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Tongue cancer epidemiology in Brazil: incidence, morbidity and mortality

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Abstract

Background: The purpose of this current research was to clarify for the scientific community the trends of tongue cancer epidemiology in Brazil.

Methods: The data came from Population Based Cancer Registries, Hospital Cancer Registries, and Mortality Information System from 2000 to 2014.

Results: The age-adjusted incidence rate are increasing in both men and women for base of tongue cancer and for other and unspecified parts of the tongue in women, and decreasing in men for other and unspecified parts of the tongue. The majority of cases were diagnosed at clinical stages III and IV. The mortality rate remained relatively stable in both men and women in the period studied.

Conclusion: The increase in age-adjusted incidence rate for tongue cancers (except for other and unspecified parts of the tongue in men), with most patients over 50 years of age, with low education levels, and advanced disease reinforces the need for interventions that address access to health promotion resources and medical care in Brazil.

KEYWORDS

Brazil, Brazilian National Cancer Institute (INCA), epidemiology, incidence, morbidity, mortality, oral cancer, oral squamous cell carcinoma, oropharyngeal cancer, tongue cancer

1 | INTRODUCTION

The incidence of tongue cancer, namely oral squamous cell carcinoma (SCC), has shown an eminent increase worldwide in the past decades, with some regions of the world demonstrating a shift trend toward women, younger patients, or both.[1]

Data from the Surveillance, Epidemiology, and End Results database corroborate the increasing incidence of oral SCC of the tongue in young white individuals and further indicate that the trend is particularly pronounced in young white women. The tumors were not often associated with human papillomavirus (HPV) infection, and, in fact, the incidence of HPV-related head and neck carcinomas is declining among women.[2]

Fifteen years ago, researchers showed an increase in the number of patients with head and neck cancer among Americans younger than 40 years from 1985 to 1997, mainly caused by increased tongue cancer. In addition, the authors concluded that since the mid-1970s, a sharply increasing trend in incidence of tongue cancer was observed, attributed to patients born between 1938 and 1947 and was less associated with a virulent disease course.[3]

Younger patients generally undergo a comparatively more comprehensive therapy than the most commonly older patients that present with oral tongue cancer but still tend to have higher recurrence and mortality rates. Another impacting fact is that younger age at presentation is a predictor of poor outcome, regardless of the low tumor stage at the time of diagnosis, lower rate of comorbidity, and lower intake of tobacco and alcohol.[4–6]

Cases of SCC of the head and neck present a 5-year survival rate of only 40%-60% in the last 50 years, despite advances in surgical techniques, radiotherapy, chemotherapy, and combined therapies.[7] The incidence of this type of cancer, especially of cancer of the mobile tongue and oropharynx, has increased significantly in the United States between 1973 and 2012, in younger patients of both sexes.[8]

In the 2017 World Health Organization classification of head and neck tumors, oral cancer is enclosed together with mobile tongue, whereas oropharynx and base of the tongue cancers are depicted in an independent chapter recognizing the uniqueness of oropharyngeal and base of the tongue tumors.[9] The HPV-positive oropharyngeal SCC possibly explains the dramatic increase of oropharyngeal tumors over the past 3 decades. Sexual behavior is usually associated with oral HPV infection, even though partners of patients with HPV-oropharyngeal cancer do not seem to have an elevated oral HPV infection incidence compared with the general population.[10] Extensive epidemiological and laboratory evidence strongly suggest the association of HPV and oropharyngeal cancer, especially tonsillar carcinoma. These HPV-associated tumors at the base of the tongue, tonsils, or oropharynx tend to present a better response to chemotherapy regardless of the pathological poorly differentiated profile, usually basaloid, of these tumors.[11] Regarding the pathological differentiation of oral cancer, the verrucous carcinoma, originally described as a variant of SCC, should be considered as a distinct entity, associated with a generally favorable prognosis. The referred neoplasia is more prevalent in the tongue, followed by the alveolar ridge and buccal mucosa.[12]

There are no nationwide data regarding incidence, morbidity, and mortality of tongue cancer in Brazil. To fill the gap, the purpose of the current research was to clarify the scientific community about the trends of tongue cancer epidemiology in the country.

2 | MATERIALS AND METHODS

2.1 | Incidence

The Brazilian National Cancer Institute (INCA) website (www.inca.gov.br) discloses the number of new cases of malignant neoplasm of the base of the tongue according to the 10th edition of the International Classification of Diseases (ICD-10-C01) and malignant neoplasm of other and unspecified parts of the tongue (ICD-10-C02) present in men and women and obtained by age group and year of diagnosis.[13] Data included 23 population-based cancer registries with at least 5 years of consolidated data between 2000 and 2012. These population-based cancer registries cover around a quarter of the Brazilian population. Data were obtained on August 7, 2017 (a detailed Supporting Information Chart is available in the online version of this article).

