Diagnosis of mucosal changes and hospitalized oral cancer patients in Brazil: influence of socioeconomic factors

Abstract: This study aimed to analyze the influence of socioeconomic factors on the frequency of diagnoses of oral mucosal changes and the number of hospitalized patients with oral and oropharyngeal cancer in Brazil. This cross-sectional study analyzed data from all Brazilian cities in the period 2011–2017. The frequency of diagnoses of oral mucosal changes and the number of hospitalized patients of oral and oropharyngeal cancer in Brazil were extracted from the Primary Care Information System (SIAB) and Brazilian National Cancer Institute (INCA) databases. The socioeconomic factors evaluated were the Gini coefficient of inequality, municipal Human Development Index (MHDI), inadequate basic sanitation rate, employment rate, illiteracy rate and expected years of schooling. Associated factors were examined using bivariate Spearman’s correlations and multivariate Poisson regressions, and statistically significant (p < 0.05) correlations between study variables and regression coefficients were obtained. A higher frequency of diagnoses of mucosal changes was observed in cities with a higher Gini coefficient (B = 11.614; p < 0.001), higher MHDI (B = 11.298; p < 0.001), and higher number of hospitalized patients with oral and oropharyngeal cancer (B = 0.001, p < 0.002). Cities with higher Gini coefficients (B = 8.159, p < 0.001), higher inadequate basic sanitation rates (B = 0.09, p = 0.001), lower expected years of schooling (B = -0.718, p < 0.001), and higher illiteracy rates (B = 0.191, p < 0.001) had a higher frequency of hospitalized patients with oral and oropharyngeal cancer. In conclusion, more developed cities showed a higher frequency of diagnoses of mucosal changes. Greater inequality and worse socioeconomic conditions are associated with a higher frequency of hospitalized patients with oral and oropharyngeal cancer in Brazil.

Keywords: Mouth Neoplasms; Diagnosis, Oral; Socioeconomic Factors.

Introduction

Lip and oral cavity cancer is one of the most prevalent cancers worldwide; it was estimated to be the 16th most common type of cancer in 2018.1,2 Oropharynx and salivary gland cancer lesions are also frequent and among the thirty most incident cases of cancer in Brazil.2 When considering lip, oral cavity, oropharynx and salivary gland cancer cases, Brazil has an age-standardized rate of 6.5 new cases per
100,000 inhabitants. The incidence of the disease is higher for males and individuals over 60 years of age. In recent decades, however, there has been a reduction in the number of affected men compared to women as well as an increase in the number of cases among young adults younger than 45 years old.

Several factors are associated with the prevalence of oral cancer, including nonmodifiable factors (such as sex and age) and modifiable factors (lifestyle). Smoking and alcohol consumption are considered the main risk factors. Infection by human papillomavirus, solar radiation, immunosuppression and unhealthy eating habits are also relevant etiological factors. Furthermore, the literature reports the influence of environmental factors resulting from the social and economic contexts of individuals. Studies suggest that oral cancer is more prevalent among individuals exposed to unfavorable socioeconomic conditions and those living in socially disadvantaged areas marked by inequality. Thus, socioeconomic vulnerability acts as a risk factor comparable to those related to lifestyle.

Studies suggest that oral cancer is more prevalent among individuals exposed to unfavorable socioeconomic conditions and those living in socially disadvantaged areas marked by inequality. Thus, socioeconomic vulnerability acts as a risk factor comparable to those related to lifestyle. The difficulty in regular access to health care and the greater prevalence of smoking and alcohol consumption, poor nutrition and greater exposure to occupational risk factors may explain this relationship. Recognition of the important role of socioeconomic factors in the development of oral cancer in a population is essential for targeting intersectoral interventions and reducing cancer rates.

Brazil is a developing country of continental size that is affected by social inequalities and a mixed population. Approximately 75% of the population is dependent on the public health system, but only 40% are registered for primary health care through the Family Health Strategy. Within the public healthcare sector in Brazil, measures are available for the diagnosis and treatment of cancer, but access to healthcare services is unequal.

