

Trends in tracheal, bronchial and lung cancer attributed to smoking in South America: Global Burden of Disease analysis 1990-2019

Pedro Rafael Vieira de Oliveira Salerno,¹ Luis Augusto Palma Dallan,¹ Gabriel Tensol Rodrigues Pereira,¹ Paulo Manuel Pego Fernandes,² Ricardo Mingarini Terra,² Sanjay Rajagopalan,¹ Sadeer G Al-Kindi,³ Juliana Vieira de Oliveira Salerno²

Suggested citation Salerno PRVO, Palma Dallan LA, Rodrigues Pereira GT, Pego Fernandes PM, Mingarini Terra R, Rajagopalan S et al. Trends in tracheal, bronchial and lung cancer attributed to smoking in South America: Global Burden of Disease analysis 1990-2019. *Rev Panam Salud Publica*. 2024;48:e30. <https://doi.org/10.26633/RPSP.2024.30>

ABSTRACT

Objective. To investigate the burden of tracheal, bronchus, and lung (TBL) cancer due to tobacco exposure in the last 30 years in 12 South American countries.

Methods. We used the Global Burden of Disease (GBD) 2019 exposure-response function to analyze the total tobacco, smoking, and secondhand smoke exposure-related TBL cancer deaths and disability-adjusted life years (DALYs), for 12 South American countries, between 1990 and 2019. Metrics were described as absolute numbers or rates per 100 000 individuals. The relative change in burden was assessed by comparing the 1990-1994 to 2015-2019 periods.

Results. In 2019, the all-ages number of TBL cancer deaths and DALYs associated with tobacco exposure in South America was 29 348 and 658 204 in males and 14 106 and 318 277 in females, respectively. Age-adjusted death and DALYs rates for the region in 2019 were 182.8 and 4035 in males and 50.8 and 1162 in females, respectively. In males, 10/12 countries observed relative declines in TBL death rates attributed to tobacco exposure while only 4 countries reduced their mortality in females.

Conclusion. While significant efforts on tobacco control are under place in South America, substantial burden of TBL cancer persists in the region with significant sex-specific disparities. Increased country-specific primary data on TBL cancer and tobacco exposure is needed to optimize healthcare strategies and improve comprehension of regional trends.

Keywords

Lung neoplasms; smoking; epidemiology; South America.

Tobacco exposure is associated with a wide range of negative health outcomes and is considered the most significant preventable cause of cancer.(1) Furthermore, according to the Global Burden of Disease (GBD) 2019, it has been considered the main cause of global tracheal, bronchus and lung (TBL) cancer burden in the last 30 years.(2) Smoking and secondhand smoke are considered extremely relevant sources of tobacco exposure and

both have been linked to increase TBL risk. (1,3) Current smoking, for instance, has been associated with an increase of up to 20-fold in lung cancer (LC) mortality.(4) Furthermore, smoking cessation reduces TBL cancer mortality by up to 38% compared to current smokers, indicating a major beneficial effect.(5) In addition, both home and work exposure to secondhand smoke has also been associated with increased LC incidence.(6)

¹ University Hospitals Cleveland Medical Center, Cleveland, United States of America

² Universidade de São Paulo, São Paulo, Brazil. ✉Juliana Vieira de Oliveira Salerno, juliana.salerno1@gmail.com

³ Houston Methodist Hospital, Houston, United States of America

However, considerable global heterogeneity in exposure patterns and burden has been described.(1) While several high-income countries are experiencing decreases in tobacco use and are currently enduring the consequences of past high consumption rates, middle and low-income countries are subject to great variability in their tobacco control status.(1,7) Data availability derived from tobacco-use series are mostly from high-income countries, while lacking for regions such as South America (SA). (8) This is particularly troublesome because LC is the leading cause of cancer death in SA (12.91% of total cancer deaths). Furthermore, since SA is composed of 12 sovereign countries, each with its particular healthcare system, access infrastructure, socioeconomic status, geography, cultural and racial composition, country-specific trends must be examined.(9)

These factors, therefore, contribute to a significant knowledge gap regarding tobacco burden in SA, including its impact in TBL cancer. Thus, in this study, we aimed to investigate the burden of TBL cancer due to tobacco exposure in the last 30 years in 12 SA countries.

METHODS

Data sources

With over 5000 collaborators from 152 countries, the Global Burden of Disease (GBD) is an international initiative that measures disability and death from a multitude of causes.(10) Data from this study was sourced from the GBD 2019 edition that is available online via the Global Health Data Exchange query tool (GHDx, <http://ghdx.healthdata.org/gbd-results-tool>).(11) This tool is capable of generating standardized reports filtered by location, time (1990 to 2019), age and sex following the World Health Organization's (WHO) Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).

TBL cancer burden attributable to tobacco

The GBD 2019 methods for estimating the TBL cancer burden has been previously thoroughly described. (12) In summary, primary input data for the estimates of TBL cancer included multiple cancer registries such as the Cancer Incidence in Five Continents, NORDCAN, and EUREG. (13) International classification of disease (ICD)-10 codes for TBL cancer included C33-C34.9, D02.1-D02.3, D14.2-D14.3, D38.1 and ICD-9 codes included 162-162.9, 212.2-212.3, 231.1-231.2, 235.7. (14) The Cause of Death Ensemble mode (CODEm), the spatiotemporal gaussian process regression (ST-GPR), and the DisMod-MR (a Bayesian meta-regression modelling tool) were the main standardized tool GDB used to generate reports and estimates. (13) The effect of risk factors and their contribution to TBL burden were also estimated. The main contributors to tobacco exposure assessed were smoking and secondhand smoke. Smoking was defined as individuals that currently use any quantity of a tobacco product on a daily or occasional basis and the primary input data derived from 3 625 cross-sectional nationally representative household surveys that described self-reported tobacco use. (12) Secondhand smoke exposure required patients to be considered non-smokers, defined as all individuals who are not daily smokers and with current exposure to secondhand tobacco at home, work or in other public spaces. (12) Primary input data for secondhand smoke was derived from

representative major survey series with household composition module and cross-sectional surveys. (12)

GBD database analysis

Our study included the 12 sovereign countries of SA (Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay, and Venezuela) with data available at the GBD 2019. Using GHDx (11), the age-adjusted prevalence per 100 000 individuals and the age-adjusted Disability adjusted Life years (DALYs) per 100 000 individuals for TBL cancer between 1990 and 2019 were obtained. Age-adjusted prevalence and DALYs rates are provided together with 95% uncertainty intervals (UI). The 95% uncertainty intervals are determined by the 25th and 75th value of the 1000 values after ordering them from smallest to largest. (15) Absolute numbers and rates (per 100 000 individuals) for 5-year age groups were also obtained. Sex-specific disparities were assessed by obtaining data for females and males. Furthermore, besides analyzing the burden of TBL cancer due to tobacco, we evaluated the contribution of smoking and secondhand smoke to TBL prevalence and DALYs.

To evaluate the trends for HF prevalence and DALYs, we calculated the relative percentage change over the study period as:

$$\left[\frac{\text{age adjusted prevalence (1990-1994)} - \text{age adjusted prevalence 2015-2019}}{\text{age adjusted prevalence (1990-1994)}} \right] * 100$$

$$\left[\frac{\text{age adjusted YLDs(1990-1994)} - \text{age adjusted YLDs2015-2019}}{\text{age adjusted YLDs(1990-1994)}} \right] * 100$$

The 95% confidence interval (CI) for the relative change was calculated using the delta method.

