Burden of Tracheal, Bronchus, and Lung Cancer and Its Attributable Risk Factors in 204 Countries and Territories, 1990 to 2019

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ABSTRACT

Introduction: Understanding trends in the annual incidence, mortality, and disability-adjusted life-years (DALYs) for tracheal, bronchus, and lung (TBL) cancer globally is important to enable appropriate targeting of resources for prevention, clinical practice improvement, and research. The aim of this study was to determine the global, regional, and national burdens of TBL cancer in 204 countries and territories from 1990 to 2019 by age, sex, and sociodemographic index.

Methods: Estimates were produced through various data inputs including the following: cancer registries (n_site-years = 5318), vital registration (n_site-years = 22,553), vital registration-sample (n_site-years = 825), and verbal autopsies (n_site-years = 516). Annual incidence, mortality, and DALYs were estimated and presented as counts and age-standardized rates per 100,000 population.

Results: There were 2.3 million (95% uncertainty interval [UI]: 2.1–2.5) incident cases of TBL cancer, with an age-standardized annual incidence rate of 27.7 (95% UI: 25.3–30), which decreased by 2.6% (95% UI: −12.4 to 6.5) between 1990 and 2019. TBL cancer was responsible for 2 million (95% UI: 1.9–2.2) deaths globally with an age-standardized death rate of 25.2 (95% UI: 23.2–27), a decrease of 7.8% (95% UI: −15.9 to 6.2) between 1990 and 2019. Moreover, TBL accounted for 45.9 million (95% UI: 42.3–49.3) DALYs at the global level, with an age-standardized rate of 551.6 (95% UI: 509–593.1) DALYs per 100,000 population. The standardized DALY rate declined by 16.2% (95% UI: −24 to −8.2) from 1990 to 2019. Greenland (77.7 [95% UI: 64.4–90.6]), Monaco (75.6 [95% UI: 61.4–90.8]), and Montenegro (56.7 [95% UI: 46.5–68.9]) had the three highest age-standardized annual incidence rates. The aforementioned three countries also had the three highest age-standardized death rates of TBL cancer. The largest increases were found in age-standardized annual incidence rates for TBL cancer during 1990 to 2019. The largest increases were found in age-standardized death rates of TBL cancer in Honduras (67.1% [95% UI: 14.7–133.1]), Cabo Verde (62.2% [95% UI: 24.1–101.3]), and Monaco (58.2% [95% UI: 19.2–109.7]).

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Age-standardized annual incidence and death rates were higher in male than female individuals and increased with population aging. There were nonlinear but generally positive associations between age-standardized DALY rates with corresponding sociodemographic index of countries. Globally, smoking (62.4%), ambient particulate matter (15.3%), and high fasting plasma glucose (9.9%) had the top three highest percent of attributable DALYs owing to TBL cancer in 2019 for both sexes.

Conclusions: This study found a decline in burden globally but with some countries having an increase. These results are crucial to set priorities for prevention and treatment of TBL cancer and would be beneficial for policymakers, government officials, clinicians, and researchers.

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Keywords: Lung cancer; Epidemiology; Risk factors; Incidence; Mortality; Global

Introduction

In 2016, it was reported that tracheal, bronchus, and lung (TBL) cancer accounted for 36 of the 213 million disability-adjusted life-years (DALYs) and 19% of all cancer deaths, making it the leading cause of DALYs and cancer-related death globally.\(^1\) The costs associated with lung cancer according to the 2011 European Lung White book are 3.35 billion Euros among European countries\(^3\) with prevalence costs of 12.1 billion dollars in the United States of America in 2010.\(^4\) Importantly, costs of TBL cancer care are increasing for the nationwide economy and the individual patient, with government organizations paying smaller and smaller portions of TBL cancer treatment over time.\(^5\) This highlights the need for recent and comprehensive incidence, mortality, and DALY data that can be used to inform updated prevalence costs for use within current practice to inform policy decisions and resource allocation.