Given the above, the aim of this study was to analyze the influence of socioeconomic indicators on the frequency of diagnoses of oral mucosal changes and the number of hospitalized patients with oral and oropharyngeal cancer in Brazilian cities. This study also included analysis of factors associated with the frequency of hospitalization in those with cancer lesions in the following sites: lip and oral cavity (C-00 to C-06), salivary glands (C-07 to C-09) and oropharynx (C-10). Analysis of socioeconomic factors should contribute to the identification of risk factors, and such information can be used for adjusting public policies in Brazil as well as in other countries and populations.

**Methodology**

An observational, cross-sectional and ecological study was conducted for the period between 2011 and 2017. All Brazilian cities were included (n=5565). The main outcome variables for this study were the number of diagnoses of mucosal changes and the number of hospitalized patients with oral and oropharyngeal cancer.

The number of diagnoses of mucosal changes was obtained from the national database of the SIAB, which is linked to the primary care services of the Brazilian public health system. The diagnosis of mucosal changes consists of a clinical procedure in which the dentist of primary care detects oral lesions during routine examination or during campaigns. According to the SIAB, mucosal changes can be nonneoplastic proliferative processes, benign neoplasms, malignant neoplasms, infectious diseases (bacterial, fungal or viral), mucocutaneous diseases and oral manifestations of systemic diseases. This variable represents the sum of individuals with oral mucosa changes between 2011 and 2015 for each municipality.

The sum of cases of oral and oropharyngeal cancer involving hospitalization registered between 2011 and 2017 was retrieved from the INCA-HRC database of the Brazilian National Cancer Institute (INCA-HRC - https://irhc.inca.gov.br/RHCNet/visualizaTabNetExterno.action).

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tongue, tongue, gingiva, floor of the mouth, palate, other unspecified parts of the mouth, parotid gland, other major salivary glands, tonsils, and oropharynx. The frequency of hospitalized patients with cancer located primarily in the lip and oral cavity (C-00 to C-06), salivary glands (C-07 to C-09) and oropharynx (C-10) was also retrieved from the INCA-HRC. All types of lesions were included, regardless of the degree of staging. A preliminary analysis of cancer data revealed that 90.2% of the cases corresponded to cases of squamous cell carcinoma.

The independent variables comprised socioeconomic information regarding the Gini coefficient of inequality, municipal Human Development Index (MHDI), inadequate basic sanitation rate (percentage of residences without water and sewage supply within the city), employment rate for individuals older than 18 years of age (percentage of employed individuals above 18 years old), illiteracy rate for individuals aged 15 years old or older (percentage of individuals above 15 years who do not know to write and read), and expected years of schooling (average years of schooling expected for a population). Data were obtained from the panel of socioeconomic indicators of Brazilian cities available at the Human Development Atlas of Brazil (http://atlasbrasil.org.br), which is linked to the United Nations Development Program (UNDP). These data correspond to the year 2010.

The data were tabulated and analyzed using IBM Statistical Package for Social Sciences (IBM SPSS, v. 24, IBM, Chicago, USA). Bivariate correlations between dependent and independent variables were obtained using Spearman’s correlation test (p<0.05). Bivariate and multivariate Poisson regressions were performed considering the number of diagnoses of mucosal changes and the number of hospitalized patients with oral and oropharyngeal cancer as dependent variables. The number of inhabitants in the Brazilian cities (2010 population, according to http://atlasbrasil.org.br) was used to weight the effect of multivariate regressions. All independent variables were included in the crude multivariate Poisson regression model, followed by a stepwise backward approach. Only variables with a p-value < 0.20 were included in the adjusted multivariate Poisson regression model.

Variables with a p-value<0.05 in the adjusted model were considered statistically significant. The incident rate ratio (IRR) and confidence interval (95%CI) were obtained for the crude and adjusted models. Regression coefficient B was used to estimate the effect of each independent variable on the dependent variable, considering p < 0.05.

Adjusted multivariate Poisson regression models were also obtained for each group of cancer sites using similar modeling and adjustment approaches. The number of hospitalized patients with cancer in the lip and oral cavity (C-00 to C-06), salivary glands (C-07 to C-09) and oropharynx (C-10) were analyzed according to the independent variables under study by using the population size as the weighting effect and the stepwise backward modeling approach.