Statistical analysis was performed using R 4.1.2 (2021) (The R Foundation for Statistical Computing) using the following packages: sf, ggplot2, ggthemes, ggprism, dplyr, cowplot. Due to the nature of the publicly available data, no institutional Review Board approval was necessary.

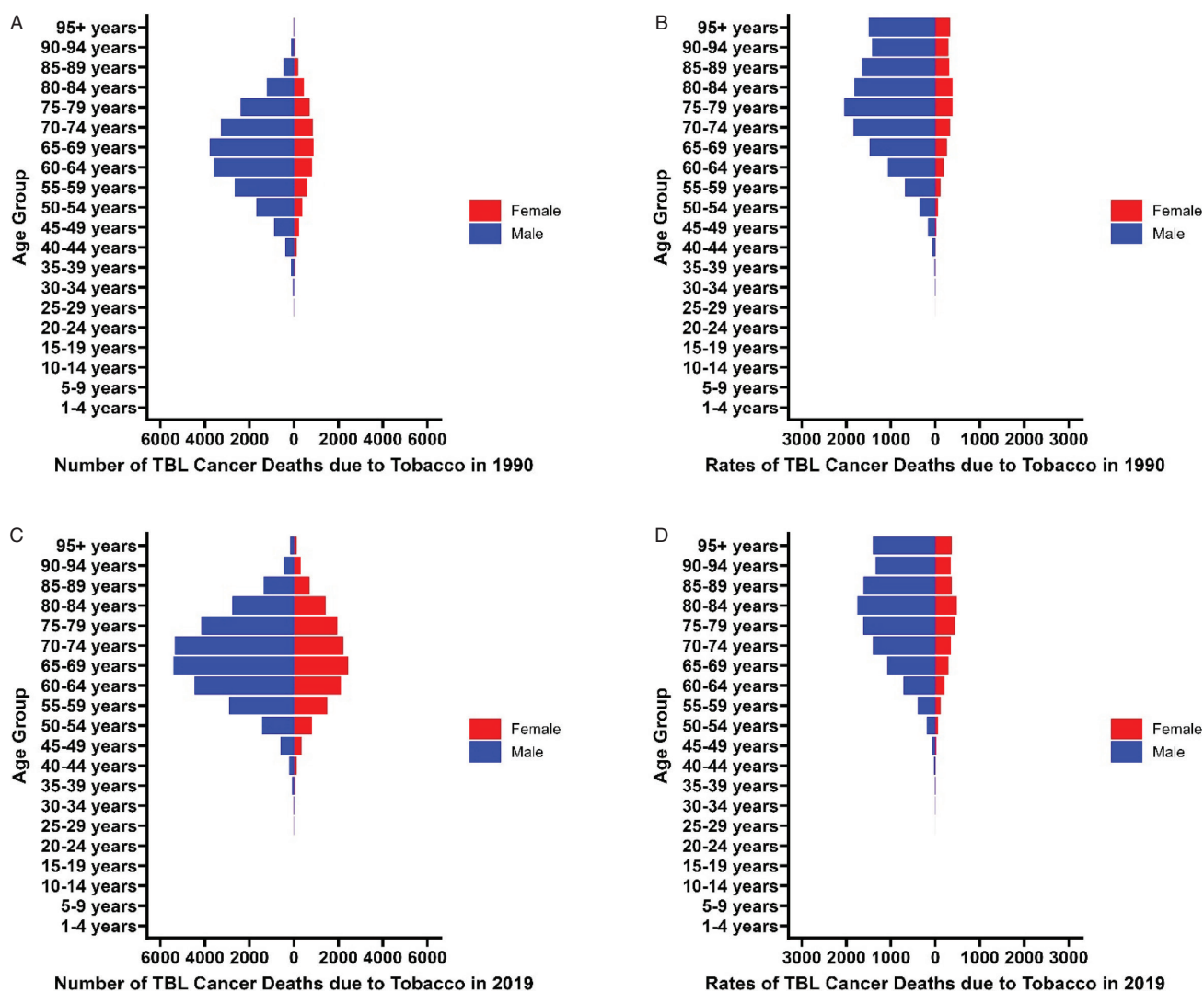
RESULTS

TBL cancer deaths due to tobacco exposure in 2019 and relative change

In 2019, the total, all ages, number of TBL cancer deaths associated with tobacco exposure in South America was 29 348 in males and 14 106 in females. The age-adjusted death rate (per 100 000 individuals) for the region in 2019 was 182.8 in males and 50.8 for females. The sex-specific 5-year absolute number of deaths and death rates for 1990 and 2019 is presented in Figure 1 and the longitudinal trends in age-adjusted death and DALYs rates for the region are showed in Figure 2. Country-specific trends in age-adjusted deaths for 1990, 2000, 2010 and 2019 are mapped in Figure 3.

Supplemental Table 1 describes the age-adjusted death and DALY rates for TBL due to exposure to tobacco. In males, Uruguay had the highest age-adjusted death rate 42.6 (95%UI, [39.5, 45.7]) followed by Argentina 28.8 (95%UI [26.8, 31.1]). Meanwhile, Peru (3.6, 95%UI [2.5, 5.0]) and Guyana (6.6, 95%UI [5.1, 8.4]) had the lowest. In females, Uruguay (9.1, 95%UI [8.2, 10.1])

FIGURE 1. The absolute death and death rates (per 100 000 individuals) for 5-year age groups for South America as a region, for males and females in 1990 (A, B) and 2019 (C, D)



and Argentina (8.8, 95%UI [7.8, 9.8]) persisted as the countries with the highest death burden while Peru (0.9, 95%UI [0.6, 1.3]) and Bolivia (1.2, 95%UI [0.7, 1.9]) had the lowest.

