



UNIVERSIDADE ESTADUAL DE CAMPINAS
Faculdade de Odontologia de Piracicaba

GISELE PEDROSO MOI

**ANÁLISE ESPACIAL DOS FATORES ASSOCIADOS À MORTALIDADE POR
NEOPLASIAS MALIGNAS DE LÁBIO, CAVIDADE ORAL E FARINGE NO
BRASIL, 2005 - 2014.**

**SPATIAL ANALYSIS OF THE ASSOCIATED FACTORS TO MORTALITY
FOR MALIGNANT NEOPLASMS OF LIPS, ORAL CAVITY AND PHARYNX
IN BRAZIL, 2005 - 2014.**

PIRACICABA

2017

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Tese de doutorado apresentada à Faculdade de Odontologia de Piracicaba da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de Doutor em Odontologia, na área de Saúde Coletiva.

Thesis presented to the Piracicaba Dental School of the University of Campinas in partial fulfillment of the requirements for the degree of Doctor in Dentistry, in Collective Health area.

Orientador: Prof. Dr. Antonio Carlos Pereira

ESTE EXEMPLAR CORRESPONDE À
VERSÃO FINAL DA TESE DEFENDIDA
PELA ALUNA GISELE PEDROSO MOI,
E ORIENTADA PELO PROF. DR.
ANTONIO CARLOS PEREIRA.

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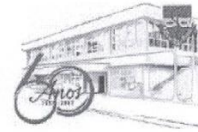
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A Ata da defesa com as respectivas assinaturas dos membros encontra-se no processo de vida acadêmica do aluno.

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ABSTRAC

Malignant neoplasms affecting the lip, oral cavity and pharynx are among the ten most common cancers and the seventh most frequent cause of death worldwide. This pathology accounts for 75% of malignant tumors of the head and neck, being the fourth most prevalent type of cancer in males. There are marked variations in the incidence and mortality rates of lip, oral cavity and pharyngeal cancer in the various geographic regions in the world, and these rates have been higher in developed countries compared to developing countries. Estimates and predictions of cancer incidence and mortality provide references to exposure to risk factors and allow the evaluation of the effectiveness of existing health interventions, making them valuable tools for redirecting programs to control, manage and distribute financial and human resources. This exploratory ecological study investigated the global spatial autocorrelation of epidemiological aspects with mortality rates due to malignant neoplasms affecting the lip, oral cavity and pharynx in the period 2005-2014 in the Brazilian states, using the "global" Moran statistic LISA method and, subsequently, a multiple spatial regression, having as variables of exposure the habits and lifestyle, sociodemographic indicators, the consumption of pesticides, the presence of comorbidities, the use of health services and food consumption; And, as a variable response, mortality rates due to malignant neoplasms affecting the lip, the oral cavity. The software used was Stata 11.0, SPSS 18.0 and GeoDa 0.95-i. Global spatial patterns were found in the distribution of mortality rates due to malignant neoplasm of lip, oral cavity and pharynx for the age of 40 years or older. In the multiple regression, statistically significant negative correlations were observed between the human development index (HDI) and the mortality rates for lip, oral cavity and pharynx standardized by age in the studied period ($p < 0.05$) and positive among the variables proportion of the population that dentist consultation in the last year, percentage of consumption of oils and fats kcal / day per capita, percentage of consumption of prepared foods and industrial mixtures kcal / day per capita and percentage of overweight adults ($BMI \geq 25 \text{ kg} / \text{m}^2$) with this type of cancer ($p < 0.05$). This is the first study that analyzed the factors associated to the spatial clusters of mortality due to oral cancer in the Brazilian Federative Units. A fairly unequal distribution of these mortality rates was found, being that these rates presented inverse association with HDI and direct association with dental appointment, consumption of oils and fats, ready-to-eat foods and industrial mixtures consumption and overweight these rates. It suggests the need to redirect Brazilian public policies

aimed at combating them so that they cease to be temporary and become permanent.