The procedures for the diagnosis of mucosal changes and the number of hospitalized patients with oral and oropharyngeal cancer were spatially distributed according to the cartographic database of the Brazilian territory (available at http://datasus.saude.gov.br/cadastros-nacionais/294-download-mapas-tabwin). The total number of records for the period was exported to the cartographic database according to the code for each municipality. The distribution considered the stratification of values into quartiles. The free software Tabwin/DATASUS was used to map the frequency distribution.

**Results**

The number of cities that registered diagnoses of oral mucosal changes between 2011 and 2015 was 3,815 (68.6%). Between 2011 and 2017, 4,252 cities (76.4%) registered at least one case of oral and oropharyngeal cancer involving hospitalization. The descriptive data for cities included in the multivariate analysis are presented in Table 1.

Cities without data for “Inadequate basic sanitation rate” and “Illiteracy rate for individuals 15 years of age or older” were excluded from the analysis. The final sample consisted of 5008 cities. Bivariate correlation analysis showed that the number of diagnoses of oral mucosal changes in primary healthcare had a significant correlation (p < 0.05) with the number of hospitalized patients with oral and oropharyngeal
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The number of hospitalized patients with oral and oropharyngeal cancer reported by the INCA showed a statistically significant correlation (p < 0.05) with all studied variables (Table 2).

Multivariate Poisson regression confirmed that Gini’s inequality coefficient, the MHDI and the number of hospitalized patients with oral and oropharyngeal cancer had a statistically significant association (p < 0.05) with the number of diagnoses of oral mucosal changes (Table 3). A higher frequency of diagnoses of mucosal changes was observed in cities with higher inequality, a higher MHDI, and a higher frequency of hospitalized patients with oral and oropharyngeal cancer.

According to the multivariate regression model (Table 4), cities with higher inequality, a higher

Table 1. Descriptive data of dependent, independent and weight variables considered for analysis.

| Variables | n   | mean | SD  | min. | max. |
|-----------|-----|------|-----|------|------|
| Dependent variables | | | | | |
| Diagnosis of oral mucosal changes (absolute frequency) | 5008 | 76.78 | 473.63 | 0 | 17690 |
| Hospitalized patients with oral and oropharyngeal cancer (absolute frequency) | 5008 | 9.92 | 61.83 | 0 | 3723 |
| Cancer cases according to primary sites | | | | | |
| Oral cavity (C-00 to C-06) (absolute frequency) | 5008 | 8.74 | 50.65 | 0 | 2649 |
| Salivary Glands (C-07 to C-09) (absolute frequency) | 5008 | 2.01 | 12.74 | 0 | 690 |
| Oropharynx (C-10) (absolute frequency) | 5008 | 2.45 | 15.73 | 0 | 799 |
| Covariate independent variables | | | | | |
| Gini’s inequality coefficient | 5008 | 0.50 | 0.06 | 0.29 | 0.80 |
| Municipality’s Human Development Index | 5008 | 0.65 | 0.07 | 0.42 | 0.85 |
| Inadequate basic sanitation rate (%) | 5008 | 9.99 | 13.08 | 0.01 | 85.36 |
| Employment rate for individuals over 18 years of age (%) | 5008 | 62.93 | 9.08 | 21.18 | 95.60 |
| Illiteracy rate for individuals 15 years of age or older (%) | 5008 | 16.79 | 9.91 | 44.40 | 0.95 |
| Expected years of schooling (years) | 5008 | 9.38 | 1.07 | 4.34 | 12.83 |
| Scale Weight | | | | | |
| Population (absolute frequency) | 5008 | 36,440.55 | 212,484.47 | 805 | 11,253,503 |

n: sample size considered for analysis; SD: standard deviation; min.: minimum value; max.: maximum value.

Table 2. Spearman’s bivariate correlation matrix for dependent and independent variables.

| Variables | Diagnosis of oral mucosal changes | Hospitalized patients with oral and oropharyngeal cancer |
|-----------|-----------------------------------|---------------------------------------------------------|
|           | p      | p-value | n   | p   | p-value | n   |
| Diagnosis of mucosal changes in primary care | -      | -       | 5008| 0.304| < 0.001| 5008|
| Hospitalized patients with oral and oropharyngeal cancer | 0.304| < 0.001| 5008| -   | -       | 5008|
| Gini’s inequality coefficient | 0.090| < 0.001| 5008| -0.067| < 0.001| 5008|
| Municipality’s Human Development Index | 0.068| < 0.001| 5008| 0.329| < 0.001| 5008|
| Inadequate basic sanitation rate | 0.030| 0.037| 5008| 0.233| < 0.001| 5008|
| Employment rate for individuals over 18 years of age | 0.016| 0.251| 5008| 0.194| < 0.001| 5008|
| Illiteracy rate for individuals 15 years of age or older | 0.018| 0.206| 5008| 0.308| < 0.001| 5008|
| Expected years of schooling | 0.009| 0.505| 5008| 0.112| < 0.001| 5008|

