Oropharyngeal Cancer Incidence and Trends in Brazil

Lady Paola Aristizabal Arboleda[1], Dyego Leandro Bezerra de Souza[2], Diego Rodrigues Mendonça e Silva[3], and Maria Paula Curado[4]

ABSTRACT

Background: Oropharyngeal cancer incidence is rising globally, predominantly in high-income countries, because of human papillomavirus infection. However, further data on oropharyngeal cancer incidence in Brazil is needed. The aim of this study was to estimate the incidence, trends, and predictions of oropharyngeal cancer in Brazilian population-based cancer registries (PBCR) by period, sex, and topography.

Methods: Data on oropharyngeal cancer were collected from PBCRs (1988–2020). Age-standardized rates were calculated from 2000 onward using the 2010 Brazilian census and world standard population. Annual average percent change was analyzed using the joinpoint regression model. Predictions up to 2034 were made using the Nordpred program and the age–period–cohort model.

Results: A total of 17,980 oropharyngeal cancer cases were recorded across 30 PBCRs (1988–2020). Most cases involved males (81.58%) ages 55 to 59 years (17.06%). The oropharynx not otherwise specified (40.58%), base of the tongue (24.98%), and tonsils (22.52%) were the sites most affected. The highest incidence rates were found in the southeastern and southern regions (3.1–9.4/100,000). Incidence trends increased for 10 PBCR regions in males and 6 regions in females. Predictions up until 2034 indicate decreasing trends for females and increasing trends for males in the north and south of Brazil.

Conclusions: The incidence of oropharyngeal cancer in Brazil differs among regions, with higher rates observed in the south and southeast. The prevalence of the human papillomavirus-attributable fraction for oropharyngeal cancer is unknown.

Impact: Analysis of oropharyngeal cancer incidence rates and regional trends aims to better understand the epidemiology of this malignancy in the Brazilian population.

Introduction

Oropharyngeal cancer represents an important public health issue, with an estimated 106,400 new cases and 52,305 associated deaths globally in 2022 (1). The incidence of oropharyngeal cancer has increased worldwide, affecting both sexes, with higher rates observed in males ages 40 to 60 years (2). Squamous cell carcinoma of the oropharynx has an attributable fraction (AF) to human papillomavirus (HPV) infection, with HPV16 representing the most common subtype (3, 4). The AF of HPV in oropharyngeal cancer is approximately 40% in developed countries. However, estimates are lower (<20%) in many countries and uncertain in others, including Brazil (5).

Oropharyngeal cancer incidence has increased more than oral cavity cancer among men in high-income countries, particularly Austria, China, the Czech Republic, Iceland, Ireland, Italy, the Republic of Korea, Lithuania, New Zealand, and Norway (2, 5–7). The true burden of oropharyngeal cancer in Brazil is unknown because its incidence is estimated collectively with oral cancer (8). However, a study from a single institution revealed that 60% of its oropharyngeal cancer cases were HPV-positive, suggesting that the incidence of this cancer and the prevalence of HPV-related oropharyngeal cancer may be increasing in the Brazilian population (9). Although global trends in oropharyngeal cancer incidence, including for Brazil, have been previously described, the data were based on only six Brazilian population-based cancer registries (PBCR), representing less than 3% of the Brazilian population (2). Therefore, given the need for a comprehensive overview of oropharyngeal cancer in Brazil, incidence rates and trends in main urban areas plus four rural areas are presented using data from all PBCRs in the country, categorized by region, sex, and age group.

Materials and Methods

Data source and anatomic histologic codes

This is an ecological study based on data from 30 PBCRs provided by the National Cancer Institute (INCA; https://www.gov.br/inca/pt-br; online resources/databases). Data were extracted and descriptively analyzed for the entire period of each PBCR by sex, age group, and anatomic site, selecting the squamous cell carcinoma morphology (8070/3), and 17 topography codes based on the International Classification of Diseases for Oncology, third edition (ICD-O-3; ref. 10). For anatomic analysis, topographies were grouped into the base of tongue (C01), uvula (C05.2 and C05.1), tonsils (C09, C09.0, C02.4, C14.2, C09.1, C09.8, and C09.9), and oropharynx (C10, C10.0, C10.1, C10.2, C10.3, C10.8, and C10.9; Supplementary Tables S1 and S2).

Of the 33 PBCRs in Brazil, the registry for São Luís, Maranhão state, was excluded from the analysis because of lack of available data. Campinas, a city in Southeast Brazil, has two PBCRs: Campinas-Unicamp (SP) and Campinas-SMS. To avoid data duplication, as both registries cover the same population, only the Campinas-SMS registry (maintained by the municipal government health authorities) was included. In Midwest Brazil, two PBCRs were identified for the state of Mato Grosso. These registries were merged because one covered the metropolitan area and the other covered the remaining population. For the analysis of incidence trends, Rondônia, Amapá, and Alagoas were excluded because of

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insufficient case numbers and continuous age-period data, components required to produce reliable incidence estimates. The years covered by the Brazilian PBCRs ranged from 1988 to 2020, with each registry covering different periods within this timeframe. All PBCRs spanned at least a full decade.

Statistical analysis

Crude incidence rates and age-standardized incidence rates (ASIR) expressed per 100,000 persons/year were calculated from the year 2000 up until 2020, according to the last update year in each PBCR. The demographic Brazilian population census (2010) provided by the Brazilian Institute of Geography and Statistics was applied because it represents the midpoint of the study period (https://datasus.saude.gov.br/populacao-residente; online resources/databases). The ASIR was calculated by the direct method using the world standard population (11). The Joinpoint Regression Program (version 4.7.0.0) was used to analyze trends in oropharyngeal cancer through the adjusted incidence rates. The calculations were performed by fitting a series of joined straight lines on a logarithmic scale to the data. PBCRs with ≥10 consecutive years of records of incident cases were included for analysis. Annual average percentage changes (AAPC) were calculated by taking a weighted average of the annual percentage change from the individual segments, with weights proportional to the length of each segment within the intervals (12). Negative AAPCs indicate decreasing trends, positive indicate increasing trends, and nonsignificant AAPCs indicate stability.