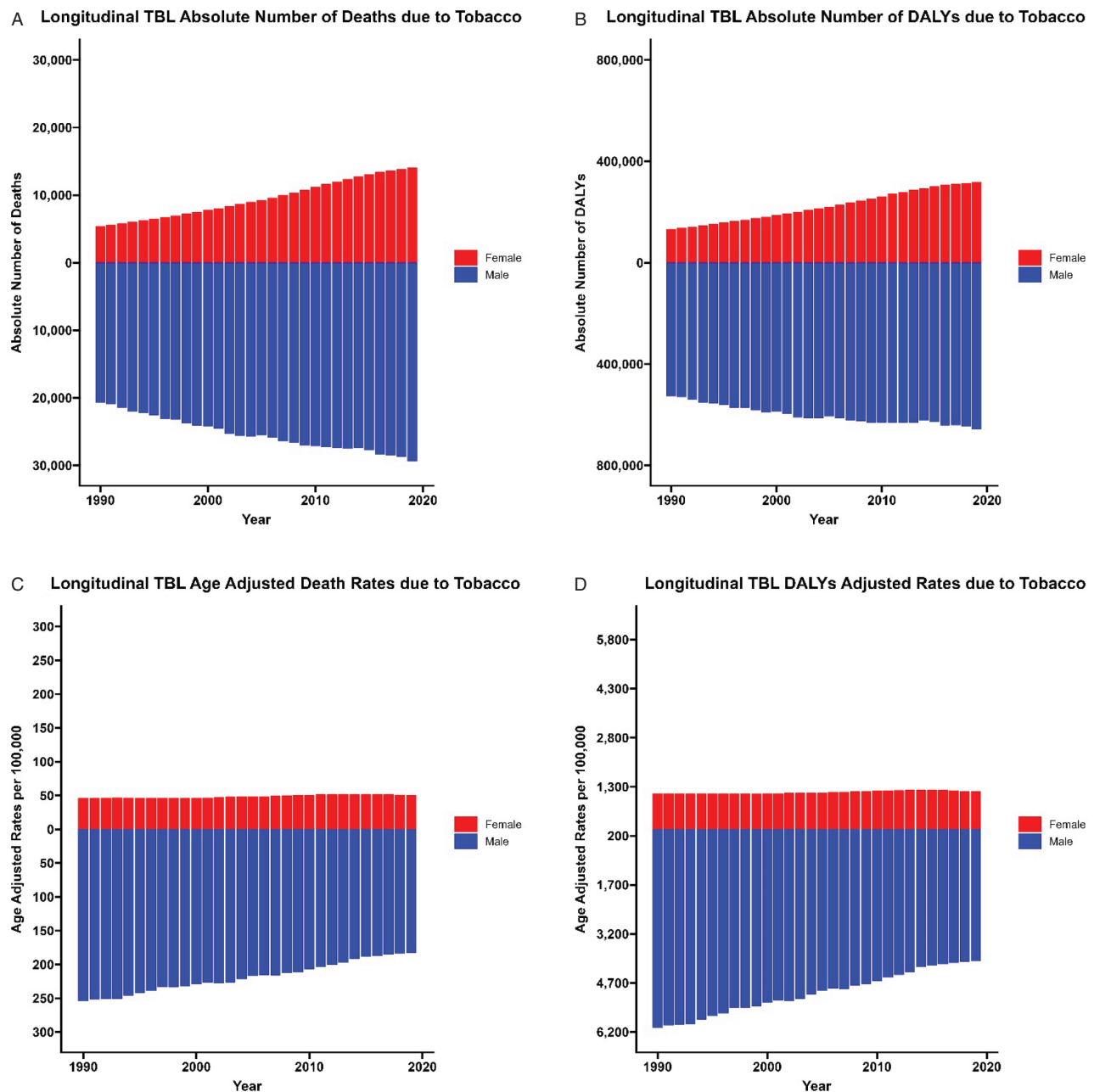
Supplemental Table 2 describes the relative change in death and DALYs rates comparing 1990-1994 to 2015-2019 across SA. When comparing 1990-1994 to 2015-2019 periods in males (Figure 4A, 4C), while most of the countries of SA markedly decreased the TBL cancer age-adjusted death rates associated with tobacco exposure, especially Colombia (-48.7%, 95%CI [-52.0, -45.3]) and Peru (-45.5%, 95%CI [-50.5, -40.5]), Suriname (3.4%, 95%CI [-1.8, 8.6]) and Paraguay (34%, 95%CI [29.7, 38.5]) distinguished themselves by observing relative increases in TBL deaths. In females, stark contrast was noted, and an opposite trend was observed with only 4 of the 12 countries experiencing relative declines in TBL deaths associated with tobacco exposure. With the largest decreases observed in Peru (-25.2, 95%CI [-29.6, -20.9]) and Colombia (-38.5, 95%CI [-41.2, -35.9]) and the largest increases observed in Uruguay (74.7, 95%CI [71.7, 77.7]) and Argentina (36.1, 95%CI [34.2, 38.0]).

TBL cancer DALYs due to tobacco exposure in 2019 and relative change

In 2019, the total, all ages, number of TBL cancer DALYs associated with tobacco exposure in South America was 658 204 in males and 318 277 in females. The age-adjusted DALYs rate (per 100 000 individuals) for the region in 2019 was 4035 in males and 1162 for females. In males, Uruguay (1000, 95%UI [925, 1076]) and Argentina (654, 95%UI [605, 704]) had the highest DALYs burden while Ecuador (128, 95%UI [98, 166]) and Peru (73, 95%UI [50, 103]) had the lowest. In females, Uruguay (224, 95%UI [200, 252]) and Argentina (216, 95%UI [192, 240]) were also the countries with the highest DALYs rates while Bolivia (27, 95%UI [15, 42]) and Peru (20, 95%UI [13, 29]) had the lowest.

When comparing 1990-1994 to 2015-2019 periods in males (Figure 4B, 4D), most countries also decreased the DALYs rate, in particular Colombia (-52.1%, 95%CI [-55.6, -48.5]) and Peru (-49.7%, 95%CI [-55.0, -44.4]). However, Suriname (1.8%, 95%CI [-3.7, 7.3]) and Paraguay (24.1%, 95%CI [19.4, 28.8]), again

FIGURE 2. Longitudinal trends (1990-2019), for South America as a region, of death and DALYs absolute, all ages, number (A, B) and age-standardized rates (per 100 000 individuals) (C, D)



experienced increases in DALYs burden attributed to tobacco. In females, substantial regional heterogeneity in SA was evident concerning TBL DALYs associated with tobacco exposure. With the largest decreases observed in Peru (-29.7%, 95%CI [-33.7, -25.7]) and Colombia (-42.6%, 95%CI [-45.8, -39.4]) and the largest increases observed in Uruguay (75.7%, 95%CI [72.4, 79.0]) and Argentina (33.3%, 95%CI [31.2, 35.5]).

TBL cancer deaths due to smoking exposure in 2019 and relative change

The longitudinal cumulative TBL death rate for SA attributable to smoking and secondhand smoke, according to sex,

is displayed in Figure 6. The age-adjusted rates for TBL cancer deaths and DALYs due to smoking in 2019 are exposed in Supplemental Table 3 and the relative change is displayed in Supplemental Table 4. In 2019, Argentina (28.2, 95%UI [26.1, 30.4]) and Uruguay (41.7, 95%UI [38.6, 44.7]) suffered with the highest age-adjusted death rates due to smoking exposure in males. While the lowest rates were found in Bolivia (1.1, 95%UI [0.6, 1.7]) and Peru (0.7, 95%UI [0.5, 1.0]). In females, the highest death rates were in Argentina (8.8, 95%UI [7.9, 9.7]) and Uruguay (8.3, 95%UI [7.4, 9.3]) and the lowest rates were found in Guyana (6.4, 95%UI [4.9, 8.1]) and Peru (3.5, 95%UI [2.4, 4.8]).

The relative change in TBL cancer deaths attributed to smoking is exposed in Supplemental Figure 1. In males, apart from

FIGURE 3. Sex-specific longitudinal trends (1990, 2000, 2010, 2019) in age adjusted death rates (per 100 000 individuals) for South American countries