Key words: Mouth Neoplasms. Spatial Analysis. Mortality. Epidemiology. Ecological Studies. Risk Factors.

RESUMO

As neoplasias malignas que acometem os lábios, a cavidade oral e a faringe estão entre os dez tipos de cânceres mais comuns e a sétima causa mais frequente de morte em todo o mundo. Esta patologia é responsável por 75% dos tumores malignos de cabeça e pescoço, sendo o quarto tipo de câncer mais prevalente no sexo masculino. Existem acentuadas variações nas taxas de incidência e mortalidade de câncer de lábio, cavidade oral e faringe nas diversas regiões geográficas no mundo, sendo que estas taxas têm se apresentado maiores nos países desenvolvidos em relação aos países em desenvolvimento. As estimativas e previsões de incidência e mortalidade por câncer fornecem referências de exposição a fatores de risco e permitem a avaliação da efetividade das intervenções de saúde existentes, tornando-se ferramentas valiosas para redirecionar os programas de controle, gerenciamento e distribuição dos recursos financeiros e humanos. Este estudo ecológico exploratório investigou a autocorrelação espacial global dos aspectos epidemiológicos com as taxas de mortalidade por neoplasias malignas que acometem o lábio, a cavidade oral e a faringe no período 2005-2014 nos estados brasileiros, usando a estatística Moran “global” pelo método LISA e, posteriormente, uma regressão múltipla espacial, tendo como variáveis de exposição os hábitos e estilo de vida, indicadores sociodemográficos, o consumo de agrotóxicos, a presença de comorbidades, a utilização de serviços de saúde e o consumo alimentar; e, como variável resposta, as taxas de mortalidade por neoplasias malignas que acometem o lábio, a cavidade oral. Os softwares utilizados foram o Stata 11.0, SPSS 18.0 e GeoDa 0.95-i. Foram encontrados padrões espaciais globais na distribuição das taxas de mortalidade por neoplasia maligna de lábio, cavidade oral e faringe para a idade igual ou superior a 40 anos. Na regressão múltipla, foram observadas correlações estatisticamente significantes negativas entre índice de desenvolvimento humano (IDH) com as taxas de mortalidade por câncer de lábio, cavidade oral e faringe padronizada por idade no período estudado ($<0,05$) e positiva entre as variáveis proporção da população que realizou consulta dentista no último ano, percentual de consumo de óleos e gorduras kcal/dia per capita, percentual de consumo de alimentos preparados e misturas industriais kcal/dia per capita e percentual de adultos com sobrepeso ($IMC \geq 25 \text{kg/m}^2$) com este tipo de câncer ($p < 0,05$). Este é o primeiro estudo que analisou os fatores associados espaciais de mortalidade por câncer bucal nas Unidades da Federação Brasileira. Verificou-se distribuição bastante desigual destas taxas de mortalidade, sendo que estas apresentaram associação inversa com IDH e associação

direta com a nomeação dentária, consumo de óleos e gorduras, consumo de alimentos prontos e consumo de misturas industriais e sobrepeso dessas taxas. Sugere a necessidade de reorientar as políticas públicas brasileiras que visam combatê-las para que elas deixem de ser temporárias e se tornem permanentes.

Palavras-chave: Neoplasias Bucais. Análise Espacial. Mortalidade. Epidemiologia. Estudos Ecológicos. Fatores de Risco.

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1 INTRODUÇÃO

O câncer bucal é um dos tipos de neoplasia maligna mais frequente em todo mundo (Siegel, Naishadham e Jemal, 2012, Listl et al., 2013), sendo considerado um problema de saúde pública mundial (Rivera, 2015). Cerca de dois terços do ônus mundial destes tumores encontram-se dentro dos países em desenvolvimento, onde os casos muitas vezes podem estar subestimados (Swaminathan, Rama e Shanta, 2008). Esta neoplasia maligna apresenta uma variação de incidência de cerca de 20 vezes nas bases de dados internacionais (Ferlay et al., 2010 e Warnakulasuriya, 2009).