Predictions of oropharyngeal cancer incidence were made for Brazilian regions by selecting PBCRs with a period of at least 15 years of data. Thus, the following PBCRs were included in the analysis: North Brazil region: Belém (PA), Manaus (AM), and Palmas (TO); Northeast Brazil region: Aracaju (SE), Fortaleza (CE), João Pessoa (PB), and Recife (PE); Midwest Brazil region: Campo Grande (MS), Mato Grosso, and Goiânia (GO); Southeast Brazil region: Belo Horizonte (MG), São Paulo (SP), Barretos-DRS (SP), and Jahú (SP); and South Brazil region: Curitiba (PR) and Porto Alegre (RS). If 1 year was missing within a given 5-year period, the number of cases from the preceding year was repeated to complete the 5-year groups. The populations used in the projections were obtained from the website of the Brazilian Institute of Geography and Statistics (http://tabnet.datasus.gov.br/cgi/deftohtm.exe?ibge/cnv/projpopuf.def; online resources/databases). For the analyses, coverage was estimated by age group and calendar year (5-year intervals) to ensure accurate estimates for each PBCR (Supplementary Tables S3 and S4). The Nordpred program (Cancer Registry of Norway) was used to predict oropharyngeal cancer incidence trends using an age–period–cohort model. The process involved fitting a generalized linear model with Poisson distribution to observed data, breaking down rates into three components: age effects (influence of aging), period effects (changes over time), and cohort effects (differences among birth groups due to risk factor exposure). The model was developed using the statistical program R, adjusted for overdispersion, and incorporates historic data trends to provide accurate predictions (13–15).

Data were pooled into 5-year periods, and the limit age group considered for analysis was that with more than 10 cases in the periods. The results were presented according to the number of cases projected for the following periods: 2020 to 2024, 2025 to 2029, and 2030 to 2034. The total ASIR for each period-year block was calculated by sex and Brazilian region. The proportion of this change, in terms of risk or change in population (size and population structure), was also calculated. These two components can be different from zero and have a positive or negative direction. The calculation can be expressed as follows (13, 14):

$$\Delta_{tot} = \Delta_{risk} + \Delta_{pop} = \left(N_{fff} - N_{off}\right) + \left(N_{off} - N_{000}\right),$$

In which Δ_{tot} is the total change, Δ_{risk} is the change as a function of risk, Δ_{pop} is the change as a function of population, N_{000} is the number of observed cases, N_{fff} is the number of predicted cases, and N_{off} is the number of expected cases when the incidence rates increase during the observed period.

Data were collected in a datasheet, systematically organized in Microsoft Office Excel 2013 software (Microsoft Corporation), and further analyzed by descriptive statistics using absolute numbers, percentages, mean values, and SDs. Subsequently, the existence of associations between sex and oropharyngeal cancer anatomic subsites were analyzed using SPSS software version 25 (IBM Corporation), and the Pearson χ^2 test or Fisher test and the Cramer V. A 5% significance level were used for all tests.

Data availability

The data generated in this study are available within the article and its supplementary data files. Additional required data are available upon request from the corresponding author.

Results

In this analysis, the PBCR coverage for the country was 24% (based on 30 PBCRs), with the highest coverage in Southeast Brazil (38.10%) and Northeast Brazil (27.37%; Supplementary Table S5). The years covered by the Brazilian PBCRs ranged from 1988 to 2020, with each registry covering different periods within this timeframe. All PBCRs spanned at least a full decade. A total of 17,980 cases were registered between 1988 and 2020, with PBCR data available for periods ranging from 1 to 25 years. Oropharyngeal cancer was more frequent in males [14,668 (81.58%)] than in females [3,312 (18.42%)]. The most frequently affected age groups were individuals ages 55 to 59 years [3,068 (17.06%)], followed by 50 to 54 [2,844 (15.82%)], 60 to 64 [2,585 (14.38%)], and 45 to 49 years [2,057 (11.44%); Supplementary Table S6]. Of the 17,980 incident oropharyngeal cancer cases, the oropharynx not otherwise specified (NOS) [7,294 (40.58%)], and subsites, including the base of tongue [4,491 (24.98%)], tonsils [4,048 (22.52%)], and uvula [2,143 (11.92%)], were affected. The oropharyngeal cancer frequency identified between 1988 and 2020 showed different proportions by sex and anatomic site, with tonsils about 5% more commonly affected in females and the oropharynx NOS about 5% more affected in males (Supplementary Table S7). The distribution of oropharyngeal cancer by age group and sex showed a predominance of cases in individuals ages 50 to 59 years in both males and females (**Fig. 1**). Regarding oropharyngeal subsites, the most frequent was the base of tongue for males (28.58%) and tonsils for females (4.83%; **Fig. 2**).

In Brazil, the ASIR of oropharyngeal cancer was 3.0/100,000 for males and 0.5/100,000 for females. The southeastern region had the highest incidence rates, with Jahú (SP; 9.4/100,000; Jahú population: 131,040 persons, 64,214 males) and Barretos (SP; 8.5/100,000; Barretos population: 409,267 persons, 202,234 males) exhibiting the highest ASIRs for men (**Fig. 3**). Higher incidence rates among men than women were found in the northern region in Manaus (AM; 3.2/100,000), the northeastern region in Fortaleza (CE; 4.4/100,000),