Another important factor to consider is despite these known societal, health, and economic impacts, a study recently found that associated research outputs for lung cancer are far fewer compared with other malignancies.\(^6\) Although some studies report on lung cancer incidence and mortality at regional levels or in selected countries,\(^7\)–\(^11\) none have comprehensively evaluated the burden of TBL cancer and global trends have not been updated since 2012.\(^1\) As such, quantifying the most recent data on incidence, deaths, and DALYs of TBL cancer is warranted.

The study of Global Burden of Disease (GBD), Injuries, and Risk Factors 2019 is the most recent comprehensive and comparable data set evaluating epidemiologic levels and trends globally, with estimates finalized and accessed in 2020. The results of GBD 2019 supersede previously published GBD estimates as the estimating methods have been changed and new data sources have been added. Therefore, the aim of this study was to use data from the GBD 2019 study to determine the global, regional, and national burdens of TBL cancer across 204 countries and territories between 1990 and 2019 by age, sex, and sociodemographic index (SDI).

Methods

Overview of GBD Study

The GBD study evaluated 204 countries, 21 regions, and seven super-regions evaluating approximately 369 diseases and 87 risk factors. General methodology and featured changes in GBD 2019 compared with previous years have been described in capstone papers.\(^12\)–\(^14\) Cancers have been categorized into 30 groups according to the 2011 International Classification of Diseases—10 codes considered for TBL cancer were C33, C34–C34.92, Z12.2, Z80.1–Z80.2, and Z85.1–Z85.20.\(^12\) The four common sequelae for cancers in GBD and their corresponding disability weights were considered for the cancer of interest (Supplementary Table 1).\(^15\) In this study, different data sources including vital registration (22,553 site-years), vital registration-sample (825 site-years), verbal autopsy (516 site-years), and cancer registries (5318 site-years) were used.\(^12\) A site-year is a unique combination of the location and calendar year and is defined as a country or other subnational geographic unit contributing data in a given year.

Mortality Estimation

Estimation of mortality occurred in the following two phases: (1) Because incidence data were more common than mortality data in many locations, this necessitated the need for mortality estimation in the first instance. The mortality-to-incidence ratio (MIR) was modeled using the locations where incidence and mortality have been provided in the same year. The MIR was firstly modeled through linear-step mixed-effects models in the presence of covariates, including the Healthcare Access and Quality Index.
Spatiotemporal Gaussian process regression was then applied using three hyperparameters including time, age, and location to smooth estimates across time and space. Estimated mortalities were then generated through multiplying incidence with modeled MIR. (2) Estimated mortalities from the previous phase and observed deaths from vital registration systems and verbal autopsies were used as inputs for the cause of death ensemble model (CODEm), and final mortality estimates were generated by this model. CODEm uses all available data and covariates developing a diverse set of plausible individual models that capture the best fit. This enables out-of-sample predictive validity to be determined for all individual models and combination of individual models to allow selection of a model with the highest predictive validity. Detailed information on estimating the TBL mortality and the covariates used in CODEm is presented elsewhere.

Incidence, Prevalence, and Disability Estimation

The final annual incidence of TBL cancer was estimated for all countries and territories from 1990 to 2019, by dividing final mortality estimates over MIR. The 10-year prevalence for this cancer was also modeled using the MIR to determine country-specific survival, divided into the following four sequelae: diagnosis/treatment, controlled, metastatic, and terminal phases (Supplementary Table 1). Sequel-specific years lived with disability (YLDs) were estimated through multiplying sequel-specific prevalence with corresponding disability weights. Years of life lost were estimated by multiplying the estimated number of deaths by age with a standard life expectancy at that age. Lastly, DALYs were calculated by summing YLDs and years of life lost. The detailed information on estimating the prevalence and YLD is presented elsewhere.

To evaluate associations of TBL cancer burden with development status of countries, the GBD used SDI. SDI is a composite indicator of total fertility rate under the age of 25, mean education for those aged 15 and older, and lag-distributed income per capita. The SDI ranges from 0 to 1, with 0 reflecting the lowest level of development and 1 the highest.