Parte destas variações de incidência podem ser decorrentes da falta de consenso na designação das localizações anatômicas envolvidas e do tipo histológico de neoplasias malignas que incluem o câncer bucal, dificultando as comparações entre os vários estudos realizados ao redor do mundo (Tapia e Goldberg, 2011). Dentre as localizações anatômicas do câncer bucal mais comumente descritas na literatura está a área situada entre o vermelhão do lábio e a junção do palato mole e duro (de Camargo Cancela et al., 2010), podendo ser acrescentada a região de orofaringe (Warnakulasuriya, 2009), nasofaringe e hipofaringe (Rodu e Cole, 2007), glândulas salivares maiores (Morse e Kerr, 2006, Zini et al., 2009), porção externa do lábio que envolve a pele (Swango, 1996). Além disso, alguns trabalhos na literatura ainda não especificam em quais sítios anatômicos bucais estas neoplasias malignas estão incluídas (Petti e Scully, 2005, Kingsley et al., 2008, Tramacere et al., 2010). Em relação a tipologia histológicos descritas na literatura com câncer bucal estão as neoplasias malignas das mucosas (Brown, Check e Devesa, 2011) e tecidos adjacentes às mucosa, tais como as glândulas salivares (Canto e Devesa, 2002), tecido conjuntivo (Ostman et al., 1995; Zini et al., 2009 e Zini, Czerninski e Sgan-Cohen, 2010), tecido epitelial adjacente ao lábio (Swango, 1996), tecido linfóide (Zini, Czerninski e Sgan-Cohen, 2010; Zini et al., 2009), tecido muscular (Ostman et al., 1995) e tecido nervoso (Canto, Devesa, 2002). Independentemente da localização anatômica ou tipologia histológica, os tumores que acometem o lábio, língua e cavidade oral e da orofaringe possuem biologia similar e vários fatores de risco em comum, sendo muitas vezes por isso agrupados em uma mesma categoria nos estudos (WHO, 2010).

As neoplasias malignas que acometem o lábio, cavidade oral e a faringe estão entre os dez tipos de cânceres mais comuns e a sétima causa mais frequente de morte em todo o mundo (Jemal et al., 2011; Mehanna et al., 2011). Esta patologia é

responsável por 75% dos tumores malignos de cabeça e pescoço (Perié et al., 2014). O risco de desenvolver este tipo de câncer aumenta com a idade, sendo que a maior parte dos casos desta patologia acomete indivíduos com idade igual ou superior a 50 anos (Warnakulasuriya, 2009). Porém, nos países que possuem alta incidência desta neoplasia no mundo, muitos casos são notificados em adultos jovens com menos de 45 anos (Llewellyn et al., 2001; Shiboski et al., 2005; Warnakulasuriya, 2009).

Existem acentuadas variações nas taxas de incidência e mortalidade de câncer de lábio, cavidade oral e faringe nas diversas regiões geográficas no mundo, sendo que estas taxas têm se apresentado maiores nos países desenvolvidos em relação aos países em desenvolvimento (Pisani et al., 1999). Estas variações de incidência refletem as diferenças de risco dos quais as populações estão expostas, porém parte destas variações pode ser atribuída a artefatos, ocasionados pelas diferenças na definição de caso, apuração incompleta, e acesso diferenciado aos cuidados e diagnóstico (Antunes et al., 2008). Já a variação na taxa de mortalidade por câncer sofre a influência de fatores representados pelo acesso aos cuidados de saúde heterogêneo e diagnóstico precoce, comorbidades dos pacientes e o risco de causas competitivas de morte (Antunes et al., 2008).

Os fatores genéticos desempenham um papel importante na carcinogênese, porém os fatores de risco ambientais, comportamentais e ocupacionais desempenham uma forte influência neste processo (Perera e Weinstein, 2000). Assim, esta patologia tem seu desenvolvimento estimulado pela interação de fatores ambientais, comportamentais e ocupacionais (agentes cancerígenos ou carcinógenos) e fatores relacionados ao próprio hospedeiro (idade, raça, sexo, mutações espontâneas e mutações herdadas) (Perera, 1997).