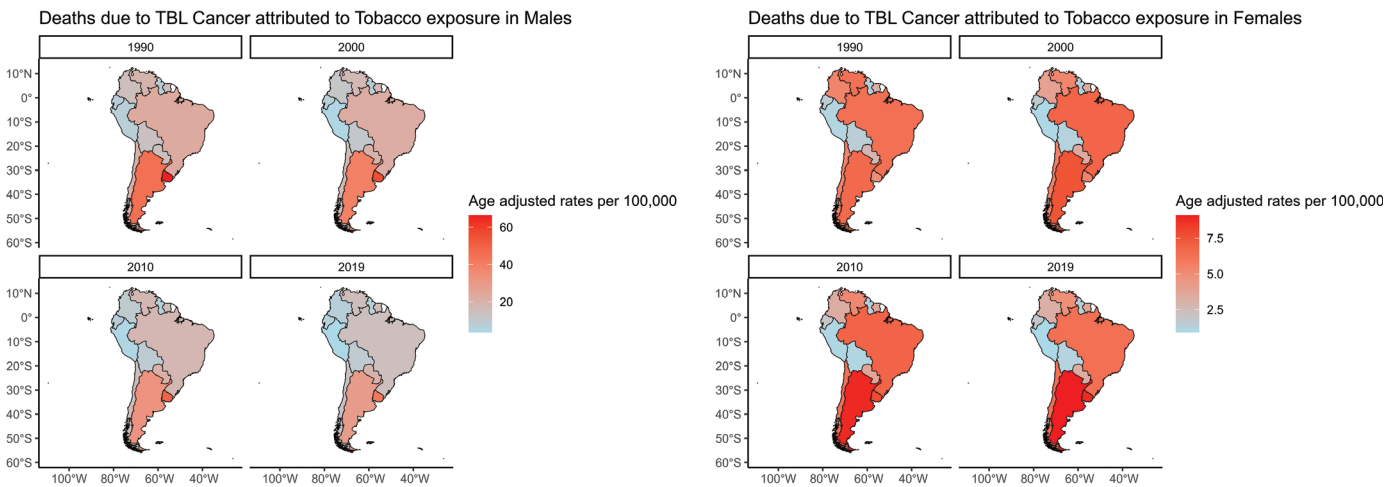
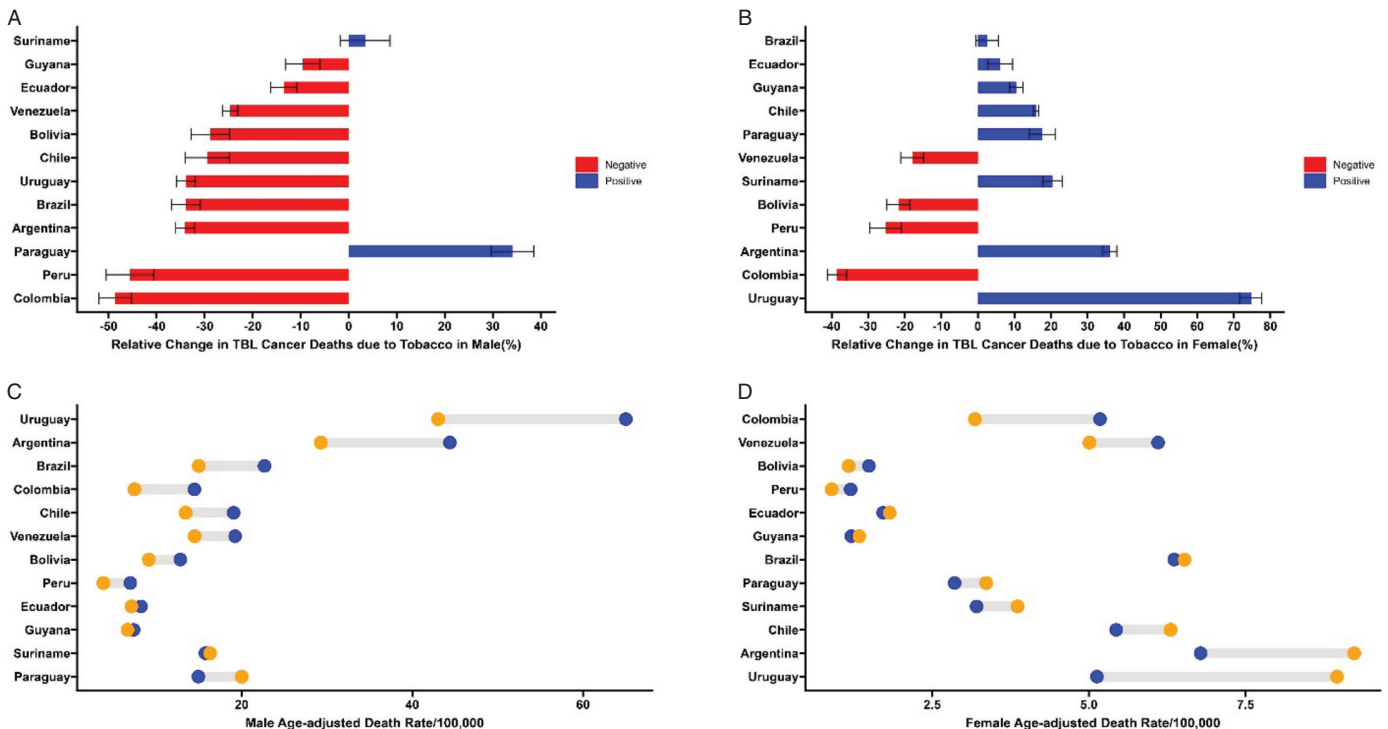


FIGURE 4. (A and B) Relative change in TBL cancer deaths rates (%) attributable to tobacco in South America comparing the periods from 1990-1994 and 2015-2019 in male and female patients. (C and D) TBL cancer age-adjusted death rates (per 100 000 individuals) due to tobacco in male and female patients. The blue dots represent the mean 5-year period for 1990-1994 and the orange dots represent the 2015-2019 period



Suriname (3.9%, 95%CI [-1.4, 9.1]) and Paraguay (33.4%, 95%CI [29.0, 37.9]), all countries experienced relative declines comparing 1990-1994 and 2015-2019. The largest declines were observed in Colombia (-49.4%, 95%CI [-52.9, -46.0]) and Peru (-45.1%, 95%CI [-50.2, -40.1]). In females, on the other hand, only one-fourth of the countries experienced relative declines. Colombia (-39.9%, 95%CI [-42.6, -37.2]) and Bolivia (-23.2%, 95%CI [-26.4, -20.0]) experienced the highest decreases. While Argentina (37.4%,

95%CI [35.5, 39.3]) and Uruguay (78%, 95%CI [74.8, 81.2]) led the countries with the highest relative increases in age-adjusted rates.

TBL cancer DALYs due to smoking exposure in 2019 and relative change

In 2019, Argentina (640.1, 95%UI [591.4, 688.7]) and Uruguay (978.9, 95%UI [905.5, 1052.3]) suffered with the highest

FIGURE 5. (A and B) Relative change in TBL cancer DALYs rates (%) attributable to tobacco in South America comparing the periods from 1990-1994 and 2015-2019 in male and female patients. (C and D) TBL cancer age adjusted DALYs rates (per 100 000 individuals) due to tobacco in male and female patients. The blue dots represent the mean 5-year period for 1990-1994 and the orange dots represent the 2015-2019 period

