countries (Bahrain and Bangladesh) showed an increasing trend in ASMR for TBL cancer among both sexes combined, whilst other regions or countries showed a flat or decreasing trend.

Similarly, both sexes combined ASDR showed a decreasing trend (AAPC, –0.9 [95% CI, –1.0 to –0.7]), where males exhibited a decrease (AAPC, –1.2 [–1.3 to –1.1]) whilst the trend of ASDR was flat in females (AAPC, 0.0 [–0.1 to 0.0]). In low-middle SDI quintile and western Sub–Saharan Africa, ASDR increased in males, whereas it increased in high-middle, low-middle, low SDI quintiles and 14 GBD regions in females (Table S4). During 2019–2021, the ASDR of TBL cancer in both sexes combined (AAPC, –0.7 [–3.3 to 1.9]), females (AAPC, 0.1 [–3.6 to 3.9]), and males (AAPC, –1.0 [–3.2 to 1.2]) showed a flat trend. At the regional and national level, only four countries (Bahrain, Bangladesh, Sudan, and Venezuela) exhibited an increasing trend in ASMR of TBL cancer for both sexes combined, whilst other regions or countries showed a flat or decreasing trend (Table S5).

From 1990 to 2021, the incidence of TBL cancer, divided into 5-year age groups, showed an increasing trend in individuals aged ≥75 years, a flat trend in those aged 70–74, and a decreasing trend in those aged <70 years. The most pronounced increase was in the 95+ years group (AAPC, 1.8 [95% CI, 1.5–2.1]), whilst the most significant decrease was seen in the 15–19 years group (AAPC, –1.7 [–1.8 to –1.5]). TBL cancer mortality and DALYs rate showed an increasing trend among individuals aged ≥80 years, a flat trend in the 75–79 years group, and a decreasing trend in those aged <75 years. The 95+ years group had the most significant increase in mortality rate (AAPC, 1.7 [1.4–2.0])and DALYs rates (AAPC, 1.6 [1.4–1.9]). Mortality rates decreased most significantly for ages 15–19 (AAPC, –1.8 [–1.9 to –1.7]), and 40–44 (AAPC, –1.8 [–1.9 to –1.6]). The most pronounced downward trend in DALYs rates was observed in the 15–19 years (AAPC, –1.8 [–1.9 to –1.7]) and 40–44 years (AAPC, –1.8 [–2.0 to –1.6]) groups (Table 1).

Between 2019 and 2021, the incidence and mortality of TBL cancer in all age groups remained stable. However, the DALYs rate for the 95+ years group showed an upward trend (AAPC, 0.2 [95% CI: 0.2–0.3) (Table 1).

Disability-adjusted life years from tracheal, bronchus, and lung cancer attributable to risk factors

In 2021, TBL cancer was estimated to cause 35.3 million (95% UI, 31.5–40.0) DALYs attributable to risk factors exposure. Table 2 illustrates the contribution of 16 factors across both sexes, five SDI quintiles, and 21 GBD regions in 2021 to DALYs caused by TBL cancer. Smoking is the primary risk factor for TBL cancer DALYs (59.5% [55.4–63.3]), followed by ambient particulate matter pollution (15.0% [9.4 to 21.0]) and asbestos exposure (7.2% [5.0–9.4]) (Table 2).

Smoking was also the primary risk factor for DALYs in both females (31.7% [95% UI, 28.1–35.0]) and males (72.9% [69.2–76.3]). Ambient particulate matter pollution was the next major risk factor, affecting females (14.1% [8.5–20.0]) and males (15.4% [9.9–21.5])

