ABSTRACT: Introduction: The global tobacco epidemic has taken pandemic proportions, with about 1.3 billion users and 6 million annual deaths. This study aimed to analyze the trends in mortality from chronic obstructive pulmonary disease (COPD) and lung, lips, oral cavity, pharynx, and esophagus cancer in Brazil between 1990 and 2015. Methods: The study was made possible through a partnership between the Metrics and Health Assessment Institute (IHME), University of Washington, Ministry of Health and the GBD Brazil technical group, using estimates from the Global Disease Charge 2015 study. Results: The mortality rates due to COPD fell; in 1990, it was 64.5/100,000 inhabitants and in 2015, 44.5, a decrease of 31%. For the various types of cancer related to smoking, the decrease was in a lower proportion than for COPD. For lung cancer, rates were 18.7/100,000 inhabitants in 1990 to 18.3 in 2015. For women, there is an upward curve for lung cancer from 1990 to 2015, with an increase of 20.7%. Discussion: The study points to smoking as a risk factor for premature mortality and disability due to COPD and cancer. The significant reduction in tobacco prevalence in recent decades could explain reductions in tobacco-related disease trends. The higher mortality from lung cancer in women may express the delayed increase in smoking in this gender. Conclusion: Nationwide actions taken in the last decades have had a great effect on reducing mortality from tobacco-related diseases, but there are still major challenges, especially when it comes to women and young people.

Keywords: Mortality. Tobacco. Pulmonary disease, Chronic Obstructive. Neoplasms.
INTRODUCTION

Tobacco originated in Latin America and began to spread throughout the world soon after its discovery. The sailors in the first caravels were already smokers. Over the next few centuries, the habit of smoking proliferated throughout Europe and tobacco became an “as valuable as gold” coin. It was unknown at the time that it was the deadliest of spices. From that period, when Brazil supplied tobacco to European courts, the tobacco leaf remained on the coat of arms of the Federative Republic of Brazil. What also remained was a habit that causes thousands of deaths and great economic cost for the Brazilian State.1

The global tobacco epidemic has taken pandemic proportions, with about 1.3 billion users and 6 million annual deaths. It involves substantial health care and economic and social costs in all countries. Health risks stem from both direct smoking and passive exposure to tobacco.2

Smoking has influenced and influences mortality in the world. A good example is the mortality rate from lung, trachea, and bronchial cancer, which, in the last century, has evolved in an upward curve in the United States. In 1930, it was 4.0/100,000, reaching 20 times higher levels in 1990.3

Tobacco contains carcinogenic substances and its use predisposes to various types of cancer, as well as heart disease, hypertension, and other conditions.4-6 Global estimates suggest that smoking accounts for 71% of lung cancer deaths, 42% of chronic respiratory
diseases, and nearly 10% of cardiovascular diseases worldwide, as well as being a risk factor for communicable diseases, such as tuberculosis. The World Health Organization (WHO) projected that tobacco-related deaths will increase to about 8 million by 2030, or 10% of global deaths, if no measures are taken to control it.

In 2014, among the 10 leading causes of death in the world responsible for half the deaths, smoking is directly related to 80% of these deaths; ischemic heart disease (first place in the classification), stroke (second place), chronic obstructive pulmonary disease (COPD) (third place), lower respiratory tract infections (fourth place), lung, or tracheal cancer (fifth place).

In Brazil, the reality is similar: in 2015, smoking is related to about half of the 10 main causes of death: ischemic heart disease (14.9%), neoplasias (17.4%), and cerebrovascular diseases including systemic arterial hypertension (12.4%) and COPD (5.3%). In contrast, the prevalence of smoking has been declining significantly, from the implementation of stricter legislation to anti-smoking campaigns. In 1989, 34.8% of the population aged over 18 years were smokers. There has been a significant drop in the last decade, with a prevalence of approximately 10.5% in Brazilian capitals. Studies have attributed these achievements to the country’s leadership in the subject, promoting educational, preventive actions, as well as regulatory actions. It is known, however, that the impact of the lowering prevalence will reflect on mortality rates in the next three to four decades.