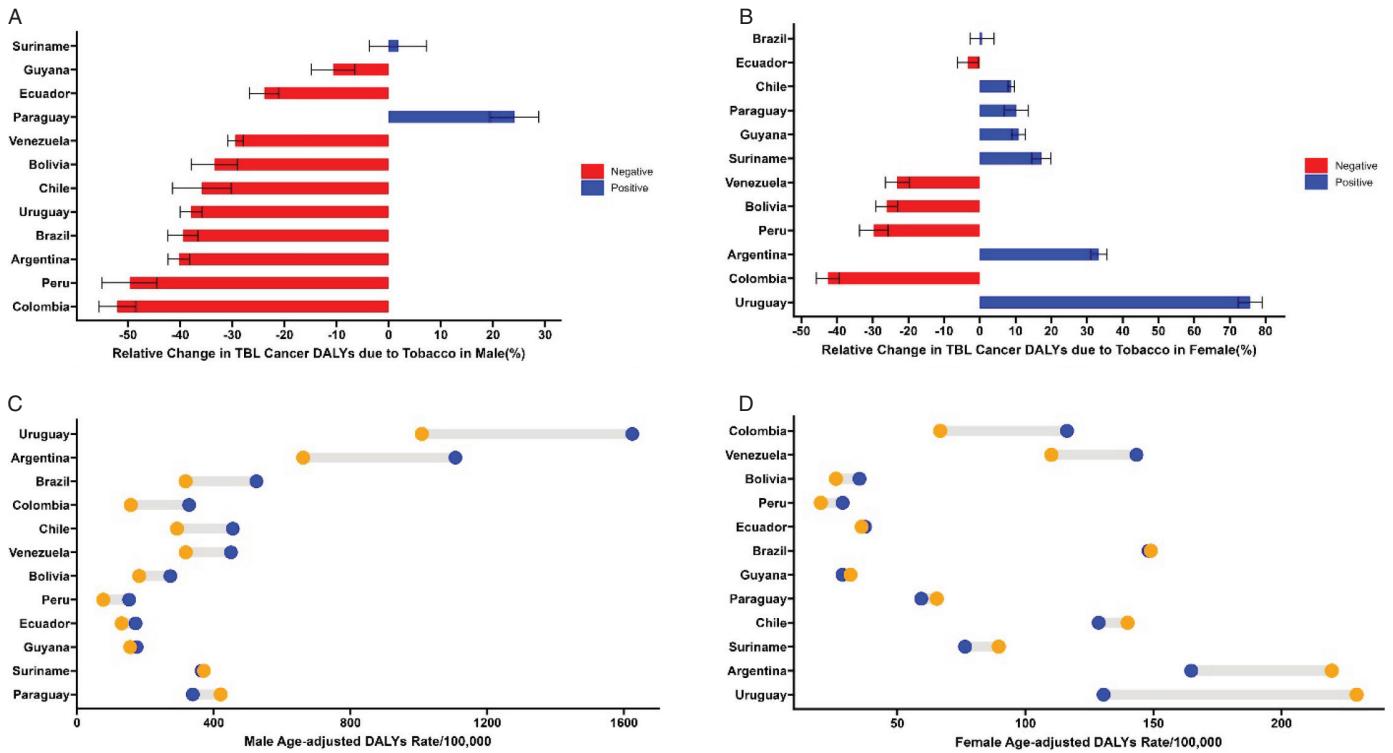
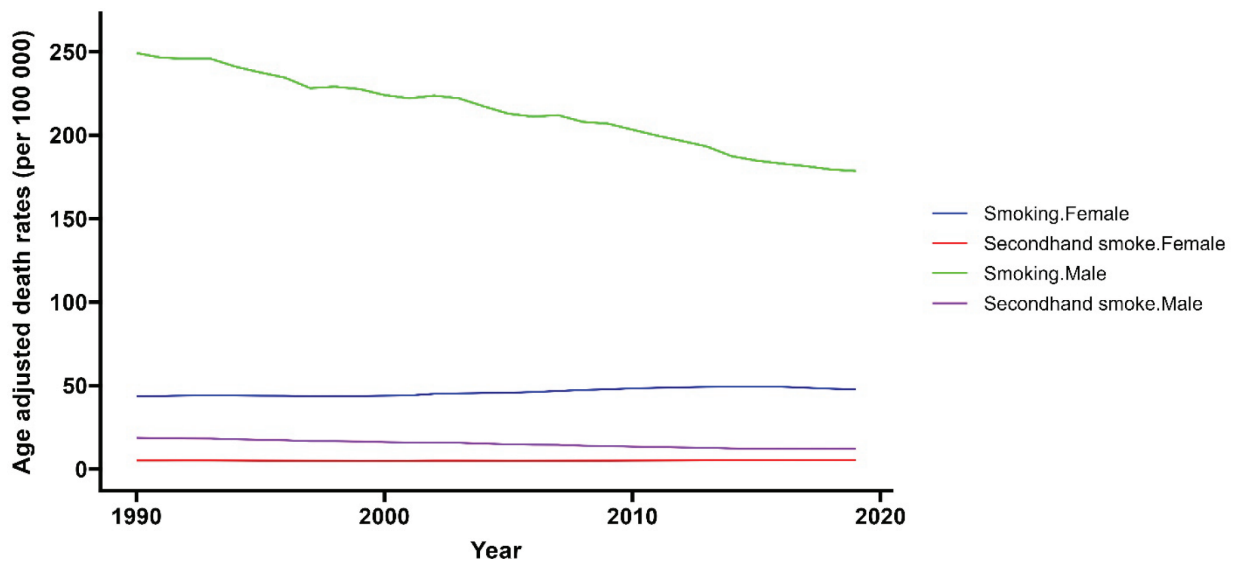


FIGURE 6. Longitudinal cumulative TBL cancer death rate (per 100 000) for South America due to smoking and secondhand smoke, according to sex



age-adjusted DALYs rates due to smoking exposure in males. The lowest rates were found in Ecuador (126.3, 95%UI [96.9, 163.6]) and Peru (69.5, 95%UI [47.1, 98.1]). In females, the highest death rates were in Argentina (208.3, 95%UI, [185.2, 231.8]) and Uruguay (212.7, 95%UI [188.8, 238.5]) and the lowest rates

were found in Guyana (16, 95%UI [10.2, 23.9]) and Peru (26.8, 95%UI [19.3, 36.7]).

The relative change in TBL cancer DALYs attributed to smoking is exposed in Supplemental Figure 2. In males, apart from Suriname (2.3%, 95%CI [-3.3, 7.9]) and Paraguay (23.4%,

95%CI [18.6, 28.1]), all countries experienced relative declines comparing 1990-1994 and 2015-2019. The largest declines were observed in Colombia (-52.8%, 95%CI [-56.4, -49.2]) and Peru (-49.3%, 95%CI [-54.7, -44.0]). In females, half of the countries experienced relative declines. Colombia (-43.9%, 95%CI [-47.2, -40.7]) and Bolivia (-27.8%, 95%CI [-30.8, -24.8]) experienced the highest decreases. While Argentina (34.5%, 95%CI [32.4, 36.8]) and Uruguay (78.7%, 95%CI [75.2, 82.2]) had the highest relative increases in age-adjusted DALYs rates.

TBL cancer deaths due to secondhand smoke exposure in 2019 and relative change

The age-adjusted rates for TBL cancer deaths and DALYs due to secondhand smoke in 2019 are exposed in Supplemental Table 5 and the relative change is displayed in Supplemental Table 6. In 2019, Argentina (2.1, 95%UI [1.2, 3.3]) and Uruguay (3.4, 95%UI [2.0, 5.2]) also had the highest age adjusted death rates due to secondhand smoke exposure in males. The lowest rates were found in Peru (0.2, 95%UI [0.1, 0.4]) and Ecuador (0.2, 95%UI [0.1, 0.3]). In females, the highest death rates were again in Argentina (0.8, 95%UI, [0.5, 1.2]) and Uruguay (1.0, 95%UI [0.6, 1.5]) and the lowest rates were found in Bolivia (0.1, 95%UI [0.1, 0.3]) and Ecuador (0.1, 95%UI [0.1, 0.2]).