Age group	AAPC of incidence rate, % (95% CI)		AAPC of mortality rate, % (95% CI)		AAPC of DALYs rate, % (95% CI)	
	1990–2021	2019–2021	1990–2021	2019–2021	1990–2021	2019–2021
15–19 years	−1.7 (−1.8 to −1.5)	−0.9 (−4.7 to 3.0)	−1.8 (−1.9 to −1.7)	−1.1 (−4.6 to 2.5)	−1.8 (−1.9 to −1.7)	−1.1 (−4.6 to 2.5)
20–24 years	−1.1 (−1.3 to −0.9)	−1.1 (−9.1 to 7.5)	−1.3 (−1.4 to −1.1)	−1.2 (−9.1 to 7.3)	−1.3 (−1.4 to −1.1)	−1.2 (−9.0 to 7.3)
25–29 years	−0.9 (−1.2 to −0.6)	−2.0 (−7.9 to 4.2)	−1.2 (−1.5 to −0.9)	−2.1 (−8.1 to 4.3)	−1.2 (−1.5 to −0.9)	−2.0 (−8.1 to 4.4)
30–34 years	−0.8 (−1.2 to −0.3)	−0.1 (−2.1 to 1.9)	−1.0 (−1.4 to −0.6)	−0.3 (−2.3 to 1.7)	−1.0 (−1.4 to −0.6)	−0.3 (−2.3 to 1.7)
35–39 years	−1.5 (−1.7 to −1.3)	0.1 (−8.0 to 8.8)	−1.7 (−1.9 to −1.5)	−0.1 (−7.8 to 8.3)	−1.7 (−1.9 to −1.5)	0.0 (−7.7 to 8.3)
40–44 years	−1.5 (−1.7 to −1.4)	−1.6 (−6.9 to 4.1)	−1.8 (−1.9 to −1.6)	−1.6 (−6.5 to 3.5)	−1.8 (−2.0 to −1.6)	−1.6 (−6.4 to 3.5)
45–49 years	−1.5 (−1.8 to −1.2)	−1.7 (−3.7 to 0.4)	−1.7 (−2.1 to −1.4)	−1.7 (−3.7 to 0.3)	−1.7 (−2.0 to −1.4)	−1.7 (−3.7 to 0.3)
50–54 years	−1.3 (−1.5 to −1.1)	−1.1 (−3.8 to 1.6)	−1.6 (−1.8 to −1.4)	−1.2 (−3.5 to 1.0)	−1.6 (−1.7 to −1.5)	−1.2 (−3.4 to 1.0)
55–59 years	−1.1 (−1.4 to −0.8)	−0.4 (−4.8 to 4.3)	−1.4 (−1.7 to −1.1)	−0.6 (−4.5 to 3.6)	−1.4 (−1.7 to −1.1)	−0.6 (−4.3 to 3.3)
60–64 years	−0.8 (−0.9 to −0.7)	−2.2 (−5.8 to 1.6)	−1.2 (−1.3 to −1.0)	−2.3 (−5.3 to 0.8)	−1.2 (−1.3 to −1.0)	−2.2 (−5.4 to 1.0)
65–69 years	−0.4 (−0.6 to −0.3)	−0.3 (−2.1 to 1.6)	−0.8 (−0.9 to −0.6)	−0.4 (−1.3 to 0.6)	−0.8 (−0.9 to −0.7)	−0.4 (−1.4 to 0.5)
70–74 years	0.0 (−0.1 to 0.1)	0.6 (−2.5 to 3.8)	−0.4 (−0.5 to −0.2)	0.3 (−1.9 to 2.6)	−0.3 (−0.5 to −0.2)	0.2 (−2.3 to 2.7)
75–79 years	0.3 (0.2–0.5)	0.6 (−1.3 to 2.4)	−0.1 (−0.2 to 0.1)	0.3 (−1.3 to 1.9)	−0.1 (−0.2 to 0.1)	0.4 (−1.5 to 2.3)
80–84 years	0.7 (0.6–0.9)	−0.4 (−3.7 to 3.0)	0.4 (0.3–0.6)	−0.6 (−2.9 to 1.8)	0.4 (0.3–0.5)	−0.5 (−2.8 to 1.8)
85–89 years	1.4 (1.3–1.5)	0.0 (−3.3 to 3.5)	1.1 (0.9–1.3)	−0.1 (−1.9 to 1.8)	1.1 (0.9–1.2)	−0.1 (−1.8 to 1.7)
90–94 years	1.7 (1.6–1.9)	0.6 (−5.2 to 6.6)	1.3 (1.2–1.4)	0.3 (−3.8 to 4.7)	1.3 (1.2–1.4)	0.3 (−3.8 to 4.7)
95+ years	1.8 (1.5–2.1)	0.1 (−0.9 to 1.2)	1.7 (1.4–2.0)	0.1 (−0.5 to 0.8)	1.6 (1.4–1.9)	0.2 (0.2–0.3)

AAPC, average annual percent change; CI, confidence interval; DALYs, disability-adjusted life-years.

Table 1: **Average annual percent change in incidence, mortality, and DALYs rates for different age groups.**

similarly. Secondhand smoke was the third leading risk factor for females (6.6% [0.8–12.4]), whereas asbestos exposure was third for males (9.3% [6.2–12.8]) (Figure S3). Moreover, risk factor proportions varied across different SDI quintiles. Smoking was the leading risk factor in high (61.3% [56.8–65.4]), high–middle (64.5% [60.0–68.5]), middle (57.1% [52.6–61.3]) and low–middle SDI quintiles (48.9% [45.6–51.9]). However, in low SDI quintile, household air pollution from solid fuels was the greatest contributor to DALYs from TBL cancer (31.8% [21.3–42.3]), whilst smoking accounted for 31.7% (28.8–34.6). As SDI decreased, the proportion of DALYs from smoking, and occupational exposure to asbestos gradually reduced, whereas the proportions from household air pollution from solid fuels gradually increased (Table 2).

Similarly, in 2021, smoking was the leading risk factor for attributable ASDR for TBL cancer globally, with an ASDR of 315.7 (95% UI, 278.2–359.9) per 100,000, affecting males (553.8 [479.3–639.6] per 100,000), and females (103.1 [89.9–118.4] per 100,000). This was consistent across all SDI quintiles and 19 GBD regions. Ambient particulate matter pollution was the second highest risk factor for TBL cancer ASDR for both sexes combined (79.6 [49.0–111.2] per 100,000), males (116.9 [71.4–165.5] per 100,000) and females (46.5 [26.9–67.1] per 100,000). However, in some high–income regions such as western Europe, high–income Asia Pacific, and high–income north America, occupational asbestos exposure was the second highest risk factor for ASDR. Details on the attribution of 16 risk factors to ASDR by GBD regions and national level are provided in Table S6.

The trend of risk factors of tracheal, bronchus, and lung cancer burden from 1990 to 2021

Attributable DALYs increased from 23.6 million (95% UI, 22.2–25.2) in 1990 to 35.3 million (31.5–40.0) in 2021. Fig. 3 illustrates the changes in attributable DALYs from 1990 to 2021 across global and five SDI quintiles. For both sexes combined, attributable DALYs in the high SDI quintile initially rose, then declined, and rose again after 2020. This trend was also observed among females and males in the high SDI quintile. High-middle SDI, middle SDI, low-middle SDI, and low SDI quintiles all exhibited a consistent year-to-year increase in TBL cancer-attributable DALYs.

