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The tobacco epidemic curve in Brazil: Where are we going?

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ABSTRACT

Background: Brazil experienced a robust decline in smoking prevalence rates as a consequence of public policies. Since lung cancer is strongly associated with smoking, trends in lung cancer mortality rates may be used as a delayed effectiveness indicator of smoking prevention interventions.
Objectives: The aim of this study was to estimate lung cancer mortality trends from 1980 through 2017 and to predict temporal trends in lung cancer mortality rates, in Brazil from 2016 through 2040.
Methods: Time trends in lung cancer mortality rates were evaluated using data from available public databases. Crude and age-standardized mortality rates were calculated for each year sex-specific mortality predictions were made for each five-year period from 2016 to 2020 through 2036–2040 using an age-period-cohort (APC) model. Sex ratios were estimated using age-standardized lung cancer mortality rates.
Results: A decline in age-standardized lung cancer mortality rates has been observed for males since 2005 and for all predicted periods. It is expected that females aged 55 or younger will experience a reduction in lung cancer mortality from 2021 to 2026 onwards, but for those aged 75 or over rates are predicted to continue increasing through 2036–2040.
Conclusion: Smoking prevention and cessation policies are essential, and it is important to commit to an ethical framework whereby equity in tobacco control activities between genders is achieved. This will avert many premature and preventable smoking-related deaths in the next decades.

1. Introduction

Smoking causes over 8 million deaths a year worldwide [1]. Lung cancer is a global public health problem associated with high mortality, which could be largely avoided by reducing smoking prevalence [2]. In Brazil, lung cancer was the leading cause of death from cancer among men in 2017; among women, breast cancer had the highest mortality, followed by lung cancer [3].

Smoking is the leading cause of avoidable death and morbidity through its effect on cancer, chronic obstructive pulmonary disease, coronary artery disease, cerebrovascular disease, influenza and pneumonia [1].

Since the late 1980s, the National Program for Tobacco Control in Brazil has led the development and implementation of effective policies and interventions to reduce smoking prevalence, using a combination of population and individual level approaches. In 2019, Brazil was declared to be the second country in the world that has passed all the World Health Organization's six proven policies to reduce tobacco use (Monitor tobacco use, Protect people from tobacco smoke, Offer help to quit, Warn about the dangers of tobacco, Enforce bans on tobacco marketing, and Raise taxes on tobacco) at the highest level [1]. As a result, there was a sharp drop in smoking prevalence rates from 1989 through 2013 in Brazil: in men, from 43.1 %–18.9 %; and in women, from 26.9 %–11.0 % [4].

As lung cancer is strongly associated with smoking, with a latency period of several decades [5], trends in lung cancer mortality rates may be used as a delayed effectiveness indicator of both smoking prevention and smoking cessation interventions [6].

Previous Brazilian publications have shown that lung cancer mortality trends are significantly different between sexes in Brazil. While age-standardized mortality rates by lung cancer have declined in males, in females they have increased [7,8], which suggests a delay in the peak time of both smoking prevalence and mortality vis-à-vis men's trends, making it unclear when a similar decline in female mortality rates will

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occur. None of lung cancer mortality trends studies predicted temporal trends.

The aim of this study is, therefore, to estimate lung cancer mortality trends from 1980 through 2017 in order to understand whether the male:female ratio in mortality has changed over time, and to estimate predicted temporal trends in lung cancer mortality rates by sex in Brazil until 2040.

2. Material and methods

We carried out a time series analysis to estimate and predict temporal trends in lung cancer sex-specific mortality rates in Brazil from 1980 to 2040, using available public databases.

The analysis was divided into two stages: *i)* in the first stage we calculated the age-standardized lung cancer mortality rates using observed data from 1980 through 2017; *ii)* in the second stage, we used observed data from 1981 through 2015 to predict temporal trends in lung cancer mortality rates in Brazil until 2036–2040.

2.1. Data source

The number of lung cancer deaths from 1980 to 2017 was obtained from the Brazilian Mortality Information System [3]. This database compiles information from death causes identified and codified routinely in death certificates for vital statistics purpose. The term "lung cancer" was used to represent malignant neoplasm of trachea, bronchus, and lung using the classification codes from the 9th and 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD). Due to modifications in ICD versions during this period, we identified the cases using the code 162 in the ICD-9 until 1995, and from 1996 to 2016 we used the codes C33 and C34 in the ICD-10 [9,10].