Crude incidence rates of malignant neoplasm of the base of tongue and malignant neoplasm of other and unspecified parts of the tongue per 100 000 men or women by age and year of diagnosis were calculated by dividing the number of new cases by the male or female population, respectively. Rates were then adjusted by the world standard population.[14] Median incidence rates accompanied by interquartile ranges, used as measures of central tendency, allowed the estimation of an annual incidence rate that synthesized the country as a whole. To adjust for short-term variability, the weighted moving average technique was applied to incidence rates. The width of the moving window was 3 years.

2.2 | Morbidity

The data of the patients with cancer came from the hospital cancer registries in the Integrator of the Brazilian National Cancer Institute and in the Oncocenter Foundation of São Paulo among 2000 to 2012. These systems were developed to store and consolidate data from hospital cancer registries and are available on the internet (www.inca.gov.br and www.fosp.saude.sp.gov.br, respectively).

According to these databases, 31 071 cases of tongue cancer were identified (ICD-10-C.01 and C02). Patients with in situ tumors and those with localized tumors on the tongue with histological types other than SCC (n = 3042) were excluded. This study includes 28 029 patients with invasive carcinoma with the following morphologies (International Classification of Diseases for Oncology [ICD-O-3]): SCC, not otherwise specified (NOS; 8070/3), SCC, keratinizing, NOS (8071/3), SCC, small cell, nonkeratinizing (8073/3), SCC, spindle-cell (8074/3), SCC, adenoid (8075/3), and SCC, large cell, nonkeratinizing, NOS (8072/3).

Descriptive statistics (mean and SD for continuous variables, frequency, and percentage for categorical variables) were used for demographic, epidemiological, and clinical characteristics. Analysis of variance and Pearson's chi-square test were used to determine the differences between the groups.

2.3 | Mortality

The number of deaths due to malignant neoplasm of the base of the tongue and malignant neoplasm of other and unspecified parts of tongue that occurred in Brazil were obtained in the web page of the National Mortality Information System from the Brazilian Public System. Crude rates of tongue cancer mortality per 100 000 men or women by age group and year of diagnosis were calculated for the country as a whole by dividing the number of new cases by the male or female population, respectively. Rates were adjusted by the world standard population.[14]

The populations used as denominator to calculate the incidence and mortality rates were estimated by the Interagency Network of Information for Health for the period between

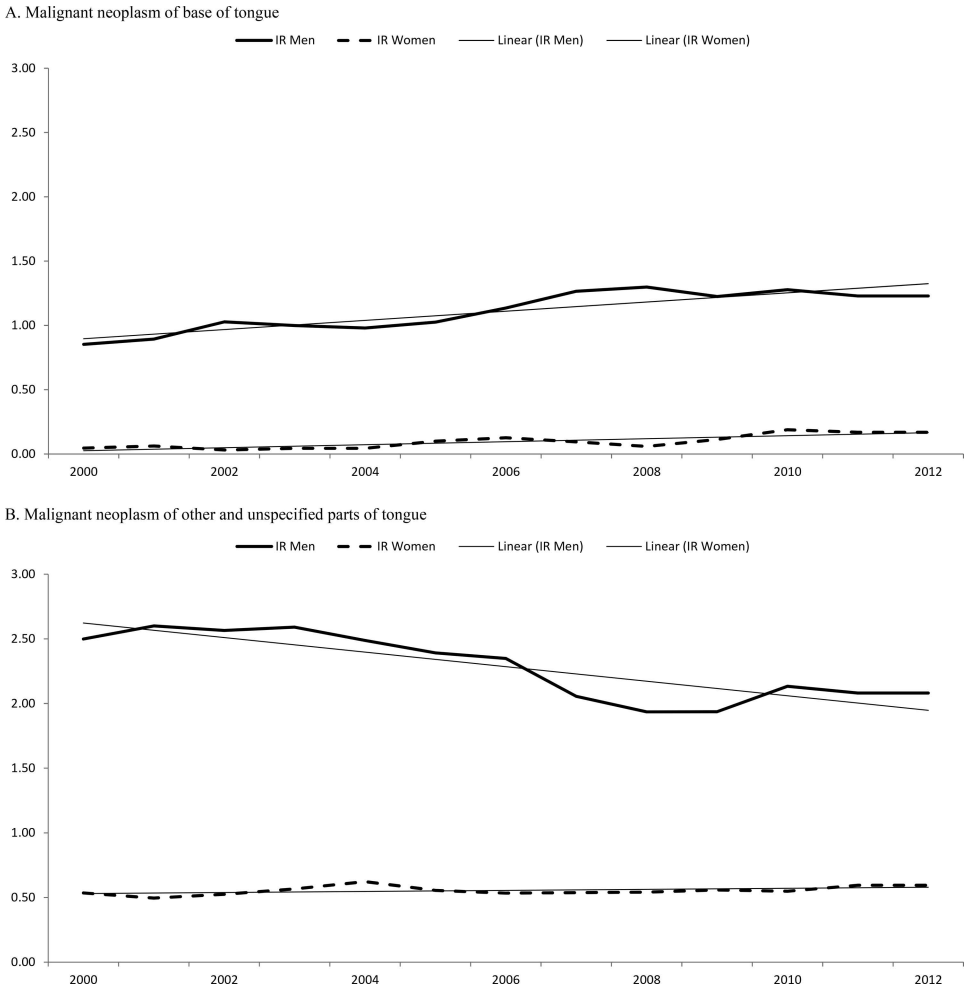

FIGURE 1 Adjusted incidence rate (IR; per 100 000) of malignant neoplasm of the base of the tongue (C01) and malignant neoplasm of other and unspecified parts of the tongue (C02). Brazil, 2000-2012. A, Malignant neoplasm of the base of the tongue. B, Malignant neoplasm of other and unspecified parts of the tongue

2000 and 2013, and by the Secretariat of Health Surveillance for 2014, captured from the website of the Department of Informatics of the Ministry of Health-Brazilian Public System (http://www.datasus.gov.br).