From 1990 to 2021, the ASDR for TBL cancer attributable to smoking decreased for both sexes combined (AAPC, −1.3 [95% CI, −1.4 to −1.2]), as well as for males (AAPC, −1.4 [−1.6 to −1.3]) and females (AAPC, −0.9 [−0.9 to −0.8]). However, increasing trends were observed in high–middle and low SDI quintiles and in seven GBD regions for females. Regarding males, a increase was determined in western Sub–Saharan Africa (Tables S7–S9). Likewise, the ASDR for TBL cancer attributable to secondhand smoke decreased for both sexes combined (AAPC, −1.1 [−1.3 to −1.0]), for males (AAPC, −1.5 [−1.6 to −1.3]), and for females (AAPC, −0.7 [−0.7 to −0.6]). Nevertheless, an increasing trend was identified in high-middle, low-middle and low SDI quintiles, south Asia and Oceania for females. In contrast, males exhibited an increasing trend only in western Sub-Saharan Africa (Tables S7–S9).

Moreover, the ASDR for TBL cancer attributable to ambient particulate matter pollution attribution displayed a stable trend in both sexes combined (−0.2

Location	Risk factors															
	Ambient particulate matter pollution, % (95% UI)	Diet low in fruits, % (95% UI)	High fasting plasma glucose, % (95% UI)	Household air pollution from solid fuels, % (95% UI)	Occupational exposure to arsenic, % (95% UI)	Occupational exposure to asbestos, % (95% UI)	Occupational exposure to beryllium, % (95% UI)	Occupational exposure to cadmium, % (95% UI)	Occupational exposure to chromium, % (95% UI)	Occupational exposure to diesel engine exhaust, % (95% UI)	Occupational exposure to nickel, % (95% UI)	Occupational exposure to polycyclic aromatic hydrocarbons, % (95% UI)	Occupational exposure to silica, % (95% UI)	Residential radon, % (95% UI)	Secondhand smoke, % (95% UI)	Smoking, % (95% UI)
Global	15.0 (9.4–21.0)	3.5 (1.8–4.9)	2.3 (−0.5 to 5.2)	4.2 (1.6–9.7)	0.6 (0.1–1.1)	7.2 (5.0–9.4)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	1.4 (1.2–1.5)	0.6 (0.1–1.5)	0.4 (0.3–0.4)	3.3 (1.5–5.1)	4.1 (−1.9 to 10.4)	5.1 (0.6–9.5)	59.5 (55.4–63.3)
Global Female	14.1 (8.5–20.0)	3.4 (1.8–4.9)	2.3 (−0.4 to 5)	4.7 (1.8–10.9)	0.7 (0.2–1.2)	2.9 (1.8–4)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	1.2 (1.0–1.5)	0.6 (0.1–1.4)	0.4 (0.3–0.5)	2.6 (1.2–4.0)	4.1 (−1.9 to 10.5)	6.6 (0.8–12.4)	31.7 (28.1–35.0)
Global Male	15.4 (9.9–21.5)	3.5 (1.8–5.0)	2.4 (−0.5 to 5.2)	4.0 (1.6–9.5)	0.6 (0.1–1.1)	9.3 (6.2–12.8)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.1 (0.1–0.1)	1.4 (1.2–1.7)	0.6 (0.1–1.5)	0.4 (0.3–0.4)	3.7 (1.6–5.6)	4.1 (−1.9 to 10.4)	4.3 (0.5–8.1)	72.9 (69.2–76.3)
5 SDI quintiles regions																
High SDI	8.2 (4.8–11.8)	2.7 (1.4–3.9)	2.9 (−0.6 to 6.4)	0.0 (0.0–0.4)	0.5 (−0.1 to 1.1)	16.2 (11.6–20.4)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.0 (0.0–0.2)	0.5 (0.4–0.6)	0.4 (−0.1 to 1.5)	0.1 (0.1–0.2)	2.7 (0.7–4.4)	4.2 (−2.0 to 11.0)	3.2 (0.4–6.0)	61.3 (56.8–65.4)