The relative change in TBL cancer deaths attributed to secondhand smoke is displayed in Supplemental Figure 3. In males, apart from Paraguay (52.4%, 95%CI [49.0, 55.9]), all countries experienced relative declines comparing 1990-1994 and 2015-2019. The largest declines were seen in Brazil (-47.5%, 95%CI [-50.1, -45.0]) and Peru (-56.5%, 95%CI [-61.6, -51.6]). In females, substantial disparities were observed and only ½ of the countries experienced relative declines. Ecuador (-26.7%, 95%CI [-29.4, -24.0]) and Peru (-37.3%, 95%CI [-42.0, -32.7]) experienced the highest decreases. Meanwhile, Uruguay (40.0%, 95%CI [38.2, 41.9]) and Paraguay (25.6%, 95%CI [21.3, 29.9]) were the countries with the highest relative increases in age-adjusted rates.

TBL cancer DALYs due to secondhand smoke exposure in 2019 and relative change

In 2019, Argentina (47.6, 95%UI [27.1, 75.2]) and Uruguay (80.7, 95%UI [47.4, 121.4]) presented the highest age-adjusted DALYs rates due to secondhand smoke exposure in males. The lowest rates were in Peru (4.7, 95%UI [2.0, 9.1]) and Ecuador (3.9, 95%UI [1.7, 7.0]). In females, the highest DALYs rates were in Argentina (19.4, 95%UI, [11.3, 29.7]) and Uruguay (24.7, 95%UI [14.5, 37.6]) and the lowest rates were found in Bolivia (3.7, 95%UI [1.6, 7.1]) and Ecuador (3.0, 95%UI [1.4, 5.3]).

The relative change in TBL cancer DALYs attributed to secondhand smoke is displayed in Supplemental Figure 4. In males, with the exception from Paraguay (41.3%, 95%CI [37.4, 45.2]), all countries observed relative declines comparing 1990-1994 and 2015-2019. The largest declines were seen in Brazil (-51.3%, 95%CI [-54.2, -48.5]) and Peru (-58.4%, 95%CI [-63.7, -53.1]). In females, 5 countries observed relative increases in DALYs rates. Uruguay (42.1%, 95%CI [40.0, 44.2]) and Paraguay (20.8%, 95%CI [16.5, 25.3]) experienced the highest increases. Meanwhile, Ecuador (32.0%, 95%CI [-34.4, -29.5]) and Peru (41.0%, 95%CI [-45.2, -36.7]) were the countries with the highest relative decreases in age-adjusted rates.

DISCUSSION

In this GBD analysis, we assessed the sex-specific trends in TBL cancer attributed to total tobacco, smoking, and secondhand smoke exposure in SA. As a region, while the absolute death and DALYs numbers for total tobacco exposure increased from 1990 to 2019, the age-adjusted rates decreased. Notwithstanding, there was substantial heterogeneity in country-level and sex-specific patterns of relative change. For instance, in males, only Suriname and Paraguay presented relative increases in TBL age-adjusted mortality rates, while 8 of the 12 SA countries had increases in females.

Our data resonates with global trends of increasing TBL cancer prevalence in women and a decreasing prevalence in men. (1) In fact, the female-to-male incidence ratio has also been narrowing in the world,(16) with multiple factors likely involved in this process. While smoking rates are decreasing throughout the world, the pace has been slower in females.(12) Several studies show that women are at higher risk for LC at the same level of smoking than men, especially in younger age groups.(17) Additionally, multiple biological pathways have been hypothesized to help understand what may be contributing to increased female susceptibility; these involve hormonal and genetic factors, as well as molecular changes. However, significant gaps in the understanding of the pathogenesis behind male and female TBL cancer differences persist.(18) Nevertheless, overall higher incidence and mortality rates are experienced in males.(19) Micheli et al. found that the earlier age at diagnosis for females was the main determinant for this increased LC survival.(19) Female patients have also been associated with higher surgical treatment rates, lower immunotherapy use rates and higher rates of endocrine complications after immunotherapy.(20)

South America is a diverse region of 12 countries with unique challenges. Healthcare systems vary considerably. Brazil provides universal coverage to all its citizens through the Sistema Único de Saúde (SUS); however, about 25% of its population relies on private health insurance. Other countries, such as Chile, ensure health access for selected diseases for their population, and Colombia provides care for its population through a contributive (more comprehensive healthcare) and a subsidized scheme.(21) While Brazil spends about 9% of its gross-domestic product in healthcare, Venezuela spends about 5%, with considerable differences in the proportion of the expenditure coming from public or private sources.(21) In addition, population in the region remains vulnerable due to gaps in access to cancer prevention strategies, treatment, early diagnosis, and palliative care services. There is sparse availability of molecular testing and targeted agents.(22) The low investment in cancer research is a major barrier to tailored strategies in SA countries, representing 3.4 times less than in developed countries.(22) Most SA countries lack population-based cancer registries, with only 7% of the population represented compared to 96% in the US registries. To understand the distribution and characteristics of the risk populations may efficiently target the screening groups and thus use appropriately the limited resources available.(22) Despite the obstacles to clinical trials, SA is a very appealing region for research with singular epidemiology, high-density population, ethnic and genetic diversity, and a prominent potential for patient recruitment.(22)

Tobacco consumption accounts for 84% of LC deaths in Latin America (which includes SA), but its use rates vary widely in

the region.(21) Overall, data from 2005 shows that Chile (35%) and Peru (33.8%) had the highest rates of adult smoking, with Ecuador (4.5%) and Paraguay (15.5%) had the lowest.(21) Differences in sex-specific smoking patterns are also notable, with large differences in consumption between males and females in Peru (males 52.5% vs. females 17.8%) and Paraguay (males 23.6% vs. females 7.4%) and narrow differences in Bolivia (males 31% vs. 28.6%) and Venezuela (males 26.7% vs. females 23.3%).(21) In fact, in urban centers such as Santiago (Chile) and Buenos Aires (Argentina), male-female smoking rates have become very similar.(21) SA also plays an important role in the production of tobacco, having 3 of the 25 largest producers in the world (Brazil, Argentina, and Ecuador). Brazil, in particular, stands out as the largest exporter of tobacco in the world.(23) Beyond the traditional market, tobacco smuggling also poses a significant challenge in the region. For instance, 87.5% of Paraguay's 40 billion cigarettes' final destination is unknown.(24)

Effective tobacco control in SA involves complex regional and international dynamics. Most of the constitutions of SA countries guarantee some form of access to healthcare; therefore, attempts to control tobacco exposure can be viewed as part of a greater public health agenda and several regional programs exist.(25) The approval of the "Smoke-free Americas" framework in 2001 by all member states of the Pan American Health Organization (PAHO), was an important step in organizing tobacco control efforts in the region.(25) In 2005, the creation and gradual adoption by the majority of the SA countries of the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC) solidified the path for more effective measures.(26) This and other collective efforts, culminated in SA achieving 100% of smoke-free environments in 2022.(25) While it is important to recognize the remarkable progress in tobacco exposure control, continued efforts are still needed, especially the development of strategies to tackle the troublesome smoking rates in females.

Exposure to secondhand smoke has been widely considered as a health hazard and public health environmental risk factor.(27) It can be further classified into mainstream smoke, exhaled by the smoker, and sidestream smoke, emitted by the tip of the cigarette.(28) The latter is derived from an incomplete combustion and produces a greater density of at least 17 carcinogens compared to mainstream smoke.(29) Our study demonstrates that, at a populational level, the burden of secondhand smoke exposure, although small, is not negligible and likely underestimated. A recent meta-analysis found a 16% increase in cancer risk in non-smokers exposed to secondhand smoke, with a stronger association in females (OR 1.253, 95%CI 1.142–1.374) and in LC (OR 1.245, 95%CI 1.026–1.511).(27) Furthermore, insights from South Korea show that adolescents with low-educated parents

were at higher risks of household secondhand smoke exposure, demonstrating that social factors play an important role in burden disparities.(30) Thus, contributing to the understanding that to truly grasp the scope of the health impacts of smoking we must also consider those surrounding the smokers.(30–32)

This study has some limitations. It presents a comprehensive review of the TBL cancer burden in SA based on the GBD; however, it is likely underestimated due to different methods of data registration management in each country. Other limitations include the fact GBD groups tracheal, bronchus and LC together as TBL, limiting the individual assessment of the specific cancer burden. Lack of high-quality primary data also leads to broad uncertainty intervals and raises awareness to the urgent need of local studies. Lastly, this study does not capture the existing geographic disparities within the studied countries.