p: Spearman’s correlation coefficient; p-value < 0.05 indicates a statistically significant correlation; N: sample size considered for analysis.
inadequate basic sanitation rate, lower expected years of schooling and a higher illiteracy rate are likely to present a higher frequency of cancer cases (Table 4).

The diagnosis of oral changes in primary care was statistically significant, but it did not significantly affect the number of cancer cases (95%CI: 1,000–1,000). Income concentration and worse socioeconomic conditions are likely associated with an increase in the number of hospitalized patients with oral and oropharyngeal cancer in Brazil.

The effect of socioeconomic variables on the frequency of cancer primarily located in the lip and oral cavity, salivary glands and oropharynx is shown in Table 5. Similar to that observed in Table 4, higher inequality, a higher inadequate basic sanitation rate, lower expected years of schooling and a higher illiteracy rate were associated with a higher frequency of cancer cases within those cancer sites (Table 5). Major effects were observed for the Gini inequality coefficient and expected years of schooling.

Many cities in Brazil did not register diagnoses of mucosal changes (Figure 1A). A higher frequency of cancer was registered along the coast, mainly for cities from the Northeast, Southeast and South regions (Figure 1B). The regional distribution of cancer cases according to cancer sites is presented in Figure 2 (A to C). A lower frequency of cases was reported for the North and Central-West regions.

**Discussion**

The results from this study suggest that socioeconomic aspects have a significant effect on access to preliminary diagnosis and hospital admission of patients with oral and oropharyngeal cancer in Brazil. Socioeconomic characteristics of Brazilian cities should be interpreted as a modulating factor for the frequency of diagnoses of oral mucosal changes and for the number of cancer cases involving hospitalization. Factors related to the fluctuation of primary care services are diverse, and etiological aspects of oral and oropharyngeal cancer have been extensively discussed. The results from this study suggest that less privileged and
Table 4. Bivariate and multivariate Poisson regressions to determine the effect of independent variables (socioeconomic factors) on the frequency of hospitalized patients with oral and oropharyngeal cancer, as based on the records of the Brazilian National Cancer Institute.

| Variable                                    | Bivariate Crude multivariate model | Adjusted multivariate model |
|---------------------------------------------|-----------------------------------|----------------------------|
|                                             | p-value | IRR (95% CI) | B | p-value | IRR (95% CI) | B | p-value | IRR (95% CI) | B |
| Gini’s inequality coefficient              | < 0.001 | 1.55×107 (3.21×106–7.52×109) | 8.492 | 0.001 | 4874.50 | 27.417–8.66×101 | 8.159 | < 0.001 | 3.494.019 | 149.212–8.18×104 |
| Municipality’s Human Development Index      | < 0.001 | 1.39×1013 (1.09×108–1.78×1019) | -2.785 | 0.069 | 0.062 | 2.658×107–1.43×104 |
| Inadequate basic sanitation                 | 0.008   | 1.549 (1.119–2.146) | 0.093 | 0.013 | 1.097 | 1.020–1.180 | 0.090 | 0.001 | 1.095 | 1.040–1.152 |
| Employment rate for individuals over 18 years of age | 0.001   | 1.070 (1.028–1.114) | -0.030 | 0.344 | 0.971 | 0.913–1.032 |
| Expected years of schooling                 | 0.010   | 1.763 (1.144–2.717) | -0.563 | 0.002 | 0.569 | 0.402–0.807 | -0.718 | < 0.001 | 0.488 | 0.352–0.675 |
| Illiteracy rate for individuals 15 years of age or older | 0.001   | 1.698 (1.255–2.298) | 0.223 | < 0.001 | 1.250 | 1.107–1.412 | 0.191 | < 0.001 | 1.211 | 1.105–1.326 |
| Diagnosis of mucosal changes in primary care | < 0.001 | 1.001 (1.001–1.001) | 0.000 | < 0.001 | 1.001 | 1.001–1.001 | 0.000 | 0.001 | 1.001 | 1.001–1.001 |

B: regression coefficient; SE: standard error; p-value: statistical significance; IRR: incident rate ratio; 95% CI: 95% confidence interval (upper-lower).