Tests for linear trends were performed using a linear least squares regression for adjusted incidence and mortality rates versus time.

Data were analyzed using Microsoft Excel (2007) and SPSS version 21.0 (São Paulo, Brazil). No ethics approval was required, as the study uses only secondary data with no risk of patient's data disclosure.

3 | RESULTS

3.1 | Incidence of tongue cancer in Brazil from the population-based cancer registry data

In men, the median incidence rate of cancer of the base of the tongue ranged from 0.67 of 100 000 to 1.47 in the period (increase of 3.6% per year, $y = 0.0356x + 0.8609$). Among women, rates ranged from 0.00 of 100 000 to 0.28 (increase of 1.2% per year, $y = 0.0117x + 0.0142$; Figure 1A). With regard to cancer of other parts of the tongue, in the same period, the rates ranged from 1.62 of 100 000 to 2.80 of 100 000 (reduction of 5.6% per year, $y = -0.0562x + 2.6786$) in men and from 0.42 to 0.66 (increase of 0.4% per year, $y = 0.0041x + 0.5264$) among women (Figure 1B).

Oral tongue cancer (C02 according to the ICD) incidence among women below 50 years old increased by only 0.1% per year (from 2000 to 2012) and decreased by 2.1% per year (from 2000 to 2012) when considering male patients (Figure 2A). Conversely, the incidence of oral tongue cancer (C02 according to the ICD) among women over 50 years old decreased by 0.2% per year (from 2000 to 2012) and decreased by 2.7% per year (from 2000 to 2012) among men (Figure 2B).

3.2 | Clinical information of patients with tongue cancer from the hospital cancer registries data

Taking into account the morbidity data, most cases of tongue cancer were from the base of the tongue (37.4%), followed

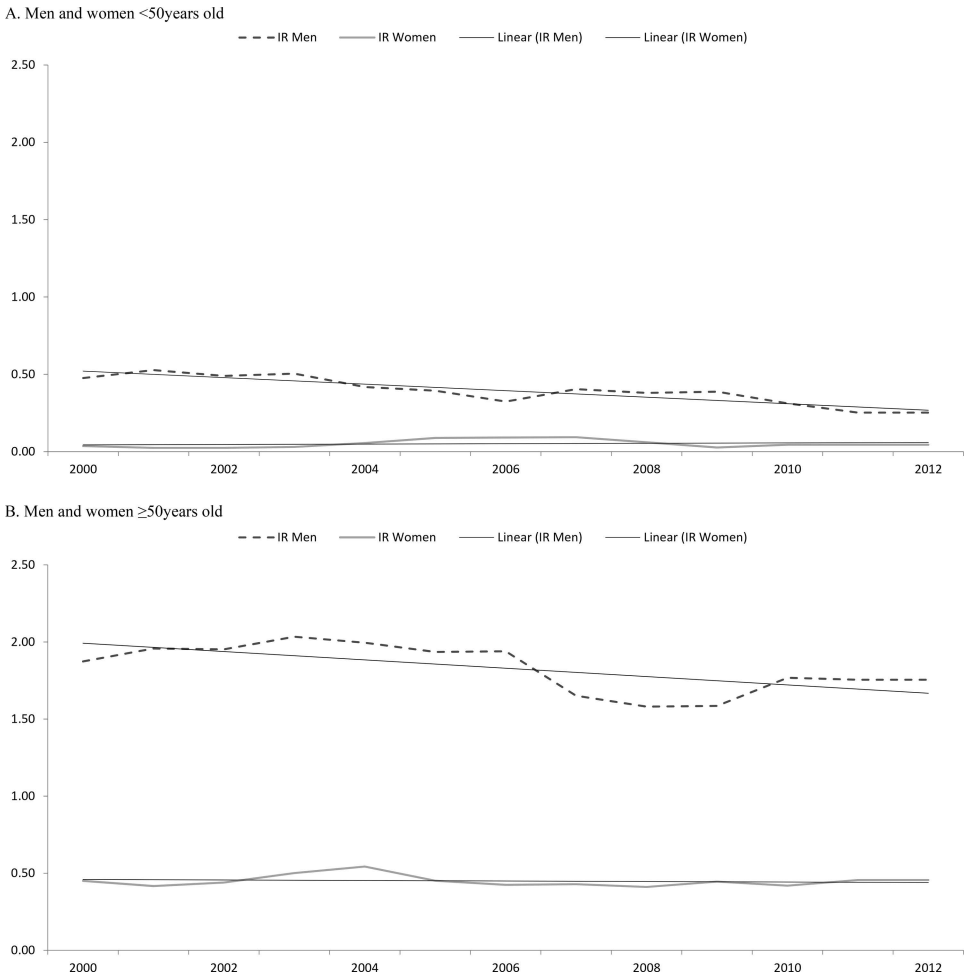

FIGURE 2 Adjusted incidence rate (IR; per 100 000) of malignant neoplasm of other location and unspecified parts of the tongue (C02) according to age. Brazil, 2000-2012. A, Men and women <50 years old. B, Men and women ≥50 years old