Risk Factors

We reported the percent of DALYs owing to TBL cancer which were attributable to smoking, ambient particulate matter, low fruit and vegetable consumption, high fasting plasma glucose levels, and exposure to pollutants, such as occupational asbestos, secondhand smoke, household air pollution, radon, occupation silica, occupational diesel, occupational arsenic, occupational nickel, and occupational polycyclic aromatic hydrocarbons. Details on definitions of these risk factors and their relative risk for TBL cancer could be found in a previous article.

Results

Global Level

This study identified 2.3 million (95% UI: 2.1–2.5) incident cases of TBL cancer in 2019, with an age-standardized annual incidence rate of 27.7 (95% UI: 25.3–30), which decreased by 2.6% (95% UI: −12.4 to 6.5) between 1990 and 2019. TBL cancer was responsible for 2 million (95% UI: 1.9–2.2) deaths in 2019 globally with an age-standardized death rate of 25.2 (95% UI: 23.2–27), which decreased by 7.8% (95% UI: −15.9 to 0.2) between 1990 and 2019. DALYs associated with TBL cancer in 2019 were 45.9 million (95% UI: 42.3–49.3), with an age-standardized rate of 551.6 (95% UI: 509–593.1) per 100,000 population that reduced by 16.2% (95% UI: −24 to −8.2) from 1990 to 2019 (Table 1).

Regional Level

The age-standardized annual incidence of TBL cancer in 2019 was found to be highest in high-income North America (45 [95% UI: 39.5–51.4]), East Asia (41.3 [95% UI: 35–48.1]) and Central Europe (25 [95% UI: 22.2–28.1]). In contrast, Eastern Sub-Saharan Africa (7 [95% UI: 5.9–8.5]), South Asia (8.4 [95% UI: 7.1–9.5]), and Western Sub-Saharan Africa (9.2 [95% UI: 7.7–10.6]) had the lowest age-standardized rates. The age-standardized death rates of TBL cancer in 2019 were also found to be highest in East Asia (38.4 [95% UI: 32.7–44.6]), Central Europe (38.3 [95% UI: 33.6–43.5]), and high-income North America (35.9 [95% UI: 33.8–37.3]), whereas, Eastern Sub-Saharan Africa (7.6 [95% UI: 6.5–9.1]), South Asia (8.8 [95% UI: 7.4–10.1]) and Western Sub-Saharan Africa (10 [95% UI: 8.5–11.6]) had the lowest rate (Table 1). The regional-level age-standardized annual incidence and death estimates for all of the GBD regions in 2019 are presented by sex in Figure 1A and B.

The percentage change in age-standardized annual incidence rates of TBL cancer during 1990 to 2019 was different across GBD regions with Central Asia (−35.8% [95% UI: −41.9 to −29.3]), Eastern Europe (−30.2% [95% UI: −37.9 to −21.9]), and high-income North America (−22.8% [95% UI: −32.5 to −11.8]) having significant decreasing trends. In contrast, East Asia (37.5% [95% UI: 11.1–71.5]) had significant increasing trends. Regions with the largest decreasing trends in age-standardized death rates of TBL cancer during the measurement period included Central Asia (−34.5% [95% UI: −40.6 to −28]), Eastern Europe (−33.3%
Table 1. Incident Cases, Deaths, and DALYs for Tracheal, Bronchus, and Lung Cancer in 2019 for Both Sexes and Percentage Change of ASRs by GBD Regions