This study aimed to analyze the trends in mortality due to COPD and lung, lips, oral cavity, pharynx, and esophagus cancer, both with higher risk of death attributable to smoking in Brazil between 1990 and 2015.

**METHODS**

This study was made possible through a partnership between Instituto Métricas e Avaliação em Saúde (IHME), University of Washington, United States, the Brazilian Ministry of Health and the GBD Brazil technical group, using analysis of the estimates of the Global Burden of Disease 2015 study.

The methodology of GBD is described in other publications, and updates procedures and conceptual principles since the first publication and others subsequent to it. The burden of disease was estimated according to the IHME method in 2015, with results accessed on its webpage. GBD 2015 used data available on causes of death in 195 countries, including data for Brazil and 27 Federative Units.

The main source of mortality data in Brazil was the death registration database of the Ministry of Health’s Mortality Information System (SIM), after adjustments by other national and international sources. Corrections were made for sub-registration and redistribution of garbage codes for defined causes. Details of clustering of causes using CID9 and CID10 (International Statistical Classification of Diseases and Related Health Problems)
have been previously described\textsuperscript{24}. Later, data modeling was performed to estimate data by age, sex, country, year, and cause. Cause of Death Ensemble Modeling-CODEm (CODEm) is a software that tests a variety of possible statistical models of causes of death and creates a combined set of models that provides the best predictive performance. DisMod-MR 2.1 software was used to calculate simultaneous estimates of incidence, prevalence, remission, disability, and mortality\textsuperscript{25,26}.

In this study, the mortality rates and years of life lost (YLL) due to death or disability, or the disability-adjusted life years (DALYs), were used as the metric. DALYs is a composite indicator that integrates premature death (YLL) and damage caused by disease, sequelae, or disability, considering different levels of severity of one or more diseases at the same time (years lost due to disability – YLD). This indicator considers the burden of lethal and non-lethal diseases to be equivalent.

In the GBD study, 95\% uncertainty intervals (95\%UI) are calculated, which provide information on the variability of estimates resulting from errors due to the sampling process, and also non-sample errors due to adjustments of data sources and modeling\textsuperscript{17}.

This study analyzed conditions that present a high-risk attributable to smoking: COPD (códigos CID 10 J40-J44.9, J47-J47.9), lung, trachea, and bronchial cancer (C33-C34.92, D02.1-D02.3, D14.2-D14.32, D38.1), esophageal cancer (C15-C15.9, D00.1, D13.0), lip and oral cavity cancer (C0-C08.9, D00.00-D00.07, D10.0-D10.5, D11-D11.9, D37.01-D37.04, D37.09), nasopharyngeal cancer (C11-C11.9, D00.08, D10.6, D37.05), and other types of pharyngeal cancer (C09-C10.9, C12-C13.9, D10.7)\textsuperscript{17}.

The analyses presented are listed below:
1. Comparisons of the attributable risk of DALY related to active and passive smoking in 1990 and 2015;
2. Comparisons of mortality rates for these diseases and the percentage of change between 1990 and 2015;
3. Analysis of trends in standardized rates of mortality, by sex and by age group, for the world and Brazil, between 1990 and 2015, for the following causes: COPD, lung, trachea, and bronchial cancer; esophageal cancer; lip and oral cavity cancer; nasopharyngeal cancer; and other types of pharyngeal cancer;
4. We also calculated trend analyzes for age-standardized DALYS, by sex, between 1990 and 2015, in the world and in Brazil, for COPD and cancer.

The Global Disease Burden Study - GDB Brasil 2015 was approved by the Research Ethics Committee of Universidade Federal de Minas Gerais (CAAE Project - 62803316.7.0000.5149).