closely by tongue unspecified (37.2%) and the border of the tongue (16.8%). Most cases of oral tongue cancer were classified as SCC, NOS (97.8%). A detailed description of the histopathology and topography of tongue cancer in Brazil can be found in Table 1.

Eighty percent (80.0%) of cases of tongue cancer affected men, representing a male:female ratio of 4:0. Case distribution of tongue cancer for patients under the age of 40 years ranged from 2.9% at the tonsil and base of the tongue to 6.5% at the oral tongue. Whereas the highest frequency was observed at the sixth decade of life, ranging from 24.1% at the oral tongue to 25.7% at the tonsil and base of the tongue. Up to 40% of cases represented patients with incomplete elementary school and only up to 3.9% of patients had finished a university degree.

Tongue cancer distribution can be seen in detail in Table 2, whereas unspecified regions of the tongue has a shocking 37.2% of cases, close to the base of the tongue (37.4%), and followed by border of the tongue, a high-risk area for oral cancer development, with almost 5000 cases (ICD C01: n = 1973 for men and n = 419 for women; ICD C02: n = 4374 for men and n = 1632 for women).

The majority of cases were diagnosed at clinical stages III and IV (78.9%). Forty-one percent of oral tongue cancers (C02.0 to C02.3) were diagnosed at stage IV, followed by nonoral tongue cancer (C02.8 and C02.9) with 54.1%, and base of the tongue and tongue tonsil (C01 and C02.4) with 70.2%. After stage IV, clinical staging III was the second highest at the morbidity evaluation.

Interestingly, the frequency of race/ethnicity in patients with tongue cancer was only slightly higher in black and mixed patients (52.5% compared with 47.5%) than white patients. All detailed data collected from the clinical examination is portrayed in Table 2.

Smoking status availability was not described in detail, although it pointed to a majority of patients currently smoking (53.9% in total). Nevertheless, over 26% of patients were missing information regarding smoking status. Regarding alcohol consumption, again, there was a lack of type, duration, and quantity of alcohol consumption, even though the majority was also currently drinking (41.3% in total). Nevertheless, over 30% of patients were missing information regarding drinking status.

TABLE 1 Histology and topography of tongue cancer in Brazil (n = 28 029)

Variables	No. of patients	%
Topography		
Base of the tongue	10 474	37.4
Border of the tongue	4715	16.8
Dorsal surface of the tongue	763	2.7
Overlapping lesion of the tongue	635	2.3
Ventral surface of the tongue	444	1.6
Lingual tonsil	310	1.1
Anterior two-thirds of the tongue, part unspecified	250	0.9
Tongue, unspecified	10 438	37.2
Histology		
SCC, NOS	27 401	97.8
SCC, keratinizing, NOS	507	1.8
SCC, large cell, nonkeratinizing, NOS	93	0.3
SCC, spindle cell	17	0.1
SCC, adenoid	4	0.01
SCC, small cell, nonkeratinizing, NOS	7	0.02
Total	28 029	100.0

Abbreviations: NOS, not otherwise specified; SCC, squamous cell carcinoma.

As expected, in accordance with how oral SCC treatment has been advocated for decades, surgery and radiotherapy at any point were present in a high percentage of cases, with the exception of the surgery of the base of the tongue or tongue tonsil, given that many of these cases can be treated with chemotherapy and radiotherapy combination without surgery. All 28 029 cases of tongue cancer, either from Integrator of the Brazilian National Cancer Institute or hospital cancer registries-Oncocenter Foundation of São Paulo, are included in a detailed description regarding their treatment in Brazil from 2000 to 2012 (Table 3).

3.3 | Mortality of tongue cancer in Brazil from the National Mortality Information System from the Brazilian Public System

A total of 6006 and 12 697 deaths were recorded at the studied time frame for base of the tongue cancer (C01) and other parts of the tongue cancer (C02), respectively. For C01 in men there were 4716 deaths in 15 years with an annual average of 314, whereas for women 839 deaths were filed in 15 years with an annual mean of 56. With regard to C02, the amount of deaths among men was 10 032 in 15 years with a mean annual death rate of 669, whereas for women there were 2665 deaths in 15 years with an annual average of 178.