In conclusion, while substantial efforts in tobacco control are under place in SA, the region continues to grapple with a significant burden of TBL cancer, exacerbated by substantial sex-specific disparities. Future research efforts are greatly needed to generate country-specific primary data on TBL cancer and tobacco exposure. Thus, allowing for a greater understanding of local trends, facilitating the development of targeted interventions tailored to geographic and sex-specific factors, and optimizing healthcare strategies to effectively address this pressing issue.

Data availability. Supplemental data for this article can be found at <https://github.com/prvosalerno/lungcancerSA>. Global Burden of Disease data is available at <http://ghdx.healthdata.org/gbd-results-tool>.

Authors contributions. PRVOS: conceptualization, data curation, formal analysis, investigation, methodology, writing—original draft, writing—review and editing; LAPD: conceptualization, writing—review and editing; GT: conceptualization, writing—review and editing; PMPF: conceptualization, writing—review and editing; RMT: conceptualization, writing—review and editing; SR: Conceptualization, Writing, review and editing; SGA: conceptualization, supervision, writing, review and editing; JVOS: conceptualization, supervision, writing—original draft, writing—review and editing. All authors approved the final version prior to publication.

Conflicts of interest. None declared.

Disclaimer. The opinions expressed in this manuscript are solely the authors' responsibility and do not necessarily reflect the views or policies of the Pan American Journal of Public Health or the Pan American Health Organization.

REFERENCES

- Deng Y, Zhao P, Zhou L, Xiang D, Hu J, Liu Y, et al. Epidemiological trends of tracheal, bronchus, and lung cancer at the global, regional, and national levels: a population-based study. *J Hematol Oncol*. 2020;13:98. doi: 10.1186/s13045-020-00915-0
- Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Lond Engl*. 2020;396(10258):1204–22. doi: 10.1016/S0140-6736(20)30925-9
- Perez-Warnisher MT, de Miguel M del PC, Seijo LM. Tobacco Use Worldwide: Legislative Efforts to Curb Consumption. *Ann Glob Health*. 84(4):571-579. doi: 10.9204/aogh.2362
- Yang JJ, Yu D, Wen W, Shu XO, Saito E, Rahman S, et al. Tobacco Smoking and Mortality in Asia. *JAMA Netw Open*. 2019 Mar 29;2(3):e191474. doi: 10.1001/jamanetworkopen.2019.1474
- Huang S, Tang O, Zheng X, Li H, Wu Y, Yang L. Effectiveness of smoking cessation on the high-risk population of lung cancer with

- early screening: a systematic review and meta-analysis of randomized controlled trials until January 2022. *Arch Public Health*. 2023;81:101. doi: 10.1186/s13690-023-01111-5
6. Sheng L, Tu JW, Tian JH, Chen HJ, Pan CL, Zhou RZ. A meta-analysis of the relationship between environmental tobacco smoke and lung cancer risk of nonsmoker in China. *Medicine (Baltimore)*. 2018;97(28):e11389. doi: 10.1097/MD.00000000000011389
 7. Warren GW, Cummings KM. Tobacco and Lung Cancer: Risks, Trends, and Outcomes in Patients with Cancer. *Am Soc Clin Oncol Educ Book*. 2013;(33):359–64. doi: 10.14694/EdBook_AM.2013.33.359
 8. Giraldo-Osorio A, Pérez-Ríos M, Rey-Brandariz J, Varela-Lema L, Montes A, Rodríguez-R A, et al. Smoking-attributable mortality in South America: A systematic review. *J Glob Health*. 2021;11:04014. doi: 10.7189/jogh.11.04014
 9. Riano I, Velazquez AI, Viola L, Abuali I, Jimenez K, Abioye O, et al. State of Cancer Control in South America. *Hematol Oncol Clin North Am*. 2024 Feb;38(1):55–76. doi: 10.1016/j.hoc.2023.05.013
 10. Institute for Health Metrics and Evaluation [Internet]. 2014 [cited 2023 Mar 29]. GBD History. Available from: <https://www.healthdata.org/gbd/about/history>
 11. Institute for Health Metrics and Evaluation [Internet]. [cited 2023 Apr 19]. GBD Results. Available from: <https://vizhub.healthdata.org/gbd-results>
 12. Global, regional, and national burden of respiratory tract cancers and associated risk factors from 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Respir Med*. 2021 Sep;9(9):1030–49.
 13. Khanmohammadi S, Saeedi Moghaddam S, Azadnajafabad S, Rezaei N, Esfahani Z, Rezaei N, et al. Burden of tracheal, bronchus, and lung cancer in North Africa and Middle East countries, 1990 to 2019: Results from the GBD study 2019. *Front Oncol*. 2023;12:1098218. doi: 10.3389/fonc.2022.1098218
 14. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Cause List Mapped to ICD Codes [Internet]. Institute for Health Metrics and Evaluation (IHME); 2020 [cited 2023 May 30]. Available from: <http://ghdx.healthdata.org/record/ihme-data/gbd-2019-cause-icd-code-mappings>
 15. von der Lippe E, Devleeschauwer B, Gourley M, Haagsma J, Hilderink H, Porst M, et al. Reflections on key methodological decisions in national burden of disease assessments. *Arch Public Health*. 2020 Dec 31;78(1):137. doi: 10.1186/s13690-020-00519-7
 16. MacRosty CR, Rivera MP. Lung Cancer in Women: A Modern Epidemic. *Clin Chest Med*. 2020 ;41(1):53–65. doi: 10.1016/j.ccm.2019.10.005
 17. Stapelfeld C, Dammann C, Maser E. Sex-specificity in lung cancer risk. *Int J Cancer*. 2020;146(9):2376–82. doi: 10.1002/ijc.32716
 18. Ragavan M, Patel MI. The evolving landscape of sex-based differences in lung cancer: a distinct disease in women. *Eur Respir Rev*. 2022 ;31(163):210100. doi: 10.1183/16000617.0100-2021
 19. Micheli A, Ciampichini R, Oberaigner W, Ciccolallo L, de Vries E, Izarzugaza I, et al. The advantage of women in cancer survival: An analysis of EUROCARE-4 data. *Eur J Cancer*. 2009;45(6):1017–27. doi: 10.1016/j.ejca.2008.11.008
 20. Stabellini N, Bruno DS, Dmukauskas M, Barda AJ, Cao L, Shanahan J, et al. Sex Differences in Lung Cancer Treatment and Outcomes at a Large Hybrid Academic-Community Practice. *JTO Clin Res Rep*. 2022 Mar 9;3(4):100307. doi: 10.1016/j.jtocrr.2022.100307
 21. Goss PE, Lee BL, Badovinac-Crnjevic T, Strasser-Weippl K, Chavarri-Guerra Y, Louis JS, et al. Planning cancer control in Latin America and the Caribbean. *Lancet Oncol*. 2013 Apr;14(5):391–436. doi: 10.1016/S1470-2045(13)70048-2
 22. Raez LE, Cardona AF, Santos ES, Catoe H, Rolfo C, Lopes G, et al. The burden of lung cancer in Latin-America and challenges in the access to genomic profiling, immunotherapy and targeted treatments. *Lung Cancer*. 2018;119:7–13. doi: 10.1016/j.lungcan.2018.02.014
 23. The Observatory of Economic Complexity [Internet]. [cited 2024 Feb 1]. Raw Tobacco (HS: Tobacco,) Product Trade, Exporters and Importers. Available from: <https://oec.world/en>
 24. Müller F, Wehbe L. Smoking and smoking cessation in Latin America: a review of the current situation and available treatments. *Int J Chron Obstruct Pulmon Dis*. 2008;3(2):285–93. doi: 10.2147/copd.s2654
 25. Severini G, Sandoval RC, Sónora G, Sosa P, Gutkowski P, Severini L, et al. Towards a smoke-free world? South America became the first 100% smoke-free subregion in the Americas. *Rev Panam Salud Pública*. 2022;46: e103. doi: 10.26633/RPSP.2022.103
 26. WHO Framework Convention on Tobacco Control, Organization WH. WHO Framework Convention on Tobacco Control [Internet]. World Health Organization; 2003 [cited 2023 Jul 12]. Available from: <https://apps.who.int/iris/handle/10665/42811>
 27. Kim AS, Ko HJ, Kwon JH, Lee JM. Exposure to Secondhand Smoke and Risk of Cancer in Never Smokers: A Meta-Analysis of Epidemiologic Studies. *Int J Environ Res Public Health*. 2018 Sep;15(9):1981. doi: 10.3390/ijerph15091981
 28. Mohtashamipur E, Mohtashamipur A, Germann PG, Ernst H, Norpoth K, Mohr U. Comparative carcinogenicity of cigarette mainstream and sidestream smoke condensates on the mouse skin. *J Cancer Res Clin Oncol*. 1990;116(6):604–8. doi: 10.1007/BF01637081
 29. Nelson E. The miseries of passive smoking. *Hum Exp Toxicol*. 2001 Feb 1;20(2):61–83. . doi: 10.1191/096032701670538508
 30. Kim H, Kang H, Choi J, Cho S il. Trends in adolescent second-hand smoke exposure at home over 15 years in Korea: Inequality by parental education level. *Tob Induc Dis*. 2023 Jun 30;21:88. doi: 10.18332/tid/166132
 31. Kim YR, Jang KA. Differences in Oral Health and Generalized Anxiety Disorder According to Secondhand Smoke Exposure in Public Places. *Behav Sci*. 2023 May 31;13(6):455. doi: 10.3390/bs13060455
 32. Diver WR, Jacobs EJ, Gapstur SM. Secondhand Smoke Exposure in Childhood and Adulthood in Relation to Adult Mortality Among Never Smokers. *Am J Prev Med*. 2018 Sep 1;55(3):345–52. doi: 10.1016/j.amepre.2018.05.005