As exposições aos agentes cancerígenos ou carcinógenos estão de alguma forma relacionada às desigualdades sócio-econômicas e podem contribuir de forma significativa com a incidência de câncer (Wünsch-Filho e Moncau, 2002). Os estratos sociais desfavorecidos apresentam um perfil de risco de maior suscetibilidade, utilizam menos o sistema de saúde para fins de prevenção (Lorant et al., 2002), possuem menor acesso ao diagnóstico precoce das neoplasias malignas, menos recursos terapêuticos e um pior prognóstico no tratamento das neoplasias malignas (Coleman et al., 2001).

Mais de 80% dos casos de câncer de lábio, cavidade oral e faringe nos países ocidentais estão associadas com o uso de tabaco e o consumo de álcool (Negri et al., 1993; MacFarlane et al., 1996; Rodriguez et al., 2004 e Bravi et al., 2013).

Adicionalmente, alguns estudos têm demonstrado também que uma dieta pobre apresenta um papel relevante na etiologia desta patologia (Negri et al., 1993; MacFarlane et al., 1996; Pelucchi et al., 2003; Rodriguez et al., 2004; Saman, 2012 e Bravi et al., 2013). Por outro lado, efeitos protetores de uma dieta saudável têm sido observados em alguns estudos (Pelucchi et al., 2003; Rodriguez et al., 2004; Saman, 2012). Dentre os achados mais consistentes, observa-se um efeito protetor associado a uma dieta rica em frutas, legumes, verduras, ao consumo regular de café e a ingestão regular de ácido fólico na dieta (Pelucchi et al., 2003; Rodriguez et al., 2004; Saman, 2012). Existem ainda outros fatores descritos na literatura que podem aumentar o risco desta neoplasia, assim como: a exposição a pesticidas, gases oriundo da exaustão de motores, queima de biomassa, exposição ao sol para câncer de lábio, exposição a alguns vírus do papiloma humano (Pelucchi et al., 2003 e Tarvainen et al., 2008) e exposição a infecções por bactérias como a *H. pylori* (Dayama et al, 2011).

O papilomavírus humano (HPV), particularmente o tipo 16, é detectado em cerca de 70% dos carcinomas da orofaringe (Westra, 2009). A infecção pelo papiloma vírus tem mudado o perfil dos pacientes com câncer oral, o que antes era prevalente em homens mais velhos, fumantes de tabaco e consumidores de bebida alcóolica, agora é encontrado em homens mais jovens (entre 40 e 60 anos), que não possuem hábito de fumar cigarros e beber álcool (D'Souza et al, 2007). Os fatores de risco tradicionais foram suplantados por outros fatores de risco poderosos, relacionados a práticas sexuais, o mais importante deles sendo o alto número de parceiros, o histórico de sexo oral-genital e sexo oral-anal (Smith et al, 2004). Certas condições e comportamentos que alteram a imunidade antitumoral podem ser importantes na transformação de uma infecção oral por HPV em uma magnificação causada por HPV. Como um exemplo, o uso de maconha tem sido identificado como um fator de risco independente para o câncer oral positivo ao HPV, e a força dessa associação aumenta com a intensidade, duração e quantidade cumulativa de anos de fumo da maconha. Canabinóides se ligam ao receptor CB2, expresso em células imunomodulatórias do tecido tonsilar humano. A ligação pode suprimir a resposta imune, diminuindo a resposta do hospedeiro aos agentes virais e atenuando a atividade antitumoral. (Westra, 2009).

A bactéria *H. pylori* tem sido associada ao desenvolvimento de úlceras pépticas e câncer gástrico. A *H. pylori* pode ser transmitida através da cavidade oral, que pode constituir reservatório natural dessa bactéria, especialmente entre os pacientes com periodontite que possuem a bactéria no trato gastrointestinal (Umeda et al, 2003).