Mortality rates for base of the tongue neoplasms (see Figure 3A) remained practically stable (0.3/100 000 in 2000 to 0.45/100 000 in 2014, $y = 0.0064x + 0.33$ in men and 0.09/100 000 in 2000 to 0.15/100 000 in 2014, $y = 0.0047x + 0.0702$ among women). With regard to neoplasms in other parts of the tongue (see Figure 3B), values remained practically the same among men (1.54/100 000 in the year 2000 to 1.54/100 000 in the year 2014, $y = -0.0025x + 1.574$) and women (0.24/100 000 in the year 2000 to 0.31/100 000 in the year 2014, $y = 0.0043x + 0.2573$).

4 | DISCUSSION

In Brazil, there is a lack of robust epidemiological studies regarding tongue cancer data. We performed a comprehensive analysis of tongue cancer data in a nationwide perspective. According to our data analysis of Brazilian patients presenting with tongue cancer, in the period studied (2000-2012), there was an increase in tongue cancer incidence with regard to the base of the tongue. In contrast, the incidence of malignant neoplasm of other locations and unspecified parts of the tongue decreased in men and barely increased in women. A recent study compiled and analyzed 22 international cancer registries and observed an annual increase in the incidence rates of tongue SCC among women in most regions studied. However, this increase was not statistically significant in Iceland, Singapore, and Hawaii, and in New Mexico, Washington, and Utah in the United States. Among men, there was also a general increase in the incidence rates of tongue SCC in all regions studied, except for Ireland and Singapore. This increase was not statistically significant in Australia, Austria, Bulgaria, Iceland, or Atlanta, Georgia, Connecticut, and San Francisco in the United States. The same authors demonstrated an annual increase in incidence

TABLE 2 Epidemiological and clinical characteristics of tongue cancer patients from Brazil (n = 28029)

Variables	No. of patients (%)				
	Oral tongue (C02.0-C02.3)	Nonoral tongue (C02.8 + C02.9)	Base of the Tongue + tongue tonsil (C01 + C02.4)	Total	*P* value
Sex					**< .001**
Male	4607 (74.6)	8559 (77.3)	9254 (85.8)	22 420 (80.0)	
Female	1565 (25.4)	2514 (22.7)	1530 (14.2)	5609 (20.0)	
Ratio male:female	2.9	3.4	6.0	4.0	
Age, mean (± SD), y	59.0 (13.3)	58.9 (12.5)	58.4 (11.3)	58.7 (12.3)	**.005**
Age in decades					**< .001**
<40 y	401 (6.5)	488 (4.4)	315 (2.9)	1204 (4.3)	
40-49 y	1033 (16.7)	2001 (18.1)	1994 (18.5)	5028 (17.9)	
50-59 y	1882 (30.5)	3631 (32.8)	3860 (35.8)	9373 (33.4)	
60-69 y	1488 (24.1)	2726 (24.6)	2773 (25.7)	6987 (24.9)	
70-79 y	932 (15.1)	1546 (14.0)	1412 (13.1)	3890 (13.9)	
≥80 y	436 (7.1)	681 (6.2)	430 (4.0)	1547 (5.5)	
Education					**< .001**
Illiterate	798 (12.9)	1419 (12.8)	1179 (10.9)	3396 (12.1)	
Incomplete elementary school	2418 (39.2)	3873 (35.0)	4309 (40.0)	10 600 (37.8)	
Complete elementary school	769 (12.5)	1633 (14.7)	1519 (14.1)	3921 (14.0)	
Complete high school	581 (9.4)	854 (7.7)	801 (7.4)	2236 (8.0)	
Complete undergraduate level	241 (3.9)	259 (2.3)	250 (2.3)	750 (2.7)	
Missing	1365 (22.1)	3035 (27.4)	2726 (25.3)	7126 (25.4)	
Race/ethnicity					**< .001**
White	1800 (43.9)	3506 (49.1)	3354 (48.0)	8660 (47.5)	
Non-white	2346 (56.6)	3685 (51.2)	3686 (52.4)	9717 (52.5)	
Smoking status[a]					**< .001**
Never	808 (18.1)	886 (11.2)	602 (7.9)	2296 (11.5)	
Former smoker	297 (6.7)	610 (7.7)	744 (9.8)	1651 (8.3)	
Current smoker	2477 (55.6)	3850 (48.7)	4418 (58.2)	10 745 (53.9)	
Missing	870 (19.5)	2556 (32.3)	1831 (24.1)	5257 (26.4)	
Alcohol consumption[a]					**< .001**
Never	1177 (26.4)	1381 (17.5)	1185 (15.6)	3743 (18.8)	
Ex-drinker	323 (7.3)	581 (7.4)	931 (12.3)	1835 (9.2)	
Current drinker	1939 (43.6)	2958 (37.4)	3340 (44.0)	8237 (41.3)	
Missing	1013 (22.8)	2982 (37.7)	2139 (28.2)	6134 (30.7)	
Hospital region					**< .001**
North	131 (2.1)	315 (2.8)	267 (2.5)	713 (2.5)	
Northeast	1672 (27.1)	2771 (25.0)	1765 (16.4)	6208 (22.1)	
Central-West	68 (1.1)	445 (4.0)	176 (1.6)	689 (2.5)	
Southeast	3357 (54.4)	5904 (53.3)	6376 (59.1)	15 637 (55.8)	
South	944 (15.3)	1638 (14.8)	2200 (20.4)	4782 (17.1)	
Diagnosis period					**< .001**
2000-2003	960 (15.6)	2077 (18.8)	1668 (15.5)	4705 (16.8)	
2004-2007	1527 (24.7)	2955 (26.7)	2622 (24.3)	7104 (25.3)	
2008-2011	2064 (33.4)	3455 (31.2)	3661 (33.9)	9180 (32.8)	
2012-2017	1621 (26.3)	2586 (23.4)	2833 (26.3)	7040 (25.1)	