<table>
<thead>
<tr>
<th>GBD Regions</th>
<th>Incidence (95% UI)</th>
<th>Deaths (95% UI)</th>
<th>DALYs (95% UI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASRs Per 100,000 (95% UI)</td>
<td>Percentage Change in ASRs Per 100,000</td>
<td>ASRs Per 100,000 (95% UI)</td>
</tr>
<tr>
<td>Global</td>
<td>2,259,998 (2,067,316, 2,451,832)</td>
<td>27.7 (25.3, 30)</td>
<td>2,042,640</td>
</tr>
<tr>
<td>High-income North America</td>
<td>285,175 (250,063, 325,229)</td>
<td>45(39.5, 51.4)</td>
<td>230,304</td>
</tr>
<tr>
<td>Australasia</td>
<td>15,301 (12,537, 18,671)</td>
<td>30.7 (25, 37.5)</td>
<td>12,036</td>
</tr>
<tr>
<td>High-income Asia Pacific</td>
<td>150,900 (126,657, 173,088)</td>
<td>31.6(27, 36.3)</td>
<td>110,970</td>
</tr>
<tr>
<td>Western Europe</td>
<td>300,654 (263,199, 341,081)</td>
<td>34.5 (30.1, 39.4)</td>
<td>260,784</td>
</tr>
<tr>
<td>Southern Latin America</td>
<td>19,657 (15,650, 24,507)</td>
<td>23.6 (18.8, 29.5)</td>
<td>19,638</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>86,319 (76,576, 97,034)</td>
<td>25 (22.2, 28.1)</td>
<td>78,716</td>
</tr>
<tr>
<td>Central Europe</td>
<td>84,020 (74,156, 94,781)</td>
<td>40 (35.2, 45.2)</td>
<td>81,333</td>
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<tr>
<td>Central Asia</td>
<td>14,342 (12,983, 15,870)</td>
<td>18.9 (17.1, 19.8)</td>
<td>13,990</td>
</tr>
<tr>
<td>Central Latin America</td>
<td>27,234 (23,161, 31,754)</td>
<td>11.7 (10, 13.6)</td>
<td>27,246</td>
</tr>
<tr>
<td>Andean Latin America</td>
<td>5970 (4813, 7309)</td>
<td>10.8 (8.7, 13.2)</td>
<td>6241</td>
</tr>
<tr>
<td>Caribbean</td>
<td>11,507 (9817, 13,472)</td>
<td>22.2 (19, 26)</td>
<td>11,233</td>
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<tr>
<td>Tropical Latin America</td>
<td>37,274 (35,041, 39,075)</td>
<td>15.4 (14.5, 16.2)</td>
<td>37,868</td>
</tr>
<tr>
<td>East Asia</td>
<td>854,582 (721,022, 1,002,044)</td>
<td>41.3 (35, 48.1)</td>
<td>778,387</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>132,529 (110,981, 153,557)</td>
<td>22 (18.4, 25.4)</td>
<td>134,566</td>
</tr>
<tr>
<td>Oceania</td>
<td>1482 (1117, 2102)</td>
<td>21.6 (16.6, 30.4)</td>
<td>1489</td>
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</tbody>
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(continued)
<table>
<thead>
<tr>
<th>GBD Regions</th>
<th>Incidence (95% UI)</th>
<th>Deaths (95% UI)</th>
<th>DALYs (95% UI)</th>
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<tbody>
<tr>
<td></td>
<td>No. (95% UI)</td>
<td>ASRs Per 100,000 (95% UI)</td>
<td>Percentage Change in ASRs Per 100,000 (95% UI)</td>
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<td></td>
<td></td>
<td>ASRs Per 100,000 (95% UI)</td>
<td>Percentage Change in ASRs Per 100,000 (95% UI)</td>
</tr>
<tr>
<td>North Africa and Middle East</td>
<td>71,681 (63,424, 81,049)</td>
<td>16.8 (14.9, 19)</td>
<td>0.7 (–20.6 to 24.1)</td>
</tr>
<tr>
<td>South Asia</td>
<td>117,195 (100,085, 133,943)</td>
<td>8.4 (7.1, 9.5)</td>
<td>9.9 (–15.5 to 34.8)</td>
</tr>
<tr>
<td>Southern Sub-Saharan Africa</td>
<td>10,284 (9,344, 11,454)</td>
<td>18.4 (16.7, 20.3)</td>
<td>–7.6 (–24.5 to 7.7)</td>
</tr>
<tr>
<td>Western Sub-Saharan Africa</td>
<td>16,155 (13,551, 18,857)</td>
<td>9.2 (7.7, 10.6)</td>
<td>18.5 (–1.5 to 42.1)</td>
</tr>
<tr>
<td>Eastern Sub-Saharan Africa</td>
<td>10,939 (9,174, 13,256)</td>
<td>7 (5.9, 8.5)</td>
<td>3 (–16.7 to 27.5)</td>
</tr>
<tr>
<td>Central Sub-Saharan Africa</td>
<td>6799 (4411, 11,653)</td>
<td>12.7 (8.4, 21.2)</td>
<td>–12.4 (–36.6 to 22.8)</td>
</tr>
</tbody>
</table>