The population denominator from 1980 to 2040 was estimated by the Brazilian Institute of Geography and Statistics using the information collected in the census of the years 1980, 1991, 2000 and 2010. Inter-census estimates are available for each age group and sex [11]. All deaths and population denominator datasets were obtained from public data available at www.datasus.gov.br website.

The proportion of ill-defined causes of death is an indicator of data quality in mortality registries [12]. In the period covered by this study the percentage of deaths due to ill-defined causes ranged from 20 % in 1980 to 6 % in 2017, without differences by sex [3]. These deaths were redistributed in the same proportion as deaths from lung cancer in relation to the total number of deaths excluding ill-defined causes. We repeated this procedure for each five-year strata of age, by year of death and sex. We used the following formula to estimate the redistributed number of lung cancer deaths [13]:

$$Redistributed\ LCD_{age\ group,year} = LCD_{age\ group,year} + IDD_{age\ group,year} * \left(\frac{LCD_{age\ group,year}}{TD_{age\ group,year} - IDD_{age\ group,year}} \right)$$

were LCD is lung cancer deaths, IDD is ill-defined deaths, and TD is total deaths.

From 1980–1995, when ICD-9 was used in Brazil, the classification codes of ill-defined causes of deaths were 780 − 799: symptoms, signs, and ill-defined conditions. Starting in 1996, when ICD-10 was adopted in Brazil, the codes used were I46 for cardiac arrest, I95-I99 for other and unspecified disorders of the circulatory system, J96 for respiratory failure, not elsewhere classified, P28 for other respiratory conditions originating in the perinatal period, and all codes corresponded to symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified category (R00-R99) [9,10].

2.2. Data analysis and predicted rates

Crude and specific five-year age group mortality rates for lung cancer were calculated per 100,000 males and females for each year between 1980 and 2017 using the estimated redistributed lung cancer deaths according to the previous calculation description. Mortality rates were age-standardized using the world standard population for global comparisons, as proposed by Segi et al. [14] in 1960 and modified by Doll et al. in 1966 [15]. We calculated the sex ratios (male/female) and their 95 % confidence intervals (95 %CI), using the age-standardized lung cancer mortality rates.

We estimated the number of deaths due to lung cancer, by sex and five-year age group from 2016 to 2020 to 2036–2040, using the Nordpred function available at the statistical package R, version 3.4.0 (The R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org). This function was developed by Norway's Cancer Registry, using a version of the age-period-cohort model (APC) that allows prediction of trends in cancer incidence and mortality rates [16–20].

To build the APC models, we compared the results based on different model parameters with observed mortality rates for the period 2011–2015 separately for males and females. The parameters used in the final models were: *i)* number of deaths and population by five-year age groups for seven periods (1981–1985, 1986–1990, 1991–1995, 1996–2000, 2001–2005, 2006–2010, 2011–2015); *ii)* average trend for the whole observation period for males (1981–2015), and average trend for the last 15 years of observation for females (2001–2015); *iii)* power-link function equal to 5. The model can be written as $R_{ap} = (A_a + D \cdot p + P_p + C_c)^5$, where R_{ap} is the mortality rate in age group a in calendar period p, D is the common drift parameter, A_a is the age component for age group a, P_p is the non-linear period component of period p and C_c is the non-linear cohort component of cohort c [16–18].

The average trend for the last 15 years of observation was used in the females' model, because the tobacco epidemic history shows that females are in a different stage of tobacco epidemic compared to males. The results of each predictive model correspond to the estimated number of deaths from lung cancer, for five periods (2016–2020, 2021–2025, 2026–2030, 2031–2035, and 2036–2040). Because mortality rates under age 40 years are unstable, due to small number of observed lung cancer deaths, we presented age-specific mortality rates for ages 40 and older.

3. Results

A total of 658,823 lung cancer deaths were detected during the study period, 441,343 in males and 217,480 in females. Crude lung cancer mortality rates were 16.8 deaths/100,000 in males (95 %CI 16.4–16.9) and 11.8 deaths/100,000 in females (95 %CI 11.6–12.0) in 2017.