**RESULTS**

Figure 1 shows the risk attributable to smoking as a cause of premature mortality and disability. The loss of DALYs is concentrated in cardiovascular diseases (2.3\% of DALYs),
COPD (1.3% of DALYs), and cancer (1.3% of DALYs). The same causes are found in relation to passive exposure to tobacco.

The age-standardized mortality rates for the main tobacco-related death causes and the percentage changes between 1990 and 2015 are shown in Table 1. Figure 2A shows the evolution of curves related to the same diseases in Brazil in the 25 years covered by this study.

![Figure 1. Standardized rates of DALYs attributable to active and passive smoking in Brazil in 2015.](image)

Table 1. Mortality rate standardized by age for causes of death and percentage change ((2015–1990)/1990), for Brazil, both sexes and by sex. Brazil, 1990 and 2015.

<table>
<thead>
<tr>
<th>Cause of death per 100,000 inhabitants</th>
<th>Brazil</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic obstructive pulmonary disease (COPD)</td>
<td>64.5</td>
<td>44.5</td>
<td>-31.0</td>
</tr>
<tr>
<td>Lung, tracheal and bronchial cancer</td>
<td>18.7</td>
<td>18.3</td>
<td>-2.1</td>
</tr>
<tr>
<td>Lips and oral cavity cancer</td>
<td>2.8</td>
<td>2.7</td>
<td>-5.2</td>
</tr>
<tr>
<td>Nasopharyngeal cancer</td>
<td>0.2</td>
<td>0.3</td>
<td>16.9</td>
</tr>
<tr>
<td>Other types of pharyngeal cancer</td>
<td>1.9</td>
<td>1.8</td>
<td>-5.0</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>7.2</td>
<td>6.0</td>
<td>-17.2</td>
</tr>
</tbody>
</table>
Death rates standardized by the age of COPD have decreased worldwide. The overall rate in 1990 was 88.6/100,000 (95% UI 93.6 – 83.5) and 51.6/100,000 (95% UI 53.3 – 50.0) in 2015, showing a decrease of 42% (both sexes standardized by age). In Brazil, in 1990, the rate for both sexes was 64.5/100,000 inhabitants (95% UI 66.3 – 62.4) and, in 2015, 44.5/100,000 inhabitants (95% UI 47.0 – 42.3), a decrease of about 31% (Figure 2B).

Mortality due to COPD accounted for 7.4% (95% UI 7.0 – 7.9) of all causes of death in the world in 1990, and, in 2015, 6.0% (95% UI 6.3 – 5.9) with a decrease of 19%. In Brazil, this decrease was lower (3.3%), from 5.8% (5.9 – 5.7) of all deaths in 1990, to 5.5% (5.9 – 5.5), in 2015 (Figure 2C).

When observing a mortality curve for COPD in the last 25 years, in Brazil, there is an upward curve from 1990 to the end of 1997, reaching a rate of 71.3/100,000 inhabitants (95% UI 73.3 – 69.0), from a rate of 43.4/100,000 inhabitants (95% UI 45.7 – 41.9) and a growth trend in recent years. The same behavior is observed in the percentage of death curves, with a higher tendency of increase in the last years after reaching a minimum percentage of 5.5% in 2012 (Figure 2B and Figure 2C). When verified separately by sex, there was a decrease in the rate in both, with a larger decrease for men (from 94.9/100,000 inhabitants to 63.9, 32.6%) in relation to women (from 44.5/100,000 inhabitants to 31.5, 29.2%) (Figure 2).

Figure 3A and Figure 3B show the evolution of mortality by sex and by age group. In the case of women, a peak of mortality is observed in the late 1990s in the highest age groups, from 75 to 79 and over 80 years. Likewise, the mortality rate in men peaked at the same time and in the same age groups, but with values approaching twice the rate of women, about 2,300/100,000 inhabitants in the late 1990s, in the age groups above 80 years.