(Continues)

TABLE 2 (Continued)

Variables	No. of patients (%)				
	Oral tongue (C02.0-C02.3)	Nonoral tongue (C02.8 + C02.9)	Base of the Tongue + tongue tonsil (C01 + C02.4)	Total	*P* value
Diagnosis and previous treatment					**< .001**
No diagnosis and without treatment	2651 (43.0)	5113 (46.2)	5043 (46.8)	12 807 (45.7)	
With diagnosis and without treatment	2873 (46.5)	4713 (42.6)	4726 (43.8)	12 312 (43.9)	
With diagnosis and with treatment	594 (9.6)	1062 (9.6)	939 (8.7)	2595 (9.3)	
Other	34 (0.6)	42 (0.4)	28 (0.3)	104 (0.4)	
Missing	20 (0.3)	143 (1.3)	48 (0.4)	211 (0.8)	
Clinical staging					**< .001**
I	740 (14.3)	661 (9.1)	289 (3.4)	1687 (8.0)	
II	1050 (20.3)	1096 (15.2)	589 (6.9)	2735 (13.0)	
III	1263 (24.4)	1562 (21.6)	1676 (19.5)	4501 (21.4)	
IV	2121 (41.0)	3913 (54.1)	6025 (70.2)	12 059 (57.5)	
Status at the end of the first course of treatment					**< .001**
Response	1727 (28.0)	2202 (19.9)	2241 (20.8)	6170 (22.0)	
No response	1044 (16.9)	1859 (16.8)	2057 (19.1)	4960 (17.7)	
Missing/does not apply	3401 (55.1)	7012 (63.3)	6486 (60.1)	16 899 (60.3)	
Early death[b]					**< .001**
Yes	1138 (18.4)	2426 (21.9)	2918 (27.1)	6482 (23.1)	
No/missing	5034 (81.6)	8647 (78.1)	7866 (72.9)	21 547 (76.9)	
Total	6172	11 073	10 784	28 029	

[a]Data not available for hospital cancer registries-Oncocenter Foundation of São Paulo (n = 8080), the percentages were calculated based on valid data.
[b]Response: partial remission, stable disease, and complete response; no response: progressive disease, relapsed disease, or death.
[b]Death at the end of first treatment (hospital cancer registries-Integrator of the Brazilian National Cancer Institute) or up to 24 months after diagnosis (hospital cancer registries-Oncocenter Foundation of São Paulo).
Figures in boldface indicate statistical significance ($P < .05$).

rate in subjects <45 years old than subjects aged >45 years in 14 of 22 registries studied. In 7 registries (Austria, Bulgaria, Denmark, Estonia, Norway and in the United States in Atlanta and Utah), the converse was true, in which the average annual increase in incidence rates for subjects aged <45 years old was lower than that in subjects >45 years old. Only in England they have found the average annual increase in the incidence rates to be equal in both age groups.[1]

Although several authors have shown an increase of oral tongue cancer incidence in younger female patients worldwide,[1,3,8] and even specifically in white females,[2] including the report of several cases of pregnant women,[15] our study has shown that the incidence of malignant neoplasm of other locations and unspecified parts of tongue in patients under 50 years of age decreased in men (−0.2% per year) and showed a slight increase (0.1% per year) in women.

Regarding hospital data, a vast majority of cases of tongue cancer were detected at stage IV clinical staging, predominantly at the base of the tongue and tongue tonsil (C01 + C02.4), with 70.2% of cases as opposed to 41.0% of cases at the oral tongue. This discrepancy highlights the challenges that represent the diagnosis of oral cancer, especially when it is located at the posterior regions of the mouth. Such findings reinforce the need for the development of epidemiological surveillance strategies. In addition, the latest edition of the TNM classification for head and neck cancer better reflects tumor biology and clinical behavior of such lesions, giving special attention and specific classification for the HPV-mediated oropharyngeal cancer.[16]

Low level of education of the patients with oral tongue cancer just reinforces the classic presentation of the disease, which usually affects low to middle income countries more often than individuals in developed countries.[17] Around 60% of cases were represented by patients who did not pass the elementary school level.