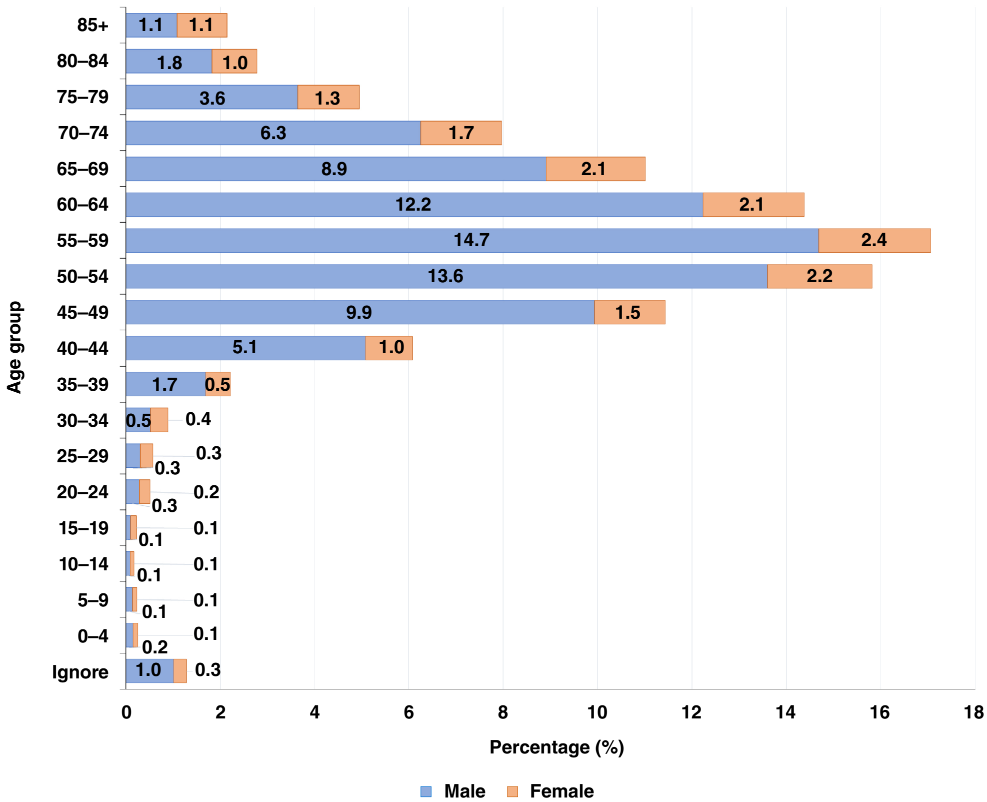


Figure 1.
Demographic distribution of oropharyngeal cancer in Brazil. The figure shows the proportion of oropharyngeal cancer cases distributed by age group and sex from 1988 to 2020.

the midwestern region in Goiânia (GO; 4.8/100,000), and the southern region in Florianópolis (SC; 7.4/100,000; **Table 1**).

Regarding incidence trends, oropharyngeal cancer in men showed an increasing trend in 10 PBCRs across all regions of Brazil (Manaus, Palmas, Fortaleza, Recife, Campo Grande, Mato Grosso, Goiânia, Belo Horizonte, Vitoria, and Curitiba) for the entire period (**Fig. 4A**). Among women, a rising trend was observed in the northeast and southeast regions (Fortaleza, Joao Pessoa, Belo

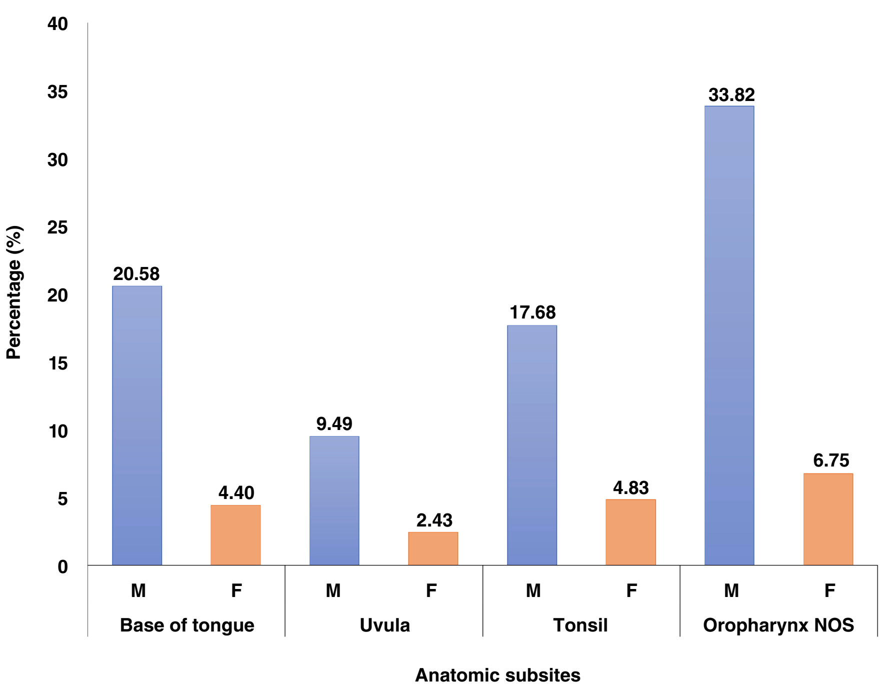


Figure 2.
Anatomic distribution of oropharyngeal cancer in Brazil. The figure shows the proportion of oropharyngeal cancer cases by anatomic subsite and sex (M, male; F, female) in Brazil from 1988 to 2020.