A associação entre *H. pylori* e câncer oral é controversa, com alguns estudos apontando a presença da bactéria em casos de câncer oral (Dayama et al, 2011; Irani et al, 2013) e outros apontando uma associação inversa entre infecção por *H. pylori* e presença de carcinoma oral de célula escamosa (Meng et al, 2016). Estudos futuros com maior amostragem devem esclarecer se a presença de *H. pylori* constitui ou não risco para desenvolvimento de câncer oral.

De modo geral, a sobrevida dos pacientes acometidos pelas neoplasias malignas do lábio, cavidade oral e faringe diminui quando seu diagnóstico é realizado tardiamente, fazendo com que as chances de inacessibilidade do tumor aumentem (Warnakulasuriya, 2009). Para a maior parte dos países, as taxas de sobrevivência de cinco anos para câncer de lábio, cavidade oral e orofaringe encontram-se em torno de 50%, sendo que o melhor resultado encontrado é para o câncer de lábio, com mais de 90% dos pacientes que sobrevivem por cinco anos (Rubin, 1993). Além disso, muitos dos que apresentam sucesso no tratamento desta patologia tem que lidar com as sequelas devastadoras decorrentes da terapêutica empregada que podem afetar a aparência e a função do paciente (comer, beber, engolir e falar), além da qualidade de vida, propiciando o desenvolvimento de depressão e deficiências nutricionais nestes pacientes (Warnakulasuriya, 2009).

As estimativas e previsões de incidência e mortalidade por câncer são de extrema relevância para o processo de planejamento de estratégias em saúde pública (Olsen et al., 2008). Pois, fornecem referências de exposição a fatores de risco e permitem a avaliação da efetividade das intervenções de saúde existentes (campanhas de prevenção, rastreio e programas de tratamento), tornando-se ferramentas valiosas para redirecionar os programas de controle e melhor distribuir os recursos financeiros e humanos (Bray e Moller, 2006). Entretanto, estas estimativas isoladamente não são suficientes para compreender a verdadeira magnitude, tendências das neoplasias malignas e avaliar as intervenções contra o câncer (Shibuya et al., 2002).

Este é o primeiro estudo que analisou os fatores associados aos clusters espaciais da mortalidade por câncer de lábio, cavidade oral e faringe nas unidades federativas brasileiras e seus resultados trazem importantes contribuições para a compreensão dos aspectos epidemiológicos espaciais envolvidos neste processo. Embora as políticas públicas de combate ao câncer bucal tenham sido introduzidas desde o início do século XXI no Brasil, este estudo mostra uma distribuição bastante desigual destas taxas de mortalidade que apresentaram associação inversa com IDH e

associação direta com proporção da população que consultou o dentista no último ano, porcentagem de consumo de óleos e gorduras, porcentagem de consumo de alimentos preparados e misturas industriais e porcentagem de adultos com sobrepeso. Sugerindo a necessidade de redirecionamento das políticas públicas brasileiras destinadas ao combate do câncer de lábio, língua e cavidade oral e da orofaringe para que deixem de ser temporárias e se tornem permanentes.

2 ARTIGO¹**SPATIAL ANALYSIS OF THE DEATH ASSOCIATED FACTORS DUE ORAL
CANCER IN BRAZIL: AN ECOLOGICAL STUDY****Gisele Pedroso Moi^{1,3*}****Ageo Mário Cândido Silva^{2,3}****Marcelo de Castro Meneghim¹****Antonio Carlos Pereira¹**

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Abstract

Objective: Oral cancer (OC) is among the ten most common cancers and the seventh most frequent cause of death worldwide. There are marked variations in the incidence and mortality rates for this type of cancer in the various geographic regions in the world. It has been reported that these incidence rates are higher in developed country and these mortality rates are higher in less developed areas. So, the objective of the present study was to analyze the spatial joint distribution and to explore possible associations of the epidemiological aspects with mortality rates due to OC in the Brazil.