Although age-standardized mortality rates among males are higher than those in females in all the periods covered, the differences declined in more recent years (Fig. 1). The sex ratio (male:female) of the age-standardized lung cancer mortality rates decreased from 3.6 (95 %CI 1.5–9.8) in 1980, to 1.7 (95 %CI 0.8–3.9) in 2017. This decrease was due to both a decrease in male rates and an increase in female rates.

There was a clear-cut decline in age-standardized lung cancer mortality rates in males from 2006 to 2010 through 2036–2040. Among females, it is predicted that rates will stop increasing after reaching their highest value in 2026–2030 (9.35 deaths/100,000, 95 %CI 9.29–9.42) (Fig. 2).

However, due to population growth and ageing, the number of deaths will increase from 46,886 (36,099 males, 10,787 females) in 1981–1985 to 264,172 (134,577 males, 129,595 females) in 2036–2040.

Age-specific lung cancer mortality rates in males are projected to decrease for most age groups in the years that follow 2006–2010,

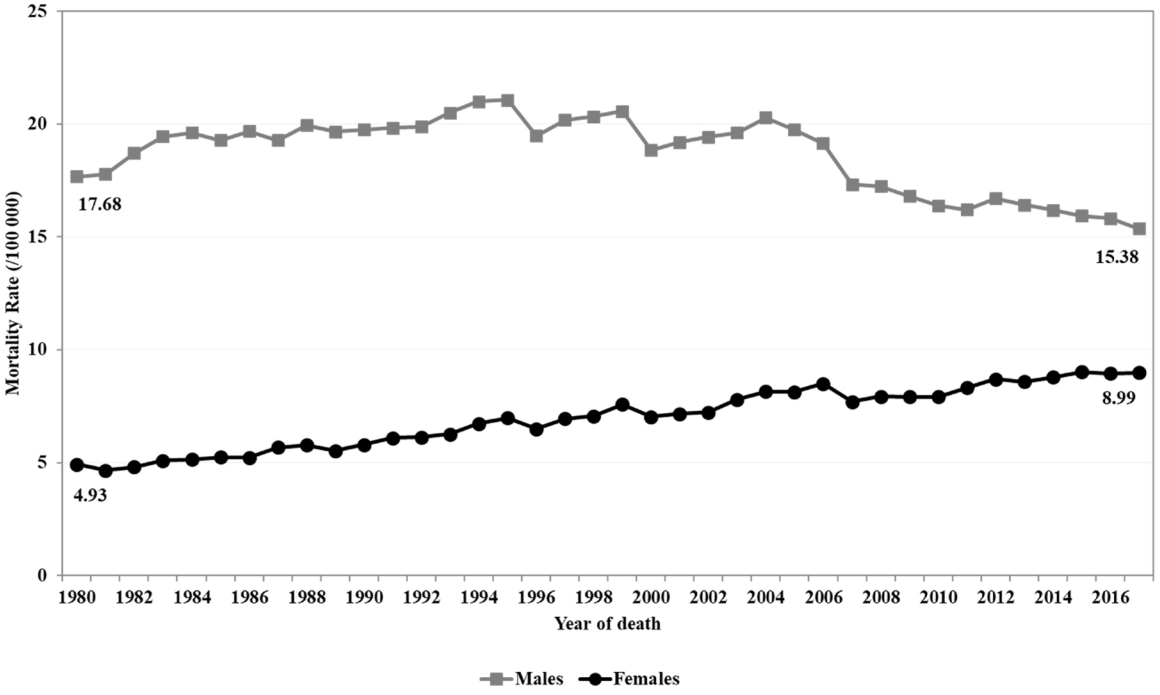

Fig. 1. Age-standardized lung cancer mortality rates, by sex, Brazil, 1980-2017.

particularly those aged 60 years and over (Fig. 3).

For females aged 40–44 years, mortality rates have declined since 2006–2010 and it is predicted that this trend will continue through 2036–2040. However, for the55 − 59 age group, it is expected that the same trend will be seen only from 2021 to 2025 onwards. For females aged 75 or over age-specific mortality rates by lung cancer are projected to increase over the whole study period (1981–2040) (Fig. 4).

4. Discussion

In this study we presented the observed lung cancer mortality rates (1981–1985 to 2011–2015) with estimated prediction of sex-specific rates from 2016 to 2020 through 2036–2040. A decline in age-standardized lung cancer mortality rates has been observed for males since 2005 and it is expected to continue during the whole predicted period (2016–2040). On the other hand, for females, it is predicted that mortality rates' increase will stop in 2031–2040. Predictions indicate a very substantial increase on the numbers of deaths due to lung cancer from 1981 to 1985 to 2036–2040.