The DALY for COPD decreased globally and in Brazil. The difference is that the decrease in Brazil from 1,099 to 702/100,000 inhabitants (36.1%) was lower than that observed globally, from 1,724 to 971/100,000 inhabitants (43.7%)27.

CANCER

There was a decline in the mortality rate for the various types of cancer related to smoking, in a lower proportion than the decrease observed for COPD. Tracheal, bronchial, and lung cancer accounted for 1.7% (1.7% – 1.6%) and 2.3% (2.4% – 2.2%) of deaths in Brazil in 1990 and 2015, respectively. There was a decline of 2.1% in mortality rates — 18.7/100,000 (95% UI 19.2 – 18.1), in 1990, to 18.3/100,000 inhabitants (95% UI 19.4 – 17.3) in 2015.

Esophageal cancer, which ranks second among tobacco-related cancers, represented 0.66% (0.68 – 0.63) in 1990 and 2015; mortality rates declined from 7.2/100,000 inhabitants (95% UI 7.4 – 6.9) to 6/100,000 inhabitants (0.80 – 0.73) of deaths in 1990 and 2015. (95% UI 6.3 – 5.6), a 17% decline. The other forms of tobacco-related cancer are lip and oral cavity, nasopharynx, and other types of pharyngeal cancer, with mortality rates, in 1990 and 2015, of 2.8 and 2.7, 0.2, and 0.3, and finally, 1.9 and 1.8, respectively. Although mortality rates from lip and oral cavity cancer showed a small
Figure 3. A) Brazil's mortality rate curve, between 1990 and 2015, for males, by age group, for COPD. http://ghdx.healthdata.org/gbd-results-tool?params=querytool-permalink/870c090f5bae8ed2414eac6c10e93f6; B) Brazil's mortality rate curve, between 1990 and 2015, for females, by age group, for COPD. http://ghdx.healthdata.org/gbd-results-tool?params=querytool-permalink/57f02b378e5d96ad1f4c7c8f52a753e4.
decrease, all three categories increased in percentage in relation to the other causes of death, in the total mortality rate — oral cavity and lip cancer, from 0.26% to 0.34%; nasopharyngeal cancer, from 0.20% to 0.03%; and other types of pharyngeal cancer, from 0.17% to 0.20%. For women, there is an upward trend in mortality from lung, bronchial, and tracheal cancer from 1990 to 2015, with respective rates of 10.6/100,000 and 12.8/100,000 inhabitants — an increase of 20.7%, showing stability or decrease in mortality from other types of cancer. In men, mortality from lung, bronchial and tracheal cancer declined in the years between 1990 and 2010, 29.4/100,000 inhabitants to 25.5/100,000 inhabitants. In the last five years, this mortality rate has shown stability, since 2015 presented the same rate of 2010. Other cancers also showed a decrease or stability in the last 25 years (Figure 4A, Figure 4B, and Figure 4C).

The behavior of the DALY curve for tobacco-related forms of cancer is very similar to that of the mortality curve27.

DISCUSSION

The study indicates smoking as a risk factor for premature mortality and disability due to cardiovascular diseases, COPD and cancer, among others. The significant reduction in the prevalence of tobacco in the last decades, as high as 70%, and consequently the lower exposure to tobacco, could explain reductions in the mortality trends of tobacco-related diseases. The decline in mortality was of approximately one third for COPD in the period studied, but, on the other hand, this rate has been showing a new upward trend in the last three years. New temporal analyses, to be conducted in the future, are needed to determine whether the positive inflection in the COPD mortality curve over the last three years represents a real upward trend.

In relation to tobacco-related cancers, the decline is much less significant. Lung, tracheal, and bronchial cancer in women show a steady increase in the last 25 years, differing from the curve for men and those that show other conditions associated with smoking. As underdiagnosis and underreporting are less common in cancer in relation to COPD, with the prevalence of smoking decreasing, there is a tendency for these rates to decline in the coming decades16.