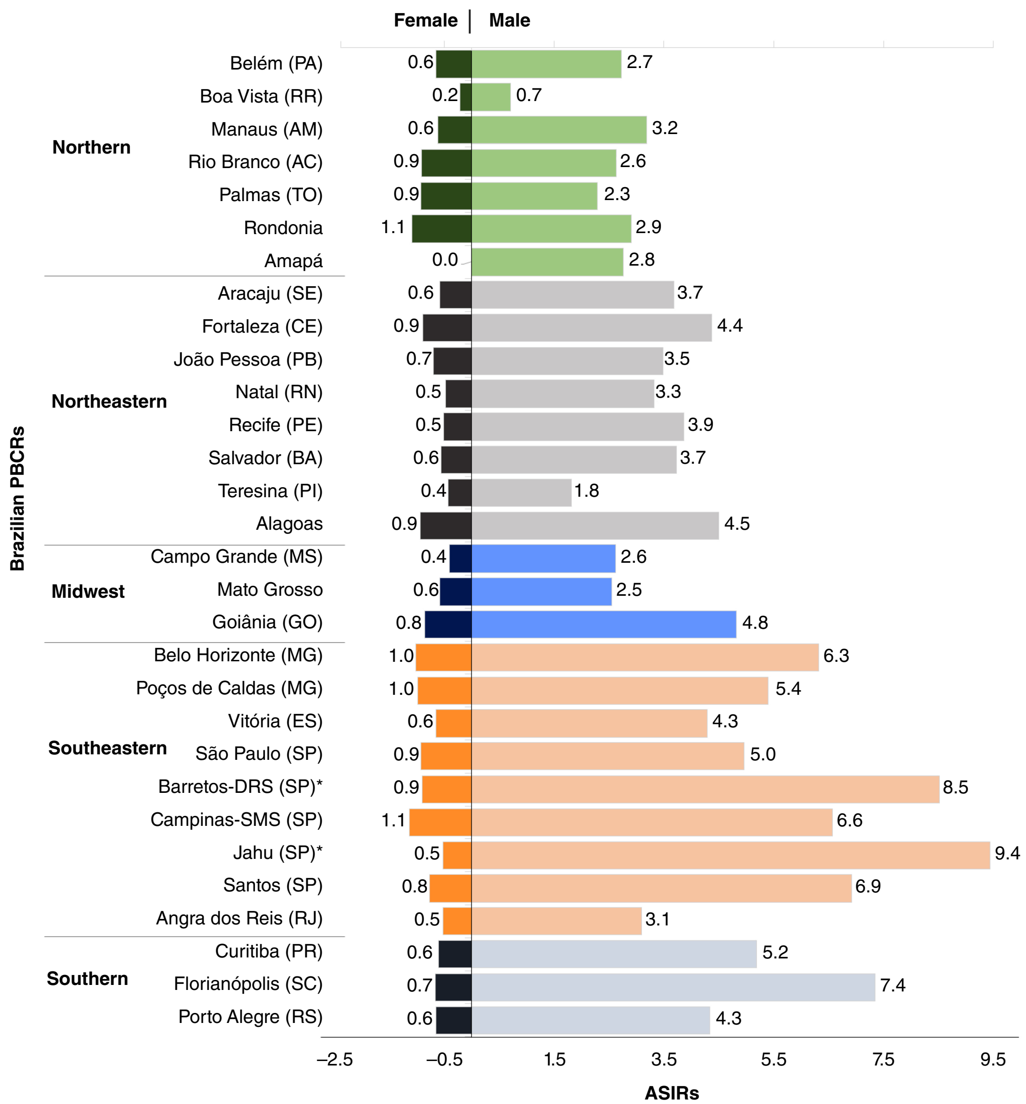


Figure 3.

ASIRs for oropharyngeal cancer in Brazil. The figure shows ASIRs of oropharyngeal cancer by Brazilian region, PBCR, and sex. An asterisk (*) represents the population numbers of two southeast region PBCRs: 131,040 inhabitants in Jahú and 409,267 inhabitants in Barretos.

Horizonte, Espirito Santo, Barretos, and Angra dos Reis; **Fig. 4B**). For both sexes, 16 PBCRs showed an increasing trend in oropharyngeal cancer over the period, whereas the remaining 17 PBCRs for men (**Fig. 4C**) and 21 for women (**Fig. 4D**) exhibited no trend.

Incidence trends according to age group (35–49, 50–64, and >65 years) indicated a rising pattern in males, except in the 35 to 49 age group for three PBCRs in the southeastern region and one in the southern region, in which trends decreased (**Fig. 5A–C**). Among females, a decreasing trend was observed in the 35 to 49 age group and in the north and northeast regions in the 50 to 64 age group. In the group ages over 65 years, an increasing trend was observed in all regions for both sexes (**Fig. 5D–F**; Supplementary Table S8).

Predictions of oropharyngeal cancer incidence rates for 2000 to 2034, grouped into 5-year periods, revealed a reduction in oropharyngeal cancer incidence across all Brazilian regions for females (**Fig. 6A**). The midwestern and southeastern regions showed decreasing trends for men, whereas the other regions (southern, northern, and northeastern) exhibited an increase in incidence rates (**Fig. 6B**; Supplementary Table S9). Due to a lack of studies in Brazil on the prevalence of HPV in oropharyngeal cancer cases by sex, it was not possible to calculate the AF of this infection for oropharyngeal cancer in the country.

Discussion

This study analyzed the incidence and trends of oropharyngeal cancer in Brazil over a 20-year period. The disease was more prevalent in males, particularly among individuals ages 45 to 69 years, with the highest incidence rates found in the southeastern and southern regions. Oropharyngeal cancer incidence significantly

Table 1. Summary of oropharyngeal cancer by PBCR with crude incidence rates, age-standardized rates, and incidence trends by sex and region in Brazil.