High-middle SDI	17.7 (11.3–24.3)	2.2 (1.2–3.3)	2.2 (−0.4 to 4.9)	1.4 (0.1–7.1)	0.7 (0.2–1.1)	5.6 (3.7–7.6)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	1.4 (1.2–1.5)	0.6 (0.1–1.5)	0.4 (0.3–0.5)	3.2 (1.5–5.0)	4.7 (−2.2 to 12.6)	6.2 (0.7–11.4)	64.5 (60.0–68.5)
Middle SDI	18.7 (10.8–26.4)	3.6 (1.9–5.1)	2.1 (−0.4 to 4.6)	5.7 (1.2–15.8)	0.7 (0.3–1.2)	2.9 (1.8–4.1)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	0.2 (0.1–0.2)	1.9 (1.7–2.1)	0.7 (0.2–1.6)	0.5 (0.5–0.6)	3.7 (1.7–5.8)	3.4 (−1.7 to 8.7)	5.8 (0.8–11.1)	57.1 (52.6–61.3)
Low-middle SDI	12.5 (7.4–18.6)	9.2 (5–12.9)	2.2 (−0.4 to 5)	17.7 (9.9–27.5)	0.6 (0.2–0.9)	2.3 (1.4–3.5)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	1.9 (1.6–2.1)	0.6 (0.1–1.4)	0.4 (0.4–0.5)	4.0 (1.9–6.2)	3.8 (−1.7 to 9.6)	4.1 (0.5–7.7)	48.9 (45.6–51.9)
Low SDI	7.7 (4.8–11.6)	9.7 (5.1–13.9)	1.8 (−0.4 to 4)	31.8 (21.3–42.3)	0.4 (0.2–0.7)	2.0 (0.8–3.9)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.1 (0.1–0.1)	1.6 (1.4–1.8)	0.5 (0.1–1.2)	0.3 (0.3–0.4)	3.4 (1.6–5.3)	4.6 (−2.2 to 11.9)	2.7 (0.3–5.2)	31.7 (28.8–34.6)
21 GBD regions																
Andean Latin America	16.1 (9.0–24.3)	2.0 (1.1–3.0)	2.0 (−0.4 to 4.6)	3.3 (0.6–10.8)	0.7 (0.3–1.1)	4.0 (2.3–5.8)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	0.2 (0.1–0.2)	2.8 (2.5–3.1)	0.7 (0.1–1.6)	0.6 (0.5–0.7)	4.0 (1.9–6.3)	4.1 (−2.0 to 14.4)	1.2 (0.1–2.2)	24.2 (21.5–27.2)
Australasia	5.2 (2.6–8.4)	2.7 (1.4–3.9)	2.6 (−0.5 to 5.7)	0.0 (0.0–0.0)	0.5 (−0.1 to 1.1)	25.8 (19.5–31.4)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.5 (0.4–0.6)	0.4 (−0.2 to 1.6)	0.1 (0.1–0.1)	3.2 (0.8–5.4)	1.5 (−0.7 to 4.7)	2.3 (0.3–5)	49.1 (44.3–54.2)
Caribbean	12.3 (5.6–20.3)	1.6 (0.8–2.3)	2.7 (−0.5 to 6.1)	3.9 (2.0–6.7)	0.6 (0.2–1.0)	2.9 (1.7–4.5)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	2.0 (1.8–2.2)	0.6 (0.1–1.3)	0.5 (0.4–0.5)	3.2 (1.5–5.0)	2.0 (−0.7 to 6.6)	3.2 (0.4–6.5)	53.6 (49.2–58.2)
Central Asia	15.9 (9.4–23.5)	3.5 (1.9–5.1)	1.8 (−0.4 to 4.1)	3.2 (1.1–7.9)	0.5 (0.2–0.8)	4.5 (2.6–6.7)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.1 (0.1–0.1)	1.9 (1.6–2.2)	0.6 (0.1–1.2)	0.4 (0.3–0.5)	3.7 (1.7–5.7)	7.3 (−3.2 to 20.1)	5.5 (0.7–10.6)	60.9 (57.4–64.1)
Central Europe	12.5 (7.8–17.7)	2.7 (1.4–3.9)	2.9 (−0.6 to 6.5)	0.8 (0.0–5.7)	0.6 (−0.1 to 1.2)	7.8 (4.9–10.5)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.4 (0.3–0.4)	0.5 (−0.2 to 1.7)	0.1 (0.1–0.1)	3.3 (0.9–5.6)	5.6 (−2.7 to 14.2)	4.6 (0.6–9)	67.3 (63.2–71.1)
Central Latin America	9.8 (6.0–14.5)	2.0 (1.0–2.9)	2.7 (−0.5 to 6.1)	2.6 (1.0–6.5)	0.6 (0.2–1.0)	4.2 (2.7–5.9)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	0.2 (0.1–0.2)	2.4 (2.1–2.6)	0.7 (0.1–1.4)	0.5 (0.5–0.6)	3.8 (1.8–5.9)	5.1 (−2.3 to 13.8)	1.9 (0.2–3.6)	32.3 (29.2–35.6)
Central Sub-Saharan Africa	7.6 (4.1–12.3)	5.0 (2.5–7.5)	2.1 (−0.4 to 4.7)	27.1 (17.4–36.9)	0.4 (0.1–0.6)	1.9 (0.4–4.7)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	1.4 (1.2–1.6)	0.4 (0.1–0.9)	0.3 (0.3–0.4)	2.5 (1.1–3.9)	3.7 (−1.8 to 13.5)	1.8 (0.2–3.5)	29.2 (25.8–32.9)