COPD

Among the six leading causes of death related to tobacco, COPD is the first of which, despite a sharp drop in the last 25 years, is still responsible for more deaths than all forms of tobacco-related cancer combined.

Despite the decline, in recent years, COPD has been rising in the general classification of deaths in the world and in Brazil. It ranked sixth among all causes of death in 1990, and fourth place in 201528.
Figure 4. A) Age-standardized mortality rate curve in Brazil between 1990 and 2015, for both sexes, for lung, tracheal and bronchial cancer; esophageal cancer; lip and oral cavity cancer; nasopharyngeal cancer; and other types of pharyngeal cancer. http://ghdx.healthdata.org/gbd-results-tool?params=querytool-permalink/31683ad84a092e4fd2c7d06e88200b7d; B) Age-standardized mortality rate curve in Brazil between 1990 and 2015, for males, lung, tracheal and bronchial cancer; esophageal cancer; lip and oral cavity cancer; nasopharyngeal cancer; and other types of pharyngeal cancer. http://ghdx.healthdata.org/gbd-results-tool?params=querytool-permalink/a58638aa059a98095daae3e577ba4df9; C) Age-standardized mortality rate curve in Brazil, between 1990 and 2015, for females, lung, tracheal and bronchial cancer; esophageal cancer; lip and oral cavity cancer; nasopharyngeal cancer; and other types of pharyngeal cancer. http://ghdx.healthdata.org/gbd-results-tool?params=querytool-permalink/66b81701010adec3423b3bd0f30f5ae9.
Importantly, the increased mortality curve for tobacco-related diseases (or, in other words, smoking-attributable mortality) often occurs after three to four decades in the corresponding increase in smoking prevalence. According to Lopez et al., who described the different stages of the smoking epidemic, the decrease in the mortality curve for COPD, which coincides with that of a decline in the prevalence of smoking, should begin some years after the onset of the prevalence decline\textsuperscript{16}. This fact may suggest a decrease in the underdiagnosis of COPD and an increase in reporting, which could justify a drop in the mortality curve earlier than expected. Although the underdiagnosis of COPD is a well-known fact, there are not yet studies that show its evolution in the last years\textsuperscript{29}.

As most smokers (70–80\%) start smoking before adulthood, smoking is currently considered a pediatric disease and should therefore be part of the overall care of the child and adolescent\textsuperscript{10}. A study published recently in Brazil, involving students aged 13–14 years, showed that cigarette experimentation in this group was of 9.6\%\textsuperscript{31}. The results of the National School Health Survey (PeNSE 2015), conducted with 9th grade students, showed that cigarette experimentation was of 18.4\%, with the highest frequency of experimentation observed in the south region (24.9\%) and the lowest frequency in the northeast region (14.2\%) and 5.6\% in the prevalence of regular smoking in the last 30 days\textsuperscript{32}. Even with the decline in the prevalence of smoking in Brazil, currently, about 11\% of adults are smokers. Thus, it is necessary to maintain the set of public policies to combat tobacco, so that growth does not resume, especially among adolescents\textsuperscript{10}.

The decrease in the prevalence of smoking in women occurs more slowly than among men. The decrease in the mortality rate in the last 25 years was also lower among women (29.2\%) than men (32.6\%)\textsuperscript{10,33-36}. Women and adolescents are the two groups that deserve greater attention from government actions.

Despite the decline in the mortality rate, worldwide and in Brazil, the DALY in Brazil (36.1\%) is lower than the worldwide (43.7\%), and it has higher rates than the global ones.

It is known that the low availability of spirometry throughout the country — the essential tool for the definitive diagnosis — and the low awareness of general practitioners and physicians can contribute to the underdiagnosis of COPD and its consequences, as well as the non-recognition of COPD as the true cause of death\textsuperscript{29,37}.