Region	PBCR (capitals)	PBCR period	Period in years	All PBCR cases	Population covered according to 2010 Brazilian census	OPC cases			Crude incidence rate			Age-standardized rate			Trends male			Trends female		
						M	F	Total	M	F	Total	M	F	Total	AAPC	Lower CI	Upper CI	AAPC	Lower CI	Upper CI
Northern	Belém (PA)	1996–2019	23	569	1,865,379	425	144	569	2.1	0.6	1.3	2.7	0.6	1.5	0.68	−1.74	3.32	0.39	−2.60	3.60
	Boa Vista (RR)	2003–2014	11	20	450,479	15	5	20	0.5	0.1	0.3	0.7	0.2	0.4	9.44	−4.21	25.04	19.42	−12.55	63.08
	Manaus (AM)	1999–2016	17	387	1,802,014	313	74	387	2.0	0.4	1.2	3.2	0.6	1.8	**4.90**[a]	3.06	7.80	5.64	−0.33	14.91
	Rio Branco (AC)	2010–2017	7	73	733,559	53	20	73	1.8	0.7	1.2	2.6	0.9	1.8	5.34	−7.29	26.86	5.56	−10.38	31.55
	Palmas (TO)	2000–2017	17	37	228,332	27	10	37	1.3	0.5	0.9	2.3	0.9	1.6	**10.32**[a]	8.60	16.00	−0.19	−3.98	3.76
	Rondonia	2015–2017	2	78	1,562,409	57	21	78	2.4	0.9	1.7	2.9	1.1	2.1	—	—	—	—	—	—
	Amapá	2016	1	7	669,526	7	0	7	2.1	—	—	2.8	—	—	—	—	—	—	—	—
Northeastern	Aracaju (SE)	1996–2016	20	193	571,149	157	36	193	3.1	0.6	1.8	3.7	0.6	1.9	0.67	−3.85	5.46	−2.24	−5.15	0.02
	Fortaleza (CE)	1990–2015	25	1,127	2,452,185	848	279	1,127	3.7	0.9	2.2	4.4	0.9	2.4	**5.33**[a]	3.63	7.72	**3.62**[a]	0.23	8.55
	João Pessoa (PB)	1999–2017	18	257	723,515	200	57	257	3.1	0.8	1.9	3.5	0.7	1.9	1.87	−1.42	6.16	**5.56**[a]	0.33	11.07
	Natal (RN)	1999–2008	9	128	803,739	104	24	128	2.6	0.5	1.5	3.3	0.5	1.5	5.55	−9.31	29.08	25.56	12.51	60.68
	Recife (PE)	1995–2018	23	714	1,537,704	575	139	714	3.8	0.7	2.1	3.9	0.5	1.9	**5.80**[a]	3.94	9.03	1.81	−1.34	5.91
	Salvador (BA)	1996–2005	9	494	2,675,656	409	85	494	3.3	0.6	1.9	3.7	0.6	1.9	11.21	0.92	26.00	−1.77	−16.23	13.93
	Teresina (PI)	2000–2006	6	53	814,230	40	13	53	1.5	0.4	0.9	1.8	0.4	1.0	−1.16	−24.33	29.04	0.80	−16.55	21.60
	Alagoas	2010–2011	1	70	3,120,494	56	14	70	3.7	0.9	2.2	4.5	0.9	2.6	—	—	—	—	—	—
Midwest	Campo Grande (MS)	2000–2012	12	146	786,797	124	22	146	2.5	0.4	1.4	2.6	0.4	1.4	**4.84**[a]	2.46	7.28	−2.72	−7.26	0.61
	Mato Grosso[b]	2000–2018	18	795	3,035,122	652	143	795	2.2	0.5	1.4	2.5	0.6	1.6	**2.49**[a]	0.95	4.57	1.50	−1.64	5.51
	Goiânia (GO)	1988–2013	25	623	1,302,001	511	112	623	4.5	0.9	2.6	4.8	0.8	2.6	**4.14**[a]	1.23	8.13	1.46	−5.26	9.32
Southeastern	Belo Horizonte (MG)	2000–2019	19	1,839	2,375,151	1,511	328	1,839	6.8	1.3	3.9	6.3	1.0	3.3	**4.87**[a]	3.87	6.39	**6.44**[a]	4.61	10.02
	Poços de Caldas (MG)[c]	2007–2014	7	44	152,435	37	7	44	6.3	1.1	3.6	5.4	1.0	3.0	−0.84	−19.08	26.34	7.67	−4.54	21.43
	Vitória (ES)	1997–2012	15	581	1,687,704	485	96	581	4.1	0.8	2.3	4.3	0.6	2.3	**6.14**[a]	3.75	9.94	**13.88**[a]	9.27	26.28
	São Paulo (SP)	1997–2015	18	6,384	11,253,503	5,180	1,204	6,384	5.0	1.1	3.0	5.0	0.9	2.7	−0.88	−2.53	0.80	1.17	−1.29	3.71
	Barretos-DRS (SP)[c]	2000–2019	19	437	409,267	388	49	437	9.6	1.2	5.3	8.5	0.9	4.5	1.12	−2.04	4.69	**4.13**[a]	0.49	7.90
	Campinas-SMS (SP)	2010–2018	8	410	1,080,113	336	74	410	7.2	1.5	4.2	6.6	1.1	3.6	−4.99	−14.75	3.55	−4.30	−9.56	0.18
	Jahú (SP)[c]	1996–2020	24	149	131,040	139	10	149	9.3	0.7	4.9	9.4	0.5	4.3	0.33	−2.39	3.19	7.67	−0.04	15.96
	Santos (SP)	2008–2013	5	130	419,400	111	19	130	9.6	1.4	5.1	6.9	0.8	3.4	−2.28	−19.22	16.86	32.52	18.03	62.29
	Angra dos Reis (RJ)[c]	2007–2019	12	37	169,511	32	5	37	2.9	0.5	1.7	3.1	0.5	1.8	8.41	−0.77	18.44	**16.44**[a]	14.13	25.18
Southern	Curitiba (PR)	1996–2018	22	1,067	1,751,907	924	143	1,067	5.3	0.8	2.9	5.2	0.6	2.8	**2.34**[a]	1.03	3.90	1.32	−2.56	5.69
	Florianópolis (SC)	2008–2016	8	156	421,240	139	17	156	7.6	0.8	4.1	7.4	0.7	3.7	10.11	0.45	26.92	−6.91	−20.27	3.21
	Porto Alegre (RS)	1993–2017	24	975	1,409,351	813	162	975	5.0	1.0	2.9	4.3	0.6	2.2	0.10	−2.31	2.47	0.20	−3.15	3.51
Total	**Brazil**	**1988–2020**	**32**	**17,980**	**46,394,912**	**14,668**	**3,312**	**17,980**	**2.8**	**0.5**	**1.6**	**3.0**	**0.5**	**1.6**	**−0.33**	**−2.34**	**1.73**	**0.12**	**−2.56**	**2.87**

Abbreviations: CI, confidence interval; F, female; M, male; OPC, oropharyngeal cancer.
[a]Indicates that the AAPC is statistically different from 0.0 at the alpha = 0.05 level.
[b]Mato Grosso region had two PBCRs, which were grouped because one covered the metropolitan area and the other the suburban area.
[c]PBCRs for rural regions.