(Table 2 continues on next page)

Location	Risk factors															
	Ambient particulate matter pollution, % (95% UI)	Diet low in fruits, % (95% UI)	High fasting plasma glucose, % (95% UI)	Household air pollution from solid fuels, % (95% UI)	Occupational exposure to arsenic, % (95% UI)	Occupational exposure to asbestos, % (95% UI)	Occupational exposure to beryllium, % (95% UI)	Occupational exposure to cadmium, % (95% UI)	Occupational exposure to chromium, % (95% UI)	Occupational exposure to diesel engine exhaust, % (95% UI)	Occupational exposure to nickel, % (95% UI)	Occupational exposure to polycyclic aromatic hydrocarbons, % (95% UI)	Occupational exposure to silica, % (95% UI)	Residential radon, % (95% UI)	Secondhand smoke, % (95% UI)	Smoking, % (95% UI)
(Continued from previous page)																
East Asia	21.5 (13.2–29.9)	2.3 (1.2–3.5)	2.0 (−0.4 to 4.5)	4.3 (0.9–13.9)	0.8 (0.3–1.3)	2.4 (1.6–3.5)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	0.2 (0.1–0.2)	1.8 (1.6–2.0)	0.8 (0.2–1.7)	0.6 (0.5–0.6)	3.5 (1.6–5.6)	3.7 (−1.8 to 9.8)	7.2 (0.9–13.3)	62.8 (57.8–68.0)
Eastern Europe	8.4 (4.6–13.3)	3.8 (2.0–5.5)	1.7 (−0.3 to 3.7)	0.3 (0.0–1.4)	0.4 (−0.1 to 0.8)	6.3 (3.9–9.1)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.3 (0.2–0.3)	0.3 (−0.1 to 1.2)	0.1 (0.1–0.1)	2.4 (0.6–4.2)	6.8 (−3.3 to 17.6)	4.0 (0.5–7.8)	67.9 (64.7–71.2)
Eastern Sub-Saharan Africa	4.5 (2.6–7.2)	9.9 (5.2–14.3)	1.1 (−0.2 to 2.5)	35.1 (23.7–45.7)	0.5 (0.2–0.9)	1.9 (0.3–4.8)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	1.8 (1.6–2.0)	0.6 (0.1–1.3)	0.4 (0.3–0.5)	3.5 (1.6–5.5)	4.0 (−1.7 to 10.7)	1.5 (0.2–2.8)	23.7 (21.3–26.0)
High-income Asia Pacific	11.1 (5.8–17.3)	3.3 (1.7–4.9)	2.9 (−0.6 to 6.3)	0.0 (0.0–0.0)	0.5 (−0.1 to 1.1)	16.1 (11.0–21.3)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.0 (0.0–0.2)	0.4 (0.3–0.4)	0.4 (−0.2 to 1.6)	0.1 (0.1–0.1)	2.9 (0.7–4.9)	2.5 (−1.3 to 7.1)	3.2 (0.4–6.4)	59.0 (54.5–63.2)
High-income North America	3.3 (1.4–5.7)	2.4 (1.2–3.6)	3.6 (−0.7 to 8.1)	0.0 (0.0–0.0)	0.5 (−0.1 to 1.1)	14.4 (10.2–18.4)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.0 (0.0–0.2)	0.4 (0.3–0.4)	0.4 (−0.2 to 1.3)	0.1 (0.1–0.1)	2.1 (0.5–3.5)	4.4 (−2.1 to 11.2)	2.6 (0.3–5.1)	62.1 (56.8–66.9)
North Africa and Middle East	19.9 (12.8–27.2)	1.2 (0.6–1.8)	2.9 (−0.6 to 6.3)	1.3 (0.7–2.3)	0.5 (0.2–0.8)	6.8 (4.1–10.1)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.1 (0.1–0.1)	1.8 (1.5–2.0)	0.5 (0.1–1.2)	0.4 (0.3–0.5)	3.5 (1.6–5.5)	3.7 (−1.7 to 10.1)	6.1 (0.8–11.8)	62.6 (58.9–66.2)
Oceania	4.4 (1.7–9.5)	4.6 (2.4–6.7)	2.7 (−0.5 to 6.1)	26.7 (16.9–36.9)	0.3 (0.1–0.5)	1.8 (0.9–3.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	1.6 (1.4–1.8)	0.4 (0.1–0.8)	0.3 (0.3–0.3)	2.2 (1.0–3.6)	3.2 (−1.3 to 12.1)	3.9 (0.5–7.6)	43.6 (37.5–50.6)
South Asia	16.7 (9.8–24.3)	16.8 (9.0–23.4)	2.5 (−0.5 to 5.5)	17 (9.0–27.8)	0.5 (0.2–0.8)	2.4 (1.3–3.8)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	1.8 (1.6–2.1)	0.6 (0.1–1.3)	0.4 (0.3–0.5)	4.1 (1.9–6.6)	4.4 (−2.0 to 11.1)	3.9 (0.5–7.4)	43.5 (39.9–46.9)
Southeast Asia	12.8 (7.4–18.9)	3.3 (1.7–4.7)	1.9 (−0.4 to 4.1)	9.0 (3.5–17.6)	0.7 (0.3–1.1)	2.0 (1.1–3.0)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	0.1 (0.1–0.2)	2.2 (1.9–2.5)	0.7 (0.1–1.6)	0.5 (0.4–0.6)	4.0 (1.9–6.3)	2.0 (−0.9 to 5.6)	4.0 (0.5–7.6)	52.7 (48.5–56.5)
Southern Latin America	10.9 (5.6–17.4)	1.6 (0.8–2.4)	2.6 (−0.5 to 5.7)	0.3 (0.0–2.3)	0.6 (0.2–0.9)	9.5 (6.3–13.4)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.2)	2.2 (1.9–2.4)	0.6 (0.1–1.3)	0.5 (0.4–0.6)	3.6 (1.6–5.6)	2.8 (−1.2 to 9.5)	3.9 (0.5–8.1)	56.6 (52.0–60.7)
Southern Sub-Saharan Africa	12.0 (7.4–17.7)	10.1 (5.2–14.5)	1.9 (−0.4 to 4.1)	5.5 (2.7–10.2)	0.2 (0.1–0.3)	11.6 (7.5–16.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.7 (0.6–0.8)	0.2 (0.0–0.5)	0.2 (0.1–0.2)	1.5 (0.7–2.3)	4.6 (−2.2 to 12.7)	3.0 (0.4–5.5)	47.7 (43.8–52)
Tropical Latin America	8.0 (3.9–12.6)	1.5 (0.8–2.2)	2.5 (−0.5 to 5.6)	1.4 (0.3–4.3)	0.6 (0.2–0.9)	6.0 (4.1–8.1)	0.0 (0.0–0.0)	0.1 (0.0–0.1)	0.1 (0.1–0.1)	2.0 (1.8–2.3)	0.6 (0.1–1.2)	0.5 (0.4–0.6)	3.4 (1.5–5.4)	4.2 (−2.0 to 11.6)	3.7 (0.4–7.4)	52.1 (47.3–56.6)
Western Europe	6.9 (4.0–10.3)	2.3 (1.2–3.4)	2.3 (−0.4 to 5.1)	0.0 (0.0–0.0)	0.5 (−0.1 to 1.1)	22.6 (16.5–28.2)	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.0 (0.0–0.2)	0.4 (0.3–0.4)	0.4 (−0.2 to 1.6)	0.1 (0.1–0.1)	2.9 (0.7–4.9)	5.9 (−2.8 to 15.8)	2.9 (0.4–5.7)	63.0 (58.3–67.1)
Western Sub-Saharan Africa	10.4 (5.7–16.8)	7.1 (3.8–10.3)	1.8 (−0.3 to 4.0)	27.8 (17.8–38.6)	0.4 (0.1–0.6)	2.2 (1.1–3.7)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.1 (0.1–0.1)	1.4 (1.3–1.6)	0.4 (0.1–0.9)	0.3 (0.3–0.3)	2.6 (1.2–4.1)	4.5 (−1.9 to 11.4)	1.9 (0.2–3.7)	24.0 (21.0–26.9)

TBL, tracheal, bronchus, and lung; DALYs, disability-adjusted life-years; UI, uncertainty interval; SDI, socio-demographic index.