ASR, age-standardized rate; DALY, disability-adjusted life-year; GBD, Global Burden of Disease; UI, uncertainty interval.
[95% UI: −40.9 to −25.6]), and Australasia (−29% [95% UI: −33.2 to −25.1]). In contrast, a statistically significant increasing trend was found in East Asia (23.8% [95% UI: 0.1–52.7]) (Table 1). Regional-level percentage change in age-standardized annual incidence and death estimates from 1990 to 2019 for all GBD regions have been presented by sex in Figures 2A and B.

The absolute number of incident cases of TBL cancer doubled from 1990 (1.1 million [95% UI: 1.1–1.2]) to
2019 (2.3 million [95% UI: 2.1–2.5]), though contributions from different GBD regions changed over this time (Supplementary Table 2). The number of deaths owing to TBL cancer also increased from 1990 (1.1 million [95% UI: 1–1.1]) to 2019 (2 million [95% UI: 1.9–2.2]) with changes to GBD region contributions over this time (Supplementary Table 3).

**National Level**

The age-standardized annual incidence rate of TBL cancer in 2019 varied significantly between countries, such that Greenland (77.7 [95% UI: 64.4–90.6]), Monaco (75.6 [95% UI: 61.4–90.8]), and Montenegro (56.7 [95% UI: 46.5–68.9]) had the three highest age-standardized annual incidence rates of all countries.
In contrast, countries with the lowest rates were Somalia (5.6 [95% UI: 3.1–9.1]), Ethiopia (5.6 [95% UI: 3.9–7.5]), and Kenya (5.6 [95% UI: 4.7–6.7]) (Fig. 3A and Supplementary Table 2). Similar results were observed for age-standardized death rates in 2019, with Greenland (78.2 [95% UI: 63.9–92]), Monaco (64.2 [95% UI: 52.3–76.9]), and Montenegro (53.4 [95% UI: 43.8–64.4]) producing the highest rates and

Figure 3. Age-standardized annual (A) incidence and (B) death rates of TBL cancer per 100,000 population by location for both sexes, 2019 (generated from data available from http://ghdx.healthdata.org/gbd-results-tool). TBL, tracheal, bronchus, and lung.
Kazakhstan (6 [95% UI: 3.4–9.8]), Ethiopia (6.1 [95% UI: 4.2–8.3]), and Kenya (6.3 [95% UI: 5.3–7.5]) had the lowest rates (Fig. 3B and Supplementary Table 3). Greenland (1769 [95% UI: 1436.9–2101.5]), Monaco (1483.3 [95% UI: 1181.9–1811.7]), and Montenegro (1343.6 [95% UI: 1092.2–1633.4]) had the highest age-standardized DALY rates of TBL cancer in 2019 among all countries. In contrast, countries with the lowest rates were Ethiopia (131.8 [95% UI: 91–178.9]), Kenya (143.5 [95% UI: 119–174.3]), and Malawi (145.3 [95% UI: 113.2–182.3]) (Supplementary Fig. 1 and Supplementary Table 4).