**Cancer**

The decrease in the mortality rate from tracheal, bronchial, and lungs cancer is a reflection of the decrease in smoking in the country. The lower decrease in mortality due to lip and oral cavity cancer and other types of pharyngeal cancer may be due to the influence of
other risk factors for these cancers, mainly alcohol use. Conversely, there was an increase in nasopharyngeal cancer mortality in 17% (0.2 – 0.3)\(^\text{18}\).

With population aging and the reduction in mortality due to infectious diseases, demographic and epidemiological transition, it is observed that despite the decrease in mortality rates, all types of tobacco-related cancers have risen in the rank among all causes of death, presenting a greater importance among the main causes of death in Brazil. Lung, bronchial and tracheal cancer represented 1.7 and 2.3% of deaths, respectively, with an increase of 37%; esophageal cancer jumped from 0.66% to 0.76%, that is, an increase of 16%; lip and oral cavity cancer went from 0.26% to 0.34%, with an increase of 33%; nasopharyngeal cancer, from 0.02% to 0.03%, with a 64% increase; and other types of pharyngeal cancer, from 0.17% to 0.22%, corresponding to a 33% increase over the 25-year period studied.

In the last five years, the mortality rate from lung, trachea, and bronchial cancer has been stabilizing, as it was 18.2% in 2009 and 18.3% in 2015 (for both sexes and standardized by age). In relation to women, there has been a continuous increase in mortality due to lung, trachea and bronchial cancer in the last 25 years, probably reflecting the increase in smoking in previous decades, differing from the other diseases analyzed\(^\text{19}\). The stabilization of smoking prevalence rates among women and the rate of experimentation and subsequent dependence on adolescents may contribute to a new growth in the trend, and these are challenges to be faced by the country, aiming at reducing the burden of these diseases.

**Tobacco and Public Policies**

Brazil is a worldwide example in the adoption of policies to fight smoking. A comparative study, published in 2012, showed that Brazil had the lowest prevalence of this condition among 16 countries — including China, Russia, Thailand, Bangladesh, Egypt, India, Mexico, Philippines, Poland, Turkey, Vietnam, and others\(^\text{40}\).

This is a result of the implementation of cost-effective measures recommended by WHO, such as

- increase of taxes and prices on tobacco products;
- a ban on smoking in public places;
- the inclusion of warnings on the dangers of tobacco consumption and the prohibition of tobacco advertising, sponsorship and promotion\(^\text{41}\).

There is ample legislation regulating tobacco products, which was consolidated through Brazilian Law No. 12.546/2011\(^\text{42}\), on tobacco-free environments, which also expanded tobacco taxation to 85% and established a minimum price for cigarettes. In addition, Presidential Decree No. 8.262/2014 regulated these measures, such as the prohibition of smoking indoors, the regulation of cigarette exposure exclusively at points of sale, as well as expanding the...
space occupied by health warnings. Thus, all the best available evidence was implemented in the country. Another factor that improved the governance of actions was Brazil’s accession to the 2005 Framework Convention on Tobacco Control.

In addition, Brazil has set as a goal, in the Strategic Action Plan for Coping with DCNT 2011-2022 and in the Global Plan of DCNT, to reduce smoking in the country by 30% in a decade.

This study is conducted by the GBD 2015 database and is the first to extract mortality data on tobacco-related diseases. The data presented in this study can be used for planning government actions and for future studies, for example, on the economic impact of the morbidity and mortality of tobacco-related diseases.

CONCLUSION

It is known that smoking has taken the proportion of a worldwide pandemic. It is the leading cause of preventable death worldwide according to the WHO. National actions in recent decades have had a major effect on reducing mortality, but mortality remains unacceptable. There are still major challenges, especially when it comes to women and young people. The targeting of global actions by WHO, such as MPOWER and Plain packaging of tobacco products, can help Brazil and other countries reduce the tobacco burden, and consequently the mortality rate from tobacco-related diseases in the coming decades.

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Received on: 02/07/2017
Final version presented on: 03/05/2017
Accepted on: 03/08/2017