Table 2: **Percentage contribution of risk factors to all-age DALYs of TBL cancer in 2021, for sexes, SDI, and by regions.**

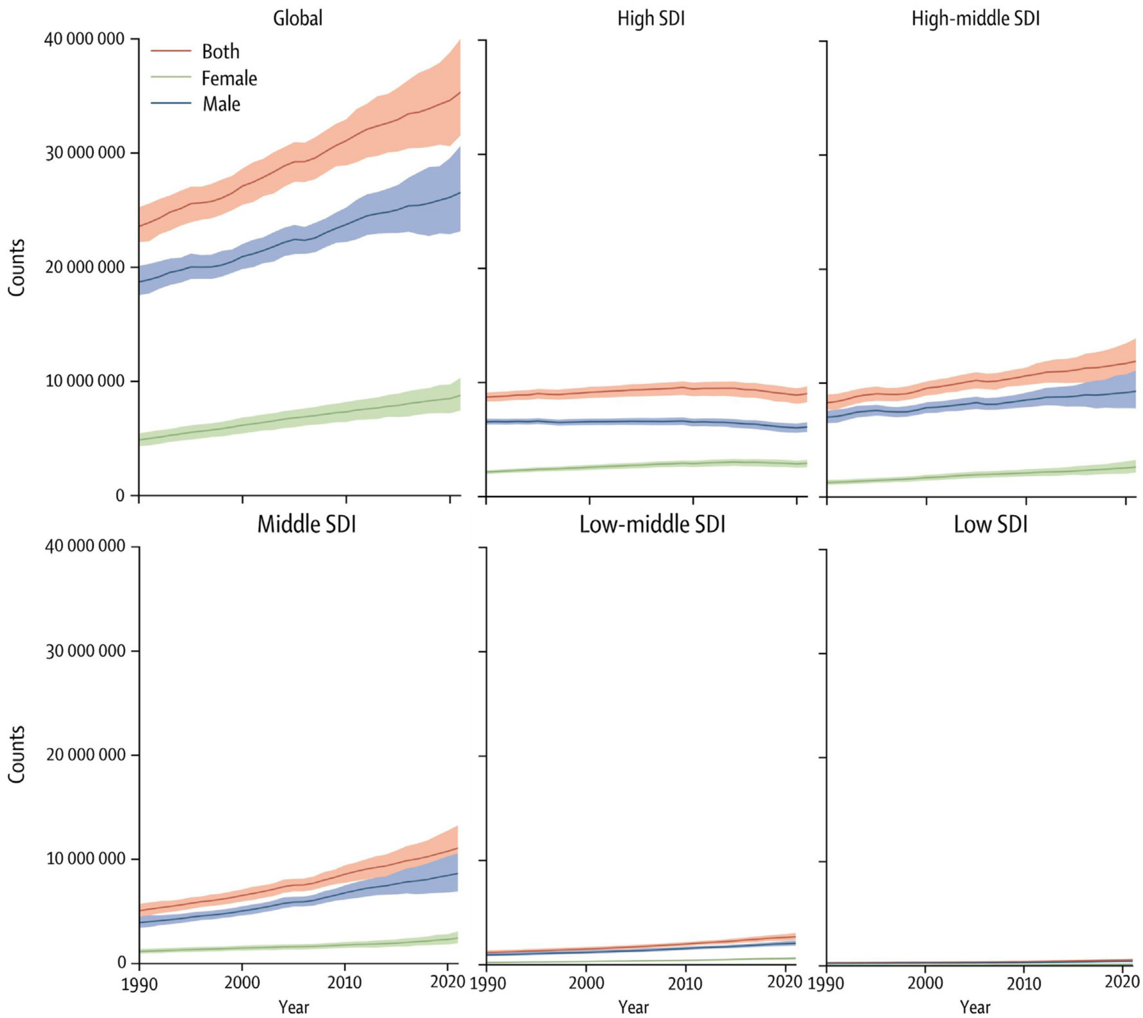

Fig. 3: Changes in total attributable DALYs for TBL cancer in both sexes combined, females and males individually, and in global and 5 SDI quintiles regions (1990–2021). DALYs, disability-adjusted life-years; SDI, Socio-demographic Index.

[95% CI, −0.4 to 0.1]). However, trends diverged by sex: males experienced a decrease (AAPC, −0.5 [−0.7 to −0.3]), whilst females saw an increase (AAPC, 0.9 [0.7–1.2]). Specifically, females showed rising trends across high-middle, middle, low-middle, low SDI quintiles and 14 GBD regions, whereas males increased in middle, low-middle and low SDI quintiles and six GBD regions (Tables S7–S9).

The ASDR for TBL cancer attributable to occupational exposure to polycyclic aromatic hydrocarbons, cadmium, chromium, and diesel engine exhaust showed upward trends in both sexes combined. Among the nine occupational exposure risk factors, only the ASDR for TBL cancer linked to asbestos decreased in females. Conversely, the ASDR for TBL cancer due to chromium, diesel engine exhaust and polycyclic aromatic hydrocarbons increased in males (Tables S7–S9).