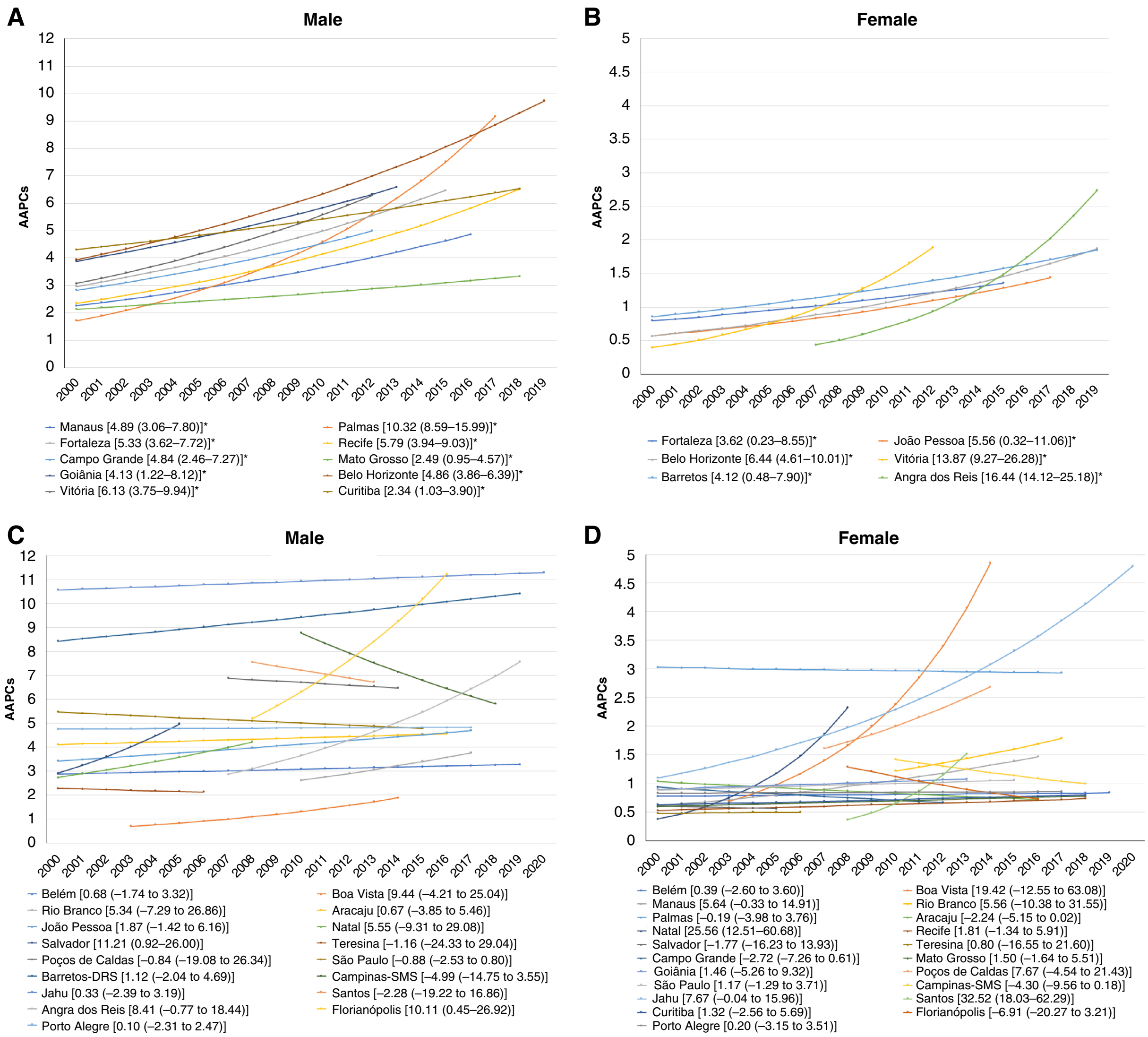


Figure 4.

Incidence trend rates of oropharyngeal cancer in Brazil. The figure displays incidence trend rates of oropharyngeal cancer per year from 2000 to 2020, by sex and PBCR for males (**A** and **C**) and females (**B** and **D**). An asterisk (*) represents a significant AAPC, with confidence intervals shown in parentheses and square brackets.

increased during the 2000 to 2020 period in 10 PBCR regions and both sexes.

Similar to reports in other Latin American countries (Colombia, Costa Rica, Ecuador, and Chile) and countries such as Korea, Turkey, China, Israel, Uganda, and the Philippines, the present study found a lower ASIR for oropharyngeal cancer from 2000 to 2020 compared with rates observed in high-income countries (2, 16, 17). For mortality rates, Brazil reported an average of 4.5/100,000 deaths for men and 0.9/100,000 deaths for women due to oral cancer and oropharyngeal cancer between 1983 and 2017 (18). As expected, regional differences in oropharyngeal cancer incidence were observed, reflecting the diversity within a country of continental size (19). For males, the highest ASIRs were found in cities situated in the southeast and south regions of Brazil. Although the cause of higher incidence is unclear, life expectancy in Brazil reached 75.5 years in 2022, with significant increases since 1998 in the southeast and south regions, where individuals over 60 have a longer disability-free life expectancy (20, 21). Moreover, these southern regions have a higher human development index (HDI) compared with other regions of the country, and an increased incidence of oropharyngeal cancer has been observed in high-HDI countries such as the United Kingdom, Canada, Germany, and Japan (2).

Incidence rates showed a rising trend in 10 PBCRs for men across all Brazilian regions, compared with 6 for women in the southeast and northeast. The other registries remained stable. From 2000 to 2013, trends in oral cancer and oropharyngeal cancer mortality in Brazil exhibited stability for males and an annual increase of 1.31% for females (22). However, oropharyngeal cancer incidence trends have risen globally since 1993 in both sexes, particularly among middle- and high-income countries (2, 5–7).