The percentage change in age-standardized annual incidence rates of TBL cancer during 1990 to 2019 differed substantially between countries, with Honduras (67.1% [95% UI: 14.5–137.7]), Cabo Verde (62.2% [95% UI: 24.1–101.3]), and Monaco (58.2% [95% UI: 19.2–109.7]) having the largest increases. In contrast, Kyrgyzstan (−54.5% [95% UI: −60.9 to −47.8]), Bahrain (−52.1% [95% UI: −64.7 to −34.8]), and Kazakhstan (−49.7% [95% UI: −57.1 to −42]) had decreasing trends (Supplementary Table 2). The percentage change in age-standardized death rates of TBL cancer (from 1990 to 2019) also differed between countries. The largest increases were found in Honduras (67.1% [95% UI: 14.7–133.1]), Cabo Verde (64.4% [95% UI: 25–103.4]), and Mozambique (49.9% [95% UI: 7.9–101.3]). In contrast, the largest decreases during this period were found in Kyrgyzstan (−53.5% [95% UI: −59.8 to −46.8]), Bahrain (−52.1% [95% UI: −64.5 to −34.7]), and Kazakhstan (−49.5% [95% UI: −56.8 to −41.7]) (Supplementary Table 3). Notably, the largest increases in age-standardized DALY rate of TBL cancer from 1990 to 2019 were found in Honduras (55.6% [95% UI: 6–120.2]), and Mozambique (53.6% [95% UI: 7.9–108]). In contrast, Kyrgyzstan (−59.1% [95% UI: −64.9 to −53]), Bahrain (−56.6% [95% UI: −68.3 to −40.2]), and Kazakhstan (−54.9% [95% UI: −61.9 to −47.6]) had largest decreasing trends (Supplementary Table 4).

Age and Sex Patterns

In male individuals, the global annual incidence and death rates of TBL cancer in 2019 increased with population aging up to the 85 to 89 age group, with a declining trend observed up to the oldest group. In contrast, an increasing trend of death rate was observed among female individuals, continuing up to the oldest age groups. Across all age groups, annual incidence and death rates were lower in female than male individuals (from 15 to 95 y), with the largest difference observed in the 85- to 89-year age group (Fig. 4A and B). An increasing trend of global DALY rate owing to TBL cancer in 2019 was found up to the 70- to 74-year and 75- to 79-year age group for male and female individuals, respectively. The global DALY rates were higher in male than female individuals across all age groups as were the number of DALYs from the 15- to 90-year age group, peaking at 65 to 69 years (Supplementary Fig. 2).

Burden of Tracheal, Bronchus, and Lung Cancer by SDI

At the regional level, there was a nonlinear association between age-standardized DALY rate of TBL cancer and SDI. A declining trend of global age-standardized DALY rate was found during 1990 to 2019 with SDI improvement, which reached the lower-than-expected DALY rate on the basis of SDI in 2019. High-income North America, Western Europe, and Central Europe had experienced a decreasing trend between 1990 and 2019, but their actual rates were still higher than the expected rates. Oceania and East Asia had an increasing trend with higher-than-expected DALY rate. Eastern Europe, Southern Latin America, Central Asia, Caribbean, Southern Sub-Saharan Africa, and Central Sub-Saharan Africa reached to lower-than-expected age-standardized DALY rate during 1990 to 2019. Australasia, high-income Asia Pacific, tropical Latin America, Central Latin America, Andean Latin America, South Asia, Eastern Sub-Saharan Africa, and Western Sub-Saharan Africa were regions with lower-than-expected DALY rate on the basis of SDI from 1990 to 2019 (Fig. 5A).

National-level analysis in 2019 found that there was a positive nonlinear association between age-standardized DALY rates of TBL cancer and SDI. Both less developed and developed regions experienced higher-than-expected levels of age-standardized DALY rates on the basis of SDI. This was observed in Greenland, Monaco, Montenegro, Hungary, People’s Republic of China, Honduras, Papua New Guinea, and several other countries. In contrast, countries such as Kuwait, Puerto Rico, Oman, Algeria, India, Nigeria, and any other countries experienced lower-than-expected rates of TBL cancer burden (Fig. 5B).