The observed age-standardized mortality rates confirmed the tendency reported in previous studies, that showed a different pattern between males and females rates [7,21–26]. While lung cancer mortality has decreased in males, it has increased in females. If the observed trend continues, it is predicted that male:female ratio will markedly

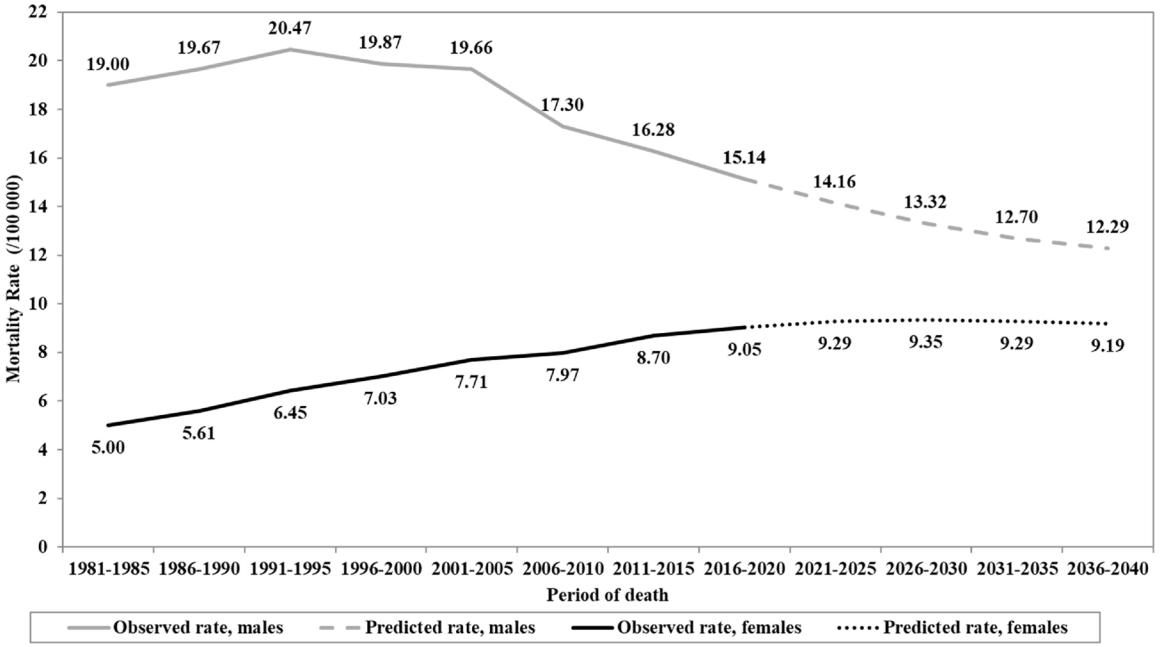

Fig. 2. Age-standardized lung cancer mortality rates observed and predicted, by sex, Brazil, 1981-2040[a].
Note: [a] Observed rates were estimated for the period 1981–2015, and predicted rates were estimated for the period 2016–2040.