Table 5. Multivariate Poisson regression adjusted models (p<0.05) to determine the effect of independent variables (socioeconomic factors) on the frequency of oral cancer primarily located in the lip and oral cavity (C-00 to C-06), salivary glands (C-07 to C-09) and oropharynx (C-10), as based on the records of the Brazilian National Cancer Institute.

| Variable                                    | Lip and oral cavity (C-00 to C-06) | Salivary glands (C-07 to C-09) | Oropharynx (C-10) |
|---------------------------------------------|-----------------------------------|--------------------------------|------------------|
|                                             | B | IRR (95% CI) | Lower | Upper | B | IRR (95% CI) | Lower | Upper | B | IRR (95% CI) | Lower | Upper |
| Gini’s inequality coefficient              | 9.938 | 20701.49 | 730.88 | 586,346.35 | 13.160 | 519,420.49 | 11,549.57 | 2,3359,976.38 | 8.396 | 4,428.67 | 197.898 | 99,107.03 |
| Municipality’s Human Development Index      | 0.097 | 1.101 | 1.059 | 1.145 | 0.134 | 1.143 | 1.055 | 1.237 | 0.015 | 1.111 | 1.062 | 1.161 |
| Inadequate basic sanitation                 | -0.388 | 0.679 | 0.522 | 0.882 | -0.684 | 0.505 | 0.406 | 0.627 |
| Employment rate for individuals over 18 years of age | 0.161 | 1.175 | 1.085 | 1.272 | 0.190 | 1.209 | 1.086 | 1.346 | 0.237 | 1.268 | 1.162 | 1.383 |
| Expected years of schooling                 | 0.161 | 1.175 | 1.085 | 1.272 | 0.190 | 1.209 | 1.086 | 1.346 | 0.237 | 1.268 | 1.162 | 1.383 |
| Illiteracy rate for individuals 15 years of age or older | 0.000 | 1.000 | 1.000 | 1.000 | 0.000 | 1.000 | 1.000 | 1.000 | 0.000 | 1.000 | 1.000 | 1.000 |

B: regression coefficient; IRR: incident rate ratio; 95% CI: 95% confidence interval.
vulnerable populations are less likely to have access to preliminary diagnosis and to hospital treatment. Nevertheless, the results should be interpreted with care, as the study was based on a secondary source of information under a cross-sectional design.

The offer of diagnostic procedures for oral mucosal changes was initially proposed by the Brazilian Ministry of Health to encourage the monitoring and planning of policies and actions aimed at health promotion, prevention and early diagnosis in primary care. However, the Brazilian primary care information system has undergone recent changes, and many professionals still do not know it thoroughly or have not received the training necessary to understand the nature of this type of notification.21 This scenario can lead to inefficient registration, even though this source of data is still reliable for monitoring Brazilian public health services.22

Figure 1. A: Frequency distribution into quartiles of diagnoses of mucosal changes among Brazilian cities. B: Frequency distribution into quartiles of hospitalized patients with oral and oropharyngeal cancer among Brazilian cities.

Figure 2. Frequency distribution into quartiles of hospitalized patients with cancer in the lip and oral cavity (A), salivary glands (B) and oropharynx (C) among Brazilian cities.
To our knowledge, data for the diagnosis of oral mucosal changes have not been used before for discussing the access of a population to oral cancer preliminary diagnosis. Data from this study suggest that more unequal and more developed cities may also have a greater number of records of diagnoses of oral mucosal changes. This is probably due to a better-structured network of health care services, mainly in larger and more populated cities. Although the frequency of diagnoses of oral mucosal changes seems well distributed among the Brazilian macroregions, many cities did not register any case of oral mucosal change between 2011 and 2015.