Risk Factors

Although the percent of attributable DALYs for risk factors was different in the GBD regions, smoking (62.4%), ambient particulate matter (15.3%), and high fasting plasma glucose (9.9%) had the top three highest percent of attributable DALYs in 2019 for both sexes in the globe (Fig. 6). This pattern was relatively similar between both sexes (Supplementary Figs. 3
and 4). In addition, the percentage of DALYs attributable to risk factors in 2019 revealed various patterns across age groups especially for smoking and occupational exposure to asbestos. The highest percent of attributable DALYs for smoking and occupational exposure to asbestos was found in 65 to 69 years and 90 to 94 years, respectively (Fig. 7). The sex-specific estimates of DALYs attributable to risk factor in 2019 were reported in Supplementary Figures 5 and 6.

Figure 4. Global number of (A) incident cases and annual incidence rate and (B) number of deaths and death rate of tracheal, bronchus, and lung cancer per 100,000 population by age and sex, 2019; dotted and dashed lines indicate 95% upper and lower uncertainty intervals, respectively (generated from data available from http://ghdx.healthdata.org/gbd-results-tool). GBD, Global Burden of Disease.
Discussion

Overall, it was found that the number of incident cases, deaths, and DALYs has increased. In contrast, age-standardized rates of annual incidence, death, and DALY are decreasing, which can be attributable to improved interventions and treatments. The Global Cancer Incidence, Mortality, and Prevalence (GLOBOCAN) registry in 2018 estimated 2.1 million incident cases and 1.8 million deaths owing to TBL cancer, which is close to the annual incidence values (2.3 million [95% UI: 2.1–2.5]) and death estimates (2 million [95% UI: 1.9–2.2]) observed in this GBD 2019 study. Comparison of GBD and GLOBOCAN estimations for the same year were not
possible as the GLOBOCAN registry does not provide comprehensive trend data for previous years. For example, annual incidence and death data for some countries have been provided by 2004, 7 2007, 8 and for some selected countries, such as the United States of America, up until 2013. 8 Hence, no previous study has been able to report trends in the annual incidence and death rates attributable to TBL cancer within the recent decade.

Global variation in age-standardized annual incidence rate between countries across these two studies (GBD and GLOBOCAN) was different such that Greenland, Monaco, and Montenegro were considered to have the highest age-standardized annual incidence rates of TBL cancer in 2019, whereas in the GLOBOCAN 2018 study, Hungary, Serbia, and France had the highest age-standardized annual incidence rates. 17 Similarly, in the GBD 2019 study, age-standardized death rates were found to be highest in Greenland, Monaco, and Montenegro, whereas in the GLOBOCAN 2018 study, it was highest in Hungary, Serbia, and France. Of note, the age-standardized annual incidence and death rates reported in GBD and GLOBOCAN cannot be compared as different standard populations have been used; however, the country rank can be compared. The two studies were more consistent in terms of age-standardized annual incidence rates, with higher rates observed for high-income North American, East Asia, Central Europe, and Western Europe within the GBD 2019 study whereas, Oceania, East Asia, Western Europe, and Central and Eastern Europe were considered to have the highest incident rates in GLOBOCAN. The differences in estimations, especially at the country level, can be attributed to input data sources and estimating methodologies used in both studies. 17