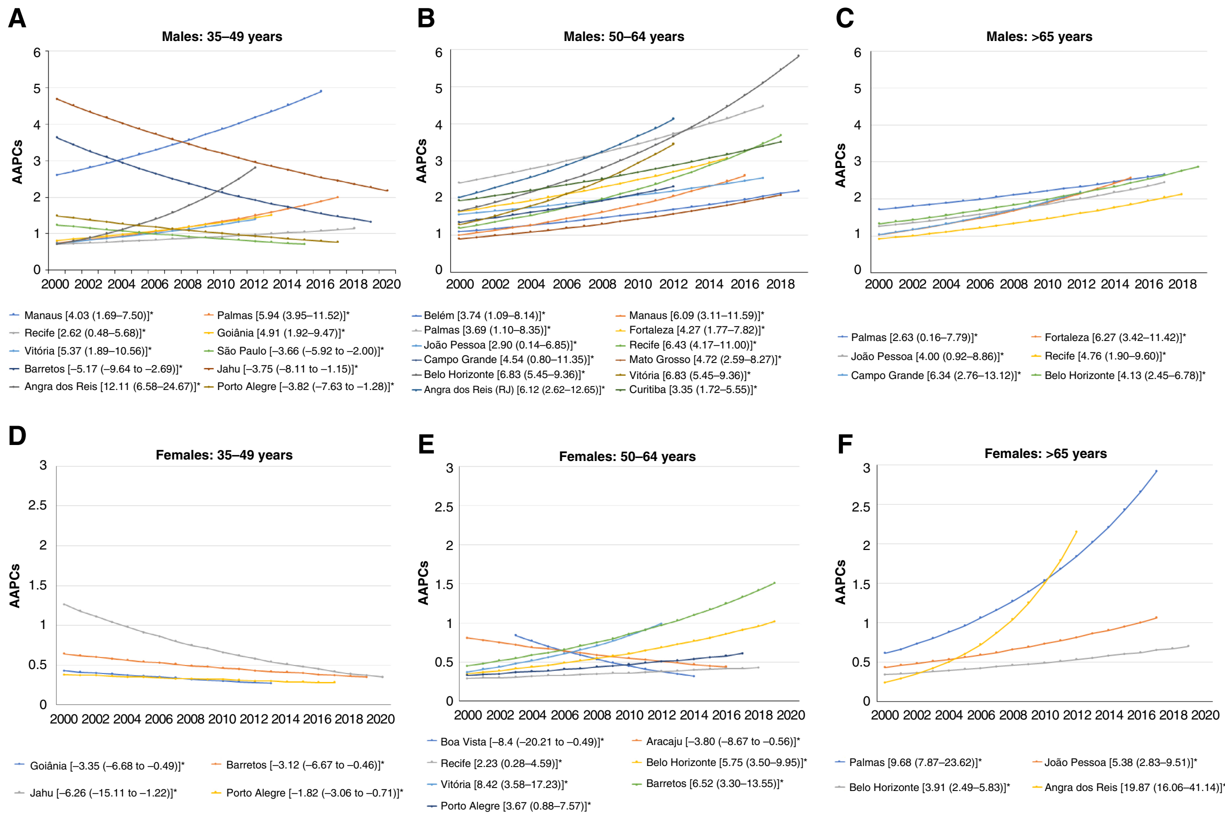


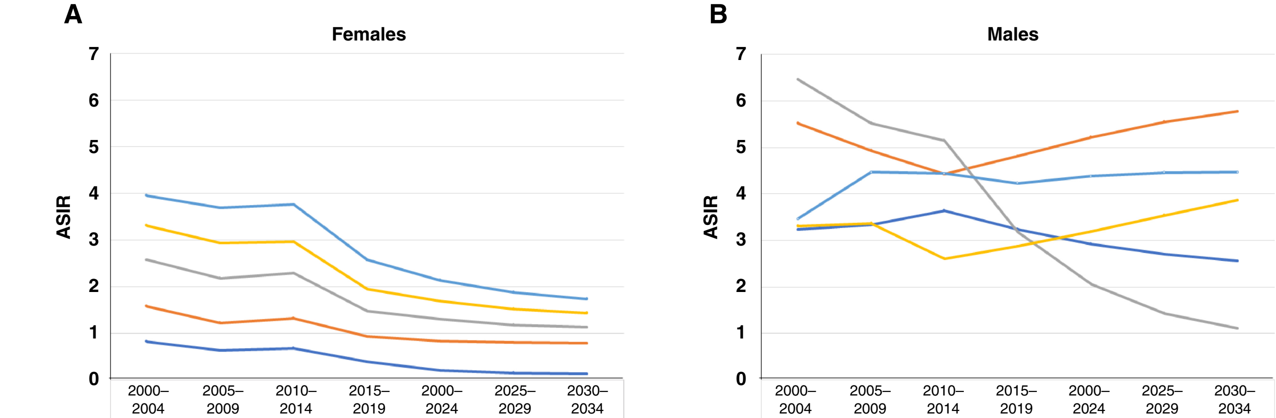
Figure 5.

Incidence trend rates of oropharyngeal cancer according to demographic characteristics. The figure shows incidence trend rates of oropharyngeal cancer per year from 2000 to 2020, with statistical significance, according to age group, sex (**A–C,** male; **D–F,** female), and PBCRs. An asterisk (*) represents a significant AAPC, with confidence intervals shown in parentheses and square brackets.