A hospital-based cancer registry in Madrid-Spain was analyzed between 1990 and 2008 for tongue malignant neoplasms. The researchers classified the SCC of the oral cavity as rare in patients under 50 years of age, suggesting it as a disease that occurs in the sixth or seventh decade of life,

TABLE 3 Treatment details of tongue cancer in Brazil (n = 28 029)

Type of treatment[a]	No. of patients (%)				
	Oral tongue (C02.0 and C02.3)	Nonoral tongue (C02.8 + C02.9)	Base of the tongue + tongue tonsil (C01 + C02.4)	Total	*P* value
No treatment	830 (13.4)	1754 (15.8)	1658 (15.4)	4242 (15.1)	**< .001**
Surgery only	910 (14.7)	1448 (13.1)	615 (5.7)	2973 (10.6)	**< .001**
Surgery at any point	2983 (48.3)	4549 (41.1)	2527 (23.4)	10 059 (35.9)	**< .001**
Radiotherapy at any point	3270 (53.0)	5846 (52.8)	6757 (62.7)	15 873 (56.6)	**< .001**
Chemotherapy at any point	1869 (30.3)	3584 (32.4)	5374 (49.8)	10 827 (38.6)	**< .001**
Surgery + radiotherapy	1343 (21.8)	2077 (18.8)	1414 (13.1)	4834 (17.2)	**< .001**
Surgery + chemotherapy	610 (9.9)	1061 (9.6)	1074 (10.0)	2745 (9.8)	**.001**
Radiotherapy + chemotherapy	1437 (23.3)	2575 (23.3)	4041 (37.5)	8053 (28.7)	**< .001**
Radiotherapy + chemotherapy + surgery	501 (8.1)	824 (7.4)	828 (7.7)	2153 (7.7)	**.001**
Total	6172	11 073	10 784	28 029	

[a]Types of treatment are not mutually exclusive.
Figures in boldface indicate statistical significance ($P < .05$).

slightly higher than our peak in Brazil at the fifth decade, although they showed a casuistic of only 610 cases and have not analyzed the trends of younger patients affected over time.[18]

Opposite to the data shown by Tota et al,[8] in the United States, there was a slight difference in tongue cancer incidence in black and mixed race patients as opposed to white patients at the Brazilian population studied, yet, risk factors here seem to be mostly the classic ones widely described in the literature: tobacco and smoking affecting usually older male patients.

The HPV-related tumors are usually present in younger patients, which may help explain the reason for the greater improvement in survival in younger patients, especially for cancer of the oral cavity, than in older patients. Nevertheless, cancer of the tongue is usually thought to be non-HPV-related, except for base of the tongue tumors.[19]

The risk factors that are contributing to the rise in oral tongue cancer cases observed among young white patients in the United States are not currently known. Thus, additional studies are needed to generate and confirm hypotheses concerning risk factors for oral tongue cancers in the presence and absence of the traditional risk factors, such as smoking. These studies could potentially focus on suspected or emerging oral cancer risk factors whose prevalence may have increased in cohorts of white individuals born after the 1940s.[8]

In the current study, although cancer incidence rates have increased for base of tongue cancer in both men and women and for other and unspecified parts of the tongue in women, mortality rates remained relatively stable in the period studied. In the Netherlands, in a study of trends in incidence and mortality rates for oral cavity cancer from 1991-2010, the most pronounced increase in incidence rates were observed in cancer of the tongue (+1.9% per year) with borderline increasing mortality rates (+0.8% per year).[20]

Given that the current study was based on 3 secondary data sources, prospective studies are needed to surpass this limitation. Another weakness that could not be overcome is that the putative HPV-associated oropharyngeal cancer had not necessarily been tested for HPV, representing another bias that surely was present in previous studies like the large epidemiological investigation from the United States.[8] High percentage of unspecified parts of the tongue highlights the need for better training of medical staff about the knowledge of high-risk regions of the tongue for cancer development and specificity of each type of local neoplasms. Including unspecified parts of the tongue was a decision based on the high rate of such stratification exactly to pinpoint the need for better classification of these lesions in Brazil, and does not spoil the evaluation of other regions with regard to tongue topography. It is also very unlikely that unspecified parts of the tongue reflects base or lingual tonsil, given it is widely known that malignant lesions of the mouth with such locations usually present a different biological behavior, with HPV etiopathogenesis probably involved, although the correlation is merely speculative given robust epidemiological databases, such as Surveillance, Epidemiology, and End Results,[19] Integrator of the Brazilian National Cancer