In 2021, household air pollution from solid fuels was a major risk factor for TBL cancer DALYs in low SDI quintile. Despite this, the ASDR for TBL cancer attributable to this risk factor decreased for both sexes combined, as well as males and females individually, from 1990 to 2021. However, the ASDR increased among females in the low SDI quintile, Oceania and in eastern and western Sub-Saharan Africa, whilst it decreased or showed a steady trend for males across all SDI quintiles and in 21 GBD regions (Tables S7–S9).

From 1990 to 2021, ASDR for TBL cancer attributable to residential radon decreased for both sexes combined (AAPC, −1.2 [95% CI, −1.4 to −1.1]). Western Sub-Saharan Africa was the only GBD region where the ASDR increased for males. Conversely, the ASDR rose among females in high-middle, low-middle, and low SDI quintiles, as well as in 14 GBD regions

(Tables S7–S9). In the same period, ASDR for TBL cancer attributable to high fasting plasma glucose increased for both sexes combined (AAPC, 0.3 [0.2–0.5]). This trend was marked by an upward trend for females (AAPC, 1.2 [1.1–1.3]) and a flat trend for males (AAPC, 0.0 [−0.2 to 0.1]). For males, the ASDR increased in the middle, low-middle and low SDI quintiles, as well as in 12 GBD regions, whereas females showed a rising trend in all SDI quintiles and 18 GBD regions (Tables S7–S9). Furthermore, the ASDR for TBL cancer attributable to the low fruit diet decreased in both sexes combined (AAPC, −2.0 [−2.1 to −1.9]), males (AAPC, −2.3 [−2.4 to −2.1]), and females (AAPC, −1.4 [−1.4 to −1.3]). On the other hand, there were upward trends among females in low-middle and low SDI quintiles, and five GBD regions, and among males in central Asia and western Sub–Saharan Africa (Tables S7–S9).

Discussion

From 1990 to 2021, the global burden of TBL cancer has generally decreased, though epidemiological trends differ by sex and region. Whilst male TBL cancer rates have mostly declined globally, female TBL cancer trends exhibit two distinct patterns: 1) In high-incidence regions in 1990, such as high–income Asia Pacific and North America, ASIR has either plateaued or declined, whilst ASMR has declined over the past 30 years. 2) Some regions in Asia, Europe, and Africa (eg, east and south Asia, west Europe, and western Sub–Saharan Africa). These variations reflect both regional and sex-based heterogeneity, likely influenced by the differences in risk factor distribution related to TBL cancer, economic development, and healthcare access.

During the study period, we determined an upward trend in TBL cancer incidence among individuals aged ≥75 years and mortality among those aged ≥80 years, indicating age-related heterogeneity in prevalence. As the global population ages, the proportion of the elderly population has increased, contributing to higher incidence and mortality rates of TBL cancer. Since older adults are exposed to various risk factors such as smoking and environmental pollution for longer periods than younger people, the cumulative effects of chronic diseases and related complications further elevate the risk of developing TBL cancer.[12,13] Notably, the burden of TBL cancer did not exhibit a clear trend during the COVID-19 pandemic.

On the other hand, we observed significant differences in attribution DALYs between different SDI quintiles (Fig. 3). For example, the high SDI quintile has attributed DALYs 21.2 times higher than the low SDI quintile, despite comparable population sizes (1,094,047,736 vs. 1,117,382,591 according to GBD 2021), and this can also be seen in other epidemiological indicators (Figure S2 and Table S3), this discrepancy is likely due to a number of reasons. For example, some lower SDI and less populated areas or countries do not have a well-established disease registration system, and systematic under-reporting may occur; of course, it cannot be ruled out that the burden associated with TBL cancer has been low in these areas. Apart from this, during the study we observed that in the high SDI quintile, smoking was the primary risk factor for TBL cancer with an attributed ASDR of 370.2 (339.8–399.7) per 100,000, whilst in the low SDI quintile, smoking was the second leading risk factor with an attributed ASDR of only 48.7 (39.4–59.3) per 100,000. Similar patterns are observed for other risk factors, indicating that regional risk factors critically impact the attribution of DALYs in TBL cancer.

Regarding risk factors trends associated with TBL cancer, regional and sex heterogeneity is evident. Smoking remains the leading risk factor for TBL cancer, but its overall burden has declined due to worldwide tobacco control efforts.[14] The Framework Convention on Tobacco Control (FCTC), implemented in 2005,[15] is an international treaty designed to support participating countries in maintaining minimum standards for tobacco control laws (e.g., reducing advertising of tobacco products and taxing tobacco). This treaty has expanded to 182 countries as of 2021.[16]

On the other hand, there remains a significant sex difference in the attributed ASDR for smoking during the study period. In particular, there was an upward trend in the ASDR attribution for female smoking in some regions. This can be partly explained by the four-stage model of the tobacco epidemic,[17] where females tend to increase smoking rates 20–30 years or more later than males, resulting in a considerable lag before the cumulative effects of smoking are observed. Additionally, females are more sensitive to specific carcinogens in tobacco, potentially due to a higher susceptibility to mutations in the p53 and K–RAS genes and interactions between tobacco carcinogens and oestrogen.[18]

Whilst the attribution burden of smoking is declining overall, it remains crucial to focus on regions with high smoking prevalence and address the increasing trend among females.