Methods: An exploratory ecological study investigated the global spatial autocorrelation of epidemiological aspects with mortality rates due to OC from the Brazilian Federative Units (n=27) in the period 2005-2014, using the "global" and "local" Moran statistic method and a multiple spatial regression, having as variables of exposure the habits and lifestyle, sociodemographic indicators, the consumption of pesticides, the presence of comorbidities, the use of health services and food consumption; and, as a variable response, mortality rates due to OC. The software used was Stata 11.0, SPSS 18.0 and GeoDa 0.95-i.

Results: The spatial distribution of OC mortality rates to age-standard was not random and showed high spatial autocorrelation and predominance of significant spatial groupings in the Central-South region of Brazil. In the multiple regression, statistically negative associations were observed between the HDI and OC age-standardized in the studied period ($p < 0.05$) and positive associations among the proportion of the population with dental appointment within last year, percentage of consumption of oils and fats, percentage of consumption of ready-to-eat foods and industrial mixtures and percentage of overweight adults with this type of cancer ($p < 0.05$).

Conclusion: This is the first study that analyzed the factors associated to the spatial clusters of mortality due to oral cancer in the Brazilian Federative Units. A fairly unequal distribution of OC mortality rates was found, being that these rates presented inverse association with HDI and direct association with dental appointment, consumption of oils and fats, ready-to-eat foods and industrial mixtures consumption and overweight these rates. It suggests the need to redirect Brazilian public policies aimed at combating them so that they cease to be temporary and become permanent.

Key words: Mouth Neoplasms. Spatial Analysis. Mortality. Epidemiology. Ecological Studies. Risk Factors.

Introduction

Oral cancer (OC) is among the ten most common cancers and the seventh most frequent cause of death worldwide¹. Its incidence increases with age, in countries with a high incidence of this malignant neoplasm in the worldwide, many cases are reported in young adults < 45 years².

This pathology has its development stimulated by the interaction of environmental, behavioral and occupational factors (carcinogens or carcinogens) and factors related to the host itself (age, race, sex, spontaneous mutations and inherited mutations)³. Exposures to carcinogens are in some way related to socioeconomic inequalities and may contribute significantly to the incidence and mortality of cancer⁴. More than 80% of OC cases occurring in Western countries are associated with tobacco use and alcohol consumption⁵. Additionally, studies have also demonstrated that a poor diet plays a relevant role in the etiology of this pathology⁵. Besides, protective effects of a healthy diet have been observed and they are associated with a diet rich in fruits, vegetables, regular coffee consumption and regular intake of folic acid in the diet⁶. There are also other factors that may increase the risk of this malignant neoplasm, as well as exposure to pesticides, combustion gases, biomass burning, human papillomavirus (HPV) exposure and sun exposure^{6,7}.

Estimates and predictions of cancer incidence and mortality are extremely relevant for the public health strategy planning process⁸. These provide references to exposure to risk factors and allow assessment of the effectiveness of existing health interventions (prevention campaigns, screening and treatment programs), making them valuable tools to redirect control programs and better distribute financial resources and humans⁹. However, these estimates alone are not sufficient to understand the true magnitude, trends of malignant neoplasms, and to evaluate interventions against cancer¹⁰. Thus, the objective of this study was to analyze the spatial joint distribution and to explore possible associations of the epidemiological aspects with mortality rates due to OC in the Brazil.

Methodos

This exploratory ecological study, approved by Research Ethics Committee of the University Center of Várzea Grande (CAAE: 62746616.1.0000.5692), included secondary data from Brazilian population.

Brazil is a continental country and the most populous country in Latin

America as well as one of the most populous in the world, has a surface area of 8,511,960 km² and with a population of 190,755,799, being divided into five geographic regions (South, Southeast, Central-West, North and Northeast) and 27 Federative Units (26 states and one Federal District)¹¹.

The geographic and spatial data of each of Brazilian Federative Units (UF), considering the latitude, longitude, perimeter, area and location of their capitals, were obtained from Brazilian Institute of Geography and Statistics (IBGE) website¹².