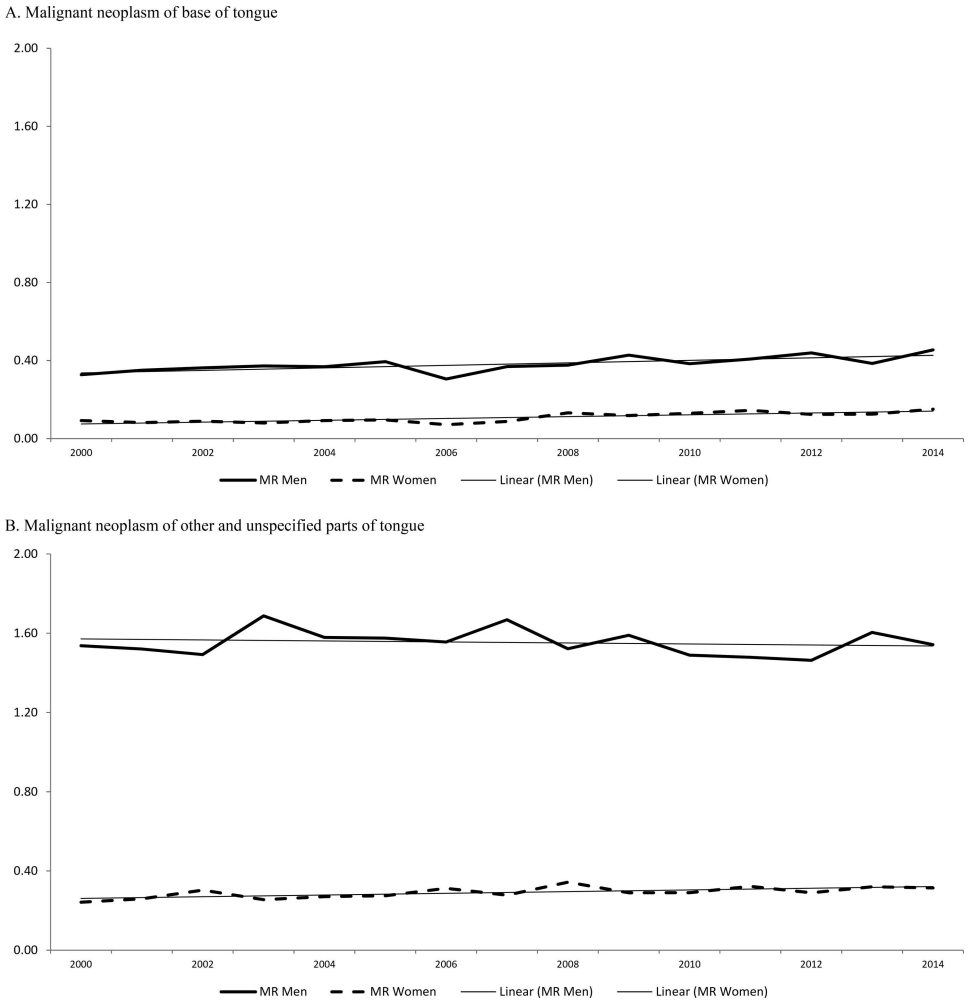

FIGURE 3 Adjusted mortality rate (MR; per 100 000) of malignant neoplasm of the base of the tongue (C01) and malignant neoplasm of other and unspecified parts of the tongue (C02). Brazil, 2000-2014. A, Malignant neoplasm of the base of the tongue. B, Malignant neoplasm of other and unspecified parts of the tongue

Institute, or hospital cancer registries-Oncocenter Foundation of São Paulo do not include HPV tumor status. On the other hand, prognosis of oral tongue cancer tends to be considered the poorest, even for cases that are diagnosed at early stages,[21–23] with opposite evidence only shown in South Korea.[24]

According to our research data, the profile of tongue cancer matches that of a developing country. Regardless of the statistically significant results of all variables concerning morbidity (see Table 2), it is also important to take into account that when a sample size is over 10 000, a significant *P* value is likely to be found even when the difference in outcomes between groups is negligible and may not justify an expensive or time-consuming intervention over another. Effect sizes should generally be calculated and presented along with *P* values for statistically significant results, and observed effect sizes should be discussed qualitatively through direct and explicit comparisons with the effects in related literature.[25] Conversely, the statistically significant increase in tongue cancer incidence referred to a population of <10 000 individuals, most of the time during the current analysis, although only a slight increase was observed.

The INCA has coordinated the National Tobacco Control Program since 1989. This program is mainly funded by the Brazilian government and the National Tobacco Control Program has achieved important positive results with Brazil being a party of the World Health Organization Framework Convention on Tobacco Control since 2006.[26] Similar strategies have to be implemented toward cessation of alcohol consumption in the Brazilian population.

5 | CONCLUSION

This study pinpointed several burdens related to tongue cancer epidemiology in Brazil ranging from lack of education to late diagnosis of the disease. All of which reach beyond the lack of widespread access to healthcare system, a historical problem found in Brazil, with approximately 4% of the population living below the extreme poverty line as of 2016,

according to the Central Intelligence Agency World Factbook.[27] Several limitations, despite the recent improvement in Brazilian economy, have also been encountered: they have ranged from the sectoral logic of health policy and the health system, as well as inherited regional inequalities.[28] Strategies to improve knowledge about oral cancer and risk factors, development of reliable public health early detection programs at the population level to diagnose oral cancer early and systematic efforts to educate the population, and to encourage cessation of causal habits and follow-up on precancerous lesions are mandatory.

Further studies have to be carried out approaching the epidemiological aspects of oral cancer, although the present study with a vast Brazilian population from 3 different databases contradicts the global tendency of a rise of tongue cancer in younger and/or female patients.

5.1 | Ethical approval

In accordance with the ethical principles established by the National Health Council (CNS), Resolution 466/12, no ethics approval was required, as the study uses only secondary data.

5.2 | Informed consent

For this type of study, informed consent is not required.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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