Ambient particulate matter pollution mainly affects high-middle and middle SDI quintiles (eg, east, central, and south Asia). According to a study, 7.3 billion people worldwide are exposed to unsafe average annual PM2.5 concentrations, with 80% living in low- and middle-income countries such as China, India, and Sub-Saharan Africa.[19] This has led to an upward trend in the attribution burden of particulate pollution from TBL cancer in these countries. The environmental Kuznets curve explains this phenomenon,[20] where middle-income countries experience the highest levels of air pollution due to pollution-causing economic activities such as manufacturing.[21] Some countries such as China, have taken action through policies to improve air quality, as seen during its 13th Five-Year Plan period, resulting in decreased PM 2.5 concentrations.[22]

This indicates great potential to reduce the global burden of TBL cancer by improving air quality. Targeted measures to reduce the pollution intensity of economic growth and transition to cleaner fuels are necessary.

In low SDI regions, household air pollution from solid fuels contributes the most DALYs, even surpassing smoking, and is particularly pronounced among females. This may be due to the high use of solid fuels (e.g., wood and coal), exposure to cooking fumes, and females' social role in indoor cooking.[23] Therefore, promoting the use of clean energy in the lower SDI regions is crucial, especially for females, to mitigate the growing burden of TBL cancer.

High fasting plasma glucose is the only attributable metabolic risk factor for TBL cancer, showing a clear upward trend in females across 194 regions and countries and in males in 125 regions and countries. This trend is concerning and may be linked to social transitions that increase the prevalence of metabolic diseases (e.g., type 2 diabetes).[24] To overcome the burden of TBL cancer, potential strategies include dietary modifications (e.g., reduced fat and low intake of sugar-sweetened beverages) and increased physical activity.

Based on the current epidemiological trends and evolving risk factors related to TBL cancer, formulating effective screening and prevention strategies is crucial. Low-dose computed tomography (LDCT) has been extensively studied for the secondary prevention of TBL cancer.[25] Randomised controlled trials, including the National Lung Screening Test (NLST)[26] and the NELSON trial,[27] have demonstrated that LDCT screening reduces lung cancer mortality.

The US Preventive Services Task Force has expanded the screening age group to include individuals aged 50–80 years and those who smoke 20 packs per year,[28] compared to the NLST (55–74 years) and NELSON (50–74 years) trials. This expansion represents a significant advancement in TBL cancer screening.

However, with declining smoking rates, TBL cancer is increasingly occurring in never-smokers.[29,30] For policymakers to consider expanding screening to at-risk populations with a history of non–smoking, it is important to evaluate the local risk factor context, current epidemiological trends, and the economic burden, especially for lower SDI regions.

In addition, the reduction in TBL cancer mortality in higher SDI regions is largely attributable to advances in therapies, including targeted therapy and immunotherapy,[31] which significantly improve patient prognosis. However, financial barriers prevent many patients from accessing these treatments. A 2021 cross-sectional survey showed that even older generic chemotherapy drugs can result in catastrophic payments for patients in low- and middle-income settings.[32] In these regions, 32% and 58% of essential cancer drugs are only available at full price,[32] indicating significant barriers to accessing essential cancer medicines, not including novel anticancer drugs. This issue is particularly severe in lower- and middle-income settings.

There are several limitations in this study. First, the availability and quality of raw data pose a limiting factor in estimating the disease burden and risk–attributed TBL cancer burden. Disease registries were particularly imperfect 30 years ago, especially in low and middle-income countries. Additionally, there is a lack of available data for some of the countries with smaller populations included in the GBD. Therefore, estimates for these regions rely on predictive covariates and neighbouring regions, which may further reduce the accuracy of the data. Second, tracheal, bronchial, and lung cancer exhibit heterogeneity in pathogenesis, pathological characteristics (e.g., squamous cell carcinoma and adenocarcinoma), and epidemic trends. However, due to the limitations of the GBD database, we cannot separate these cancers for statistical analysis. Third, the COVID-19 pandemic has significantly impacted the global healthcare system, affecting the diagnosis, treatment and care of TBL cancer patients. This may lead to an increased burden of TBL cancer in the period following the pandemic. However, GBD 2021 lists COVID-19 as a separate disease, so the impact of COVID-19 and other respiratory diseases (e.g., asthma and respiratory infections) on TBL cancer has not been fully considered. The short time interval since the pandemic's onset may not fully reflect the trend. Therefore, further observation is needed to determine the true impact of COVID-19 and other respiratory diseases on TBL cancer.

In conclusion, although the overall burden of TBL cancer is gradually decreasing, significant regional and sex-based epidemiological differences persist. The annual death toll of TBL cancer remains substantial, and the post-COVID-19 impact on this cancer still needs further follow–up observation. Reducing the prevalence of modifiable risk factors and maximising the clinical efficacy and cost-effectiveness of screening are important strategies to alleviate the burden of TBL cancer.

Contributors
Jie Li conceived the study. Ziyu Kuang designed the protocol. Ziyu Kuang, Jiaxi Wang and Kexin Liu analysed the GBD data. Ziyu Kuang, Jiaxi Wang, Kexin Liu, Jingyuan Wu, Yuansha Ge, Guanghui Zhu, Luchang Cao and Xinyi Ma contributed to the statistical analysis and interpretation of data. Ziyu Kuang, Jiaxi Wang and Kexin Liu drafted the manuscript, and other authors critically revised the manuscript. Jie Li and Ziyu Kuang accessed and verified the underlying data. All authors have read and approved the final version of the manuscript.

Data sharing statement
Data used for the analyses are publicly available from the Institute of Health Metrics and Evaluation (http://www.healthdata.org/; http://ghdx.healthdata.org/gbd-results-tool).

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Declaration of interests
All authors declare no competing interests.

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Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102804.

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