When evaluating country-specific profiles, it is possible to categorize these observations into two classes. Within class A, all three age-standardized rates have decreased over time. This was observed in countries such as Kyrgyzstan, Bahrain, and Kazakhstan. In class B, all three measures have increasing trends over time. This was observed in countries such as Honduras, Cabo Verde, and Monaco. Knowing these trends and interactions across countries is fundamental for optimal allocation of scarce societal resources. By evaluating countries with similar characteristics regarding population exposure to lung cancer risk factors, gross domestic product, economic status, and others, it is possible to benchmark a country and then explore factors across similar countries that may be contributing to differences in incidence, death, and DALYs associated with TBL cancer. Hence, national health policymakers should check their countries’ category and make appropriate decisions on the basis of their positioning alongside other countries. In particular, there are several known lung cancer risk factors that can be controlled through public policy initiatives that can reduce the impact of TBL cancer. These include the following: smoking,
ambient particulate matter, low fruit and vegetable consumption, high fasting plasma glucose levels, and exposure to pollutants, such as occupational asbestos, secondhand smoke, household air pollution, radon, occupation silica, occupational diesel, occupational arsenic, occupational nickel, and occupational polycyclic aromatic hydrocarbons. Cigarette smoking is the putative leading modifiable risk factor, as cessation can halve the risk of developing lung cancer within 10 years. Even cessation in later life has been found to reduce the risk of cancer development, whereas smoking cessation among people already diagnosed with lung cancer can still reduce the societal impact of morbidity and premature mortality. Although the global prevalence of tobacco use has reduced by 28.4% and 34.4% during 1990 to 2015 in men and women, respectively, greater success can be achieved through education, increased taxation, and government legislation, such as smoking bans and introduction of plain cigarette packaging. Programs focusing on other modifiable risk factors, such as poor nutrition and reducing exposure to occupational risk factors, particularly where these are known to be poorly managed, have the potential for substantial benefits in reducing the impact of TBL cancer. This is particularly relevant for high-income Asia Pacific, high-income North America, Western Europe, and Australasian regions as tobacco use (smoking) was found to be a very strong risk factor contributing to DALYs. Occupational exposures to asbestos and other pollutants are also areas in dire need for further intervention, particularly in developed countries. Reducing exposure through industry regulation with standardized occupational exposure limits remains a key factor to prevent disease development. Other challenges to reducing the burden of disease include compliance with personal protective equipment among workers, stigma on use of personal protective equipment, medical testing for diseases, and management of conditions, which all desperately require further resource investment and attention. Research should be undertaken to evaluate implementation and program impact for these initiatives on a small scale, to enable cost-effective identification of successful programs that can be scaled up to a population-wide level.

The development level of countries and association with TBL cancer burden is evaluated across some studies using the human development index (HDI), which should be interpreted with caution. First, one of the components of HDI is related to health and therefore should not be used to compare health outcomes between countries. To address this problem, we used SDI instead of HDI. Second, other studies have assumed only linear associations between incidence and mortality with HDI, which may be problematic as there are complex associations between the developing status of countries and burden of diseases. To address this problem, we evaluated the nonlinear association between age-standardized DALY rates of TBL cancer with SDI. Third, previous
studies have not imported all countries in their analysis to evaluate associations between development level and burden of TBL cancer, which may also lead to a biased result. In this regard, results from our study produced two interesting findings. First, although there is a positive association between TBL cancer and the developing status of a county, there were some developed countries that had low rates of TBL cancer burden and vice versa. Second, countries should not be judged on the basis of their observed burden of TBL cancer alone, as the corresponding expected level of burden should be compared to determine whether regions are performing better or worse than expected on the management of TBL cancer.

As with all research, this study had a number of limitations. Detection biases may be partly responsible for variations observed in incidence and mortality rates owing to the changes in screening protocols over time and across countries. There was also a scarcity of data available for some countries included in the GBD, with estimations conducted on the basis of predictive covariates and neighboring locations, which may further reduce the accuracy of this data. However, to our knowledge, this is the most comprehensive and recent data set available that evaluates the annual incidence, death rates, and DALYs associated with TBL cancer and its attributable risk factors over time across a global scale.

In conclusion, substantial fluctuations were observed in the burden of TBL cancer across 204 countries and territories. Although global age-standardized annual incidence, death, and DALYs associated with TBL cancer and its attributable risk factors over time across a global scale.

In conclusion, substantial fluctuations were observed in the burden of TBL cancer across 204 countries and territories. Although global age-standardized annual incidence, death, and DALY rates are decreasing, there were countries found to have increasing trends in age-standardized annual incidence, death, and DALY rates. The data could be used to develop and implement preventive and curative programs. The repeated GBD will provide a means to evaluate these programs and whether they are contributing to a decline in burden.

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Data Availability Statement
Data are available in a public, open-access repository.

Supplementary Data
Note: To access the supplementary material accompanying this article, visit the online version of the Journal of Thoracic Oncology at www.jto.org and at https://doi.org/10.1016/j.jtho.2021.03.030.

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