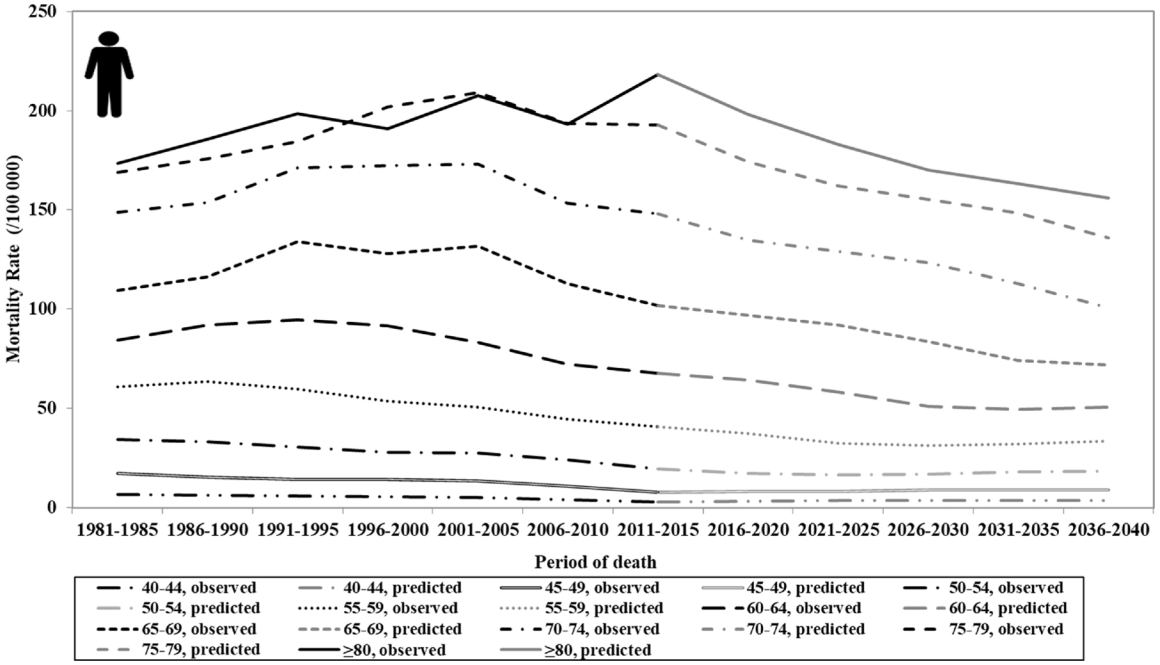

Fig. 3. Age-specific lung cancer mortality rates observed and predicted, males, Brazil, 1981-2040[a].
Note: [a] Observed rates were estimated for the period 1981–2015, and predicted rates were estimated for the period 2016–2040.

diminish by 2036–2040 in Brazil, US and Australia [23,26]. The sex difference is also reported in similar studies in Brazil [7,21,22], Latin America and different parts of the world [23–31]. Bosetti et al., for example, has reported that in most Latin American countries, lung cancer mortality rates for males has been stable or decreasing over time, but a similar pattern is not seen in females [32].

Considering the predicted lung mortality rates among females, we expect that it will s stop to increase starting in 2031–2035.This pattern is consistent with the observed pattern of female lung cancer mortality trends in many countries, particularly in developed countries [23,26–28].

The tobacco epidemic history shows that it has increased first among males and later among females [33]. The peak in smoking prevalence among women is likely to be lower than that for men due to the increasing knowledge about the health hazards of tobacco and, as a consequence, the generally widespread implementation of tobacco control measures. Furthermore, in some countries, smoking continues to be culturally unacceptable for females. Since smoking usually begins during adolescence [34,35], and given that lung cancer has a long latency period [5], the decline observed/predicted in lung cancer mortality rate among young males is probably a result of nationwide anti-tobacco interventions targeted at youth, such as the law prohibiting the