It is important to highlight that an absence of registered diagnosis of oral mucosal changes does not mean an absence of cases, a lower frequency of oral mucosal examination, or inefficiency of the healthcare network. Indeed, it is probably due to a lack of registration or low coverage of primary care within the municipality. Overall, the frequency of diagnoses of oral mucosal changes might not be reliable for monitoring the frequency of early diagnosis of oral cancer. Nevertheless, this parameter is unique and may provide some evidence regarding population access to oral mucosal examination as a preventive measure for oral cancer in Brazilian primary care.

Although statistically significant bivariate correlations between the number of diagnoses of oral mucosal changes and the frequency of hospitalized cancer cases were detected in the present study, it is not possible to affirm that those variables are strictly associated. In fact, adjusted multivariate models demonstrated very limited associations between those variables.

The frequency of hospitalization of patients with oral and oropharyngeal cancer obtained from the INCA-HRC may not be considered as a measure of cancer prevalence in Brazil. Although the absolute frequency of cases is not the best parameter for evaluation, it is uniquely related to the cancer frequency in Brazil. The INCA-HRC does not currently provide age-standardized rates for each municipality in different periods of time, which would be recommended. Thus, the data used in this study correspond to the absolute frequencies of hospitalized patients retrieved from the INCA-HRC. To reduce the influence of hospital-based data, the authors used the population size to weight the effects, in addition to harvesting the number of cases according to the municipality of residence.

The absence of records should not be interpreted as a lack of realistic cases because not all cases of cancer in Brazil are linked to the INCA-HRC. For example, the lower frequency of cases recorded for the North and Central-West regions may be associated with a lower proportion of cancer treatment units, which are more concentrated in the Northeast (19.1%), Southeast (46.3%) and South (23.5%) regions. Therefore, it is important to assume that eventually, cases of cancer may not be registered due to the limited access of the population to health services.

The healthcare network for cancer patients in Brazil is preferentially part of the public healthcare system, and it is mostly located in capitals and better-developed centers. The absence of a statistical association between the MHDI and the frequency of hospitalized cases of cancer is probably because we analyzed data based on the municipality of residence. Nevertheless, other relevant socioeconomic aspects were significantly associated with a higher frequency of cases, irrespective of the primary site of cancer.

The effect of socioeconomic factors on the frequency of oral cancer primarily located in the lip and oral cavity (C-00 to C-06), salivary glands (C-07 to C-09) and oropharynx (C-10) is novel, as previous studies have analyzed those different primary sites as a single entity. This study found similar socioeconomic factors associated with the frequency of hospitalized patients with cancer in the lip and oral cavity, salivary glands and oropharynx. Overall, the inequality coefficient was the most significant socioeconomic variable, considering both the general number of hospitalized cancer patients and those stratified by primary site.

The impact of socioeconomic inequality has been discussed in a previous meta-analysis, which considered unjust differences regarding monthly household income, occupational social class and educational level. According to this previous review, socioeconomic inequalities are potentially associated with lifestyle risk factors in a complex manner. Data from our study confirm that higher education and access to better living conditions (access to water and
sewage supply) have a general impact on the frequency of hospitalization of patients with oral cancer.

The influence of the MHDI on oral cancer rates in Brazil varies; some found an inversely proportional effect,\textsuperscript{5,13,17} whereas others suggest a positive association\textsuperscript{27}. In the present study, despite showing a positive correlation with hospitalized patients with oral and oropharyngeal cancer in bivariate analysis, the effect of the variable MHDI was lower than that of other socioeconomic factors that seem to have greater strength of association from the perspective of Brazilian cities. Although they may be considered developed, many cities have strong income concentration, segregation and social inequalities.\textsuperscript{28} In this sense, the factors included in the analysis comprise aspects such as education and income, which themselves are part of the MHDI. Therefore, exclusion of the MHDI from the adjusted model does not suggest a problematic analysis or a collinearity issue.

The results and inferences of the present study should be analyzed carefully, considering the cross-sectional design and the secondary data source. Regardless, the data from this study are representative of the Brazilian population and are from all of its cities for the last decade. Oral and oropharyngeal cancer is a complex disease, and several etiological and modifying factors must be taken into account. Further analyses of other countries and socioeconomic contexts may corroborate the findings of this study.

**Conclusion**

A higher frequency of diagnoses of mucosal changes was observed in more developed cities and those with inequality. Greater inequality and worse socioeconomic conditions are associated with a higher frequency of hospitalized patients with oral and oropharyngeal cancer in Brazil.

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