Predictions for oropharyngeal cancer incidence for 2000 to 2034 revealed a decrease in all Brazilian regions for females. This predicted decline for women may be associated with the beneficial effects of HPV vaccination, which are expected to become evident over the next 15 years. Brazil's public health system provides free access to cervical cancer screening through cytology, Pap smears, HPV detection tests, and vaccination against high-risk HPV subtypes, constituting an essential secondary prevention strategy for both cervical and oropharynx cancers in women (23, 24). HPV vaccination has been part of Brazil's National Immunization Program since 2014, with the quadrivalent HPV vaccine (covering subtypes 6, 11, 16, and 18) offered to girls ages 9 to 13 years. The national coverage goal is approximately 83% (25). However, actual coverage rates vary by region: North Brazil (61.5%), Northeast Brazil (75.6%), Midwest Brazil (67.3%), Southeast Brazil (84.1%), and South Brazil (77.8%). A notably lower coverage rate was observed in Amazonas (21.5%), a microregion in North Brazil, where household inequities in suburban and rural areas are evident (26). These rates were likely affected by the COVID-19 pandemic but are expected to improve as the vaccine is now also offered free of charge to boys ages 9 to 14 and to individuals up to 45 years old with human immunodeficiency virus, organ transplants, or cancer (26). As incidence remains higher among older men, modeling studies project a significant increase in oropharyngeal cancer over the next two decades, as the full effect of vaccination is unlikely to be evident until around 2045 (27).

The incidence of oropharyngeal cancer was higher in males and the 50 to 59 years age group, with increasing incidence trends among men ages 50 years and older. These demographic results are in line with previous reports (28–31). Oral HPV infection exhibits a sex difference in oropharyngeal cancer rates, particularly among men owing to sexual practices. Men are at higher risk of oral HPV infection through oral sex and experience slower clearance of the virus once infected. Conversely, women have a lower risk of oral HPV as the lifetime number of vaginal sex partners increases (32). The present study results revealed a higher frequency of oropharyngeal cancer in oropharyngeal NOS, likely due to the challenges determining the primary subsite when the tumor is in advanced stages. However, oropharyngeal cancer showed a 5% predominance in tonsils among women and in oropharynx NOS among men. This result may seem random, but differences in oropharyngeal cancer by subsite and sex have been previously shown (33).

Despite the increased significance of HPV infection as an etiologic factor in oropharyngeal cancer worldwide, with the HPV16 genotype responsible for most cases (4, 5, 7, 30, 34), the number of cases attributable to HPV could not be ascertained using previously reported studies for Latin America and Brazil due to uncertainty in the fractions (5, 35). However, the



A (Females)	2000–2004	2005–2009	2010–2014	2015–2019	2000–2024	2025–2029	2030–2034
Northeastern	0.64	0.76	0.8	0.62	0.45	0.36	0.3
Northern	0.74	0.75	0.67	0.47	0.39	0.34	0.31
Southeastern	0.99	0.96	0.97	0.55	0.47	0.38	0.34
Southern	0.76	0.59	0.64	0.54	0.63	0.65	0.66
Midwest	0.82	0.63	0.68	0.39	0.2	0.15	0.13

B (Males)	2000–2004	2005–2009	2010–2014	2015–2019	2000–2024	2025–2029	2030–2034
Midwest	3.23	3.34	3.64	3.24	2.92	2.7	2.56
Southern	5.52	4.93	4.42	4.81	5.22	5.55	5.77
Southeastern	6.46	5.52	5.15	3.18	2.06	1.43	1.11
Northern	3.31	3.37	2.61	2.87	3.19	3.54	3.86
Northeastern	3.46	4.47	4.44	4.23	4.38	4.46	4.47

Figure 6.
Prediction of oropharyngeal cancer in Brazil. The figure shows the predicted ASIRs of oropharyngeal cancer per year up until 2034, according to sex (**A,** female; **B,** male) and Brazilian region.

oropharyngeal cancer cases attributable to HPV according to Latin American or Brazilian references differed substantially as the literature was based on retrospective data, likely from genital infections (35, 36). Additionally, the study by de Martel and colleagues (5) used data up to 2012 from the Cancer Incidence in Five Continents database, which is based on six Brazilian cancer registries. Therefore, accurately predicting the actual AF in Brazil and Latin America as a whole is challenging due to inequalities between urban and rural regions and particularly a lack of information on HPV prevalence by sex. This is the main limitation of the study, although it does highlight the actual situation regarding the unknown prevalence of HPV in oropharyngeal cancer in Brazil. Unlike genital HPV infections, in which the prevalence of HPV16 is well-documented (36), there are limited studies on head and neck cancer, with reported HPV16 DNA prevalence rates ranging from 3.1% to 3.5% (37, 38). Consequently, it was not possible to estimate the AF for oropharyngeal cancer incidence in Brazil.

Concerning the limitations of the study, the data presented primarily represent the population covered in urban areas across all regions of Brazil. Although these data do not represent the country as a whole, they provide a clear overview of urban areas and four small rural populations. Furthermore, clusters are evident in some PBCR regions, particularly in the south and southeast regions, where rising incidence rates can be observed. These regional differences can be expected in a country with disparities like Brazil, where the northern (Amazon) and northeastern regions have a deficit in health support, as well as in the maintenance of PBCRs. However, there are potential differences in the quality of PBCR data across different regions of Brazil, which could partly explain the variation in oropharyngeal cancer incidence reported in this study. The highest incidence rates were observed in the southeastern and southern regions, which are the most developed, have the highest HDI, and have nationally recognized oncology institutions, including Barretos, possibly reflecting more reliable cancer registries, although this could be a coincidence. The incidence trend results among women in the northern region of Brazil should be interpreted with caution given that they are based on small populations with low incidence rates and, hence, on few cases over the period.

This study described the incidence of oropharyngeal cancer in Brazil, showing higher incidence rates in males ages 55 to 59 years from the southeastern and southern regions, with trends indicating a projected increase in the coming years. Thus, the study results can help support future public health actions for preventing oropharyngeal cancer in Brazil by raising awareness about the HPV vaccine for high-risk subtypes in the population.

Authors' Disclosures

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Authors' Contributions

L.P.A. Arboleda: Conceptualization, resources, data curation, formal analysis, validation, investigation, visualization, methodology, writing–original draft. **D.L.B. de Souza:** Data curation, visualization, methodology, writing–review and editing. **D.R. Mendonça e Silva:** Data curation, software, visualization, writing–review and editing. **M.P. Curado:** Conceptualization, resources, supervision, validation, visualization, project administration, writing–review and editing.

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Note

Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

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