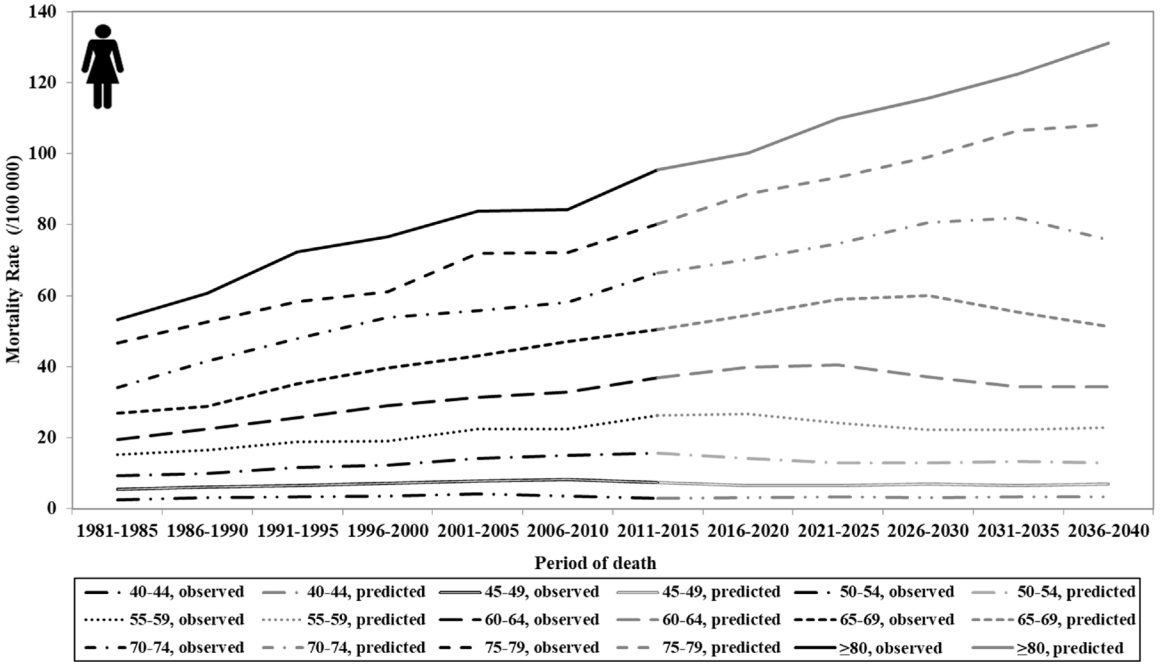

Fig. 4. Age-specific lung cancer mortality rates observed and predicted, females, Brazil, 1981-2040[a].
Note: [a] Observed rates were estimated for the period 1981–2015, and predicted rates were estimated for the period 2016–2040.

sale of cigarettes to minors, advertising restrictions, and/or price increases, which likely contributed to strong declines in smoking prevalence among adolescents in Brazil for both sexes [1,36,37].

In addition to a decrease in smoking initiation, cessation rates among adults have increased in recent years, and remaining smokers seem to be making more quitting attempts [4]. Notwithstanding the implementation of strong anti-tobacco policies in Brazil, a possible mechanism that could also explain sex differences in lung cancer mortality trends is that the interventions designed to prevent smoking did not take fully into account the gender-related, social-structural and psychosocial contributions to vulnerability to tobacco use and exposure [38].

There are many other reports using APC predicted models to estimate future mortality rates in different countries [39–43]. Is important to bear in mind that APC models consider age, birth cohort and period effects simultaneously. This is one of main strengths of this approach, since all these effects play a role in defining future mortality, as smoking-related mortality is strongly influenced by birth cohort smoking behaviors [7,44,45]. APC models' main assumption is the stability of tobacco control policies and treatments for lung cancer. Thus, future predictions may be conservative if there is a substantial improvement in tobacco control strategies or treatments that substantially modify survival [5]. Alternatively, predictions can be too optimistic if Brazil does not keep raising taxes on tobacco products [37] and, at the same time, does not implement the Protocol to Eliminate Illicit Trade in Tobacco Products [46].

4.1. Limitations

We used previous information, on observed rates, to select the APC model with the best predictive power. However, there are other models [7,47,48]. Variability in the predicted rates estimated using different models may be a common limitation of using time-related predictive models.

Although the quality of mortality data in Brazil has improved significantly since 1980 [49,50], lthe proportion of ill-defined causes varies greatly by region and time, and this heterogeneity may have introduced additional bias in time trend studies like ours [50]. An additional problem is that, in our study, we redistributed ill-defined deaths according to the proportion of lung cancer deaths in each age group and sex, for each year. There are, however, other proposed methods to solve this problem in addition to the approach we used [51].

Consistent with many other studies performed with aggregated information derived from vital statistics, we could not adjust for potential confounding factors, such as occupation and education, due to the unavailability of information in mortality data. Additionally, a change in ICD version from ICD-9 to ICD-10 could also have introduced bias in the identification of ill-defined causes. However, this change is unlikely to have affected the lung cancer mortality detection.

5. Conclusion

Our study of predictive lung cancer mortality rates by sex in Brazil may inform future policy, help in organizing public health system and in developing public health interventions. Smoking prevention and cessation policies are essential, and it is important to commit to an ethical framework, whereby equity in tobacco control activities between sexes is achieved. This will avert many premature and preventable smoking-related deaths in the next decades.

Declaration of Competing Interest

None.

CRediT authorship contribution statement

Mirian Carvalho de Souza: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration. **Diego H. Giunta:** Methodology, Investigation, Resources, Writing - original draft, Project administration. **André S. Szklo:** Writing - original draft, Writing - review & editing. **Liz Maria de Almeida:** Resources, Writing - original draft. **Moyses Szklo:** Writing - original draft, Writing - review & editing.

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