Manuscript submitted on 31 August 2023. Revised version accepted for publication on 5 February 2024.

Tendencias del cáncer de tráquea, bronquios y pulmón atribuido al tabaquismo en Sudamérica: análisis de la carga mundial de morbilidad 1990-2019

RESUMEN

Objetivo. Investigar la carga del cáncer de tráquea, bronquios y pulmón por exposición al tabaco en los últimos 30 años en 12 países de Sudamérica.

Métodos. Se utilizó la función de relación entre exposición y respuesta de la carga mundial de morbilidad del 2019 para analizar las muertes por cáncer de tráquea, bronquios y pulmón asociadas a la exposición total al tabaco, al tabaquismo activo y al tabaquismo pasivo, así como los años de vida ajustados en función de la discapacidad (AVAD), en 12 países de Sudamérica, entre 1990 y el 2019. Los resultados se presentaron en forma de número absoluto o de tasa por 100 000 personas. Se evaluó el cambio relativo de la carga mediante la comparación de los períodos 1990-1994 y 2015-2019.

Resultados. En el 2019, el número de muertes por cáncer de tráquea, bronquios y pulmón y los AVAD asociados a la exposición al tabaco para todas las edades en Sudamérica fueron de 29 348 y 658 204 en los hombres y de 14 106 y 318 277 en las mujeres, respectivamente. La tasa de mortalidad y los AVAD ajustados por la edad correspondientes al 2019 en la región fueron de 182,8 y 4035 en los hombres y de 50,8 y 1162 en las mujeres, respectivamente. En el caso de los hombres, en 10 de los 12 países se observaron disminuciones relativas de la tasa de mortalidad por cáncer de tráquea, bronquios y pulmón atribuido a la exposición al tabaco, mientras que en el caso de las mujeres solo en 4 países hubo una reducción de la mortalidad.

Conclusión. Aunque en Sudamérica se están llevando a cabo iniciativas importantes para el control del tabaco, en esta región persiste una carga considerable de cáncer de tráquea, bronquios y pulmón, con diferencias significativas en función del sexo. Es preciso contar con más datos primarios específicos de cada país sobre el cáncer de tráquea, bronquios y pulmón, así como sobre la exposición al tabaco, para optimizar las estrategias de atención de salud y mejorar la comprensión de las tendencias regionales.

Palabras clave Neoplasias pulmonares; fumar; epidemiología; América del Sur.

Tendências em câncer de traqueia, brônquios e pulmão atribuídas ao tabagismo na América do Sul: análise da carga global de doença de 1990 a 2019

RESUMO

Objetivo. Investigar a carga de câncer de traqueia, brônquios e pulmão (TBP) decorrente da exposição ao tabaco nos últimos 30 anos em 12 países da América do Sul.

Métodos. A função de exposição-resposta do estudo Carga Global de Doença (GBD, na sigla em inglês) 2019 foi usada para analisar o número de mortes e de anos de vida ajustados por incapacidade (AVAI) por câncer de TBP relacionado à exposição total ao tabaco e ao tabagismo e ao fumo passivo em 12 países da América do Sul entre 1990 e 2019. Os índices foram descritos em números absolutos ou taxas por 100 mil pessoas. A variação relativa da carga foi avaliada comparando-se os períodos de 1990 a 1994 e de 2015 a 2019.

Resultados. Em 2019, os números de mortes e de AVAI por câncer de TBP associado à exposição ao tabaco na América do Sul, em todas as idades, foram, respectivamente, 29.348 e 658.204 em homens e 14.106 e 318.277 em mulheres. As taxas de mortalidade e os AVAI ajustados por idade na região foram, respectivamente, 182,8 e 4.035 em homens e 50,8 e 1.162 em mulheres em 2019. Em homens, 10 dos 12 países registraram uma diminuição relativa das taxas de mortalidade por câncer de TBP atribuído à exposição ao tabaco, mas somente 4 países obtiveram uma redução da mortalidade em mulheres.

Conclusão. Apesar dos consideráveis esforços atuais para o controle do tabaco na América do Sul, ainda há uma expressiva carga de câncer de TBP na região, com disparidades significativas entre os sexos. É necessário dispor de mais dados primários sobre câncer de TBP e exposição ao tabaco específicos para cada país para aprimorar as estratégias de atenção à saúde e melhorar a compreensão das tendências regionais.

Palavras-chave Neoplasias pulmonares; fumar; epidemiologia; América do Sul.