The dependent variable of this study was determined from the mortality rates for oral cancer (OC) from individuals aged ≥ 40 years at a Brazilian UF in the period 2005-2014. The International Classification of Diseases for Oncology of possible sites for malignant neoplasms is accepted by World Health Organization and defines the sites belonging to OC with those involving the topographic regions of the lip, oral cavity and pharynx¹³. The crude data of mortality from OC in individuals aged ≥ 40 years were selected in the Mortality Information System of the Ministry of Health from the deaths with a basic cause coded as C00-C14, in Chapter II of the 10th Revision of the ICD, according to distribution by Brazilian UF¹⁴. The data of the total population resident in the Brazilian UF during the study period were based on the 2010 population census and estimates for the years among census that were obtained from IBGE website¹². The mortality rates from OC were calculated from the division of mortality data from OC in individuals aged ≥ 40 years in each Brazilian UF by the data of the total population resident in the same place. The independent variables selected for this study was obtained from several databases of national scope in the period studied and are described in detail below:

- The *percentage of current tobacco consumption*, the *percentage overweight* (BMI ≥ 25 kg / m²) and *obesity* (BMI ≥ 30 kg / m²) was recovered from a national survey of risk factors and protection for chronic non-communicable diseases that was conducted through telephone interviews directed to the adult population (≥ 18 years) of the Brazilian UF¹⁴.
- The *rate of contamination by (HPV)* was determined from the proxy variable rates represented by the results of pathological anatomical examinations of the uterine cervix which were recorded in the Cancer Information System of the Uterine Cervix (procedure 12.012.03-3), being selected the diagnoses of benign lesions with

cytoarchitectural alterations compatible with HPV viral action¹⁴.

- The *consumption of pesticides* (tons of active ingredient and similar registered) was obtained from records of pesticides consumption which are available on the website of the Brazilian Institute of Environment and Natural Renewable Resources¹⁵.
- The *percentage of physical inactivity* (adults aged ≥ 18 years who reported not practicing any physical activity in all domains studied), *the socioeconomic status* (illiteracy rate, proportion of population with per capita household income below 1/2 salary, Human Development Index - HDI), *the health care utilization* (proportion of the population that had a medical appointment in the last year, proportion of the population who did dental appointment in the last year, proportion of the population who have never been in any dental appointment, proportion of the population covered by health plan, proportion of population with hospitalization in the last year, performance index of the single health system, percentage of population coverage by family health strategy teams, percentage of population coverage by oral health teams) and the *percentage of food consumption in kcal / day per capita* (total food consumption, cereals, meat, dairy products, fish, fruits, vegetables, oils and fats, sugars, soft drinks, alcoholic beverages, ready-to-eat foods and industrial mixtures) were recovered from IBGE website¹².

Statistical Analysis

Univariate exploratory analysis of the spatial data was performed for global spatial autocorrelation investigation of the OC mortality rates in the Brazilian UF by Moran index I, under the assumptions of normality and randomization¹⁶.

The variables of this study were grouped into six blocks to jointly evaluate the indicators associated with OC mortality by Pearson correlation coefficient (r), where the direction and magnitude of the associations among the independent variables were evaluated through a correlation matrix: 1) habits and lifestyle; 2) sociodemographic indicators; 3) consumption of pesticides; 4) presence of comorbidities; 5) use of health services and 6) food consumption. For this analysis, all variables were standardized with mean zero (0,0) and standard deviation equal to one (1.0), due to their different

dimensions, which could impair their inclusion and interpretation in the model.

Spatial multiple regression was performed in the last phase of analysis. The fit quality of the spatial regression model is similar to the traditional linear regression model, verified by residue analysis and also based on the Moran index I^{17} . The following criteria were used for the inclusion or withdrawal of the variables of the model: 1) Selection of variable with higher statistical correlation; 2) Inclusion of variables that, when analyzed together, obtained higher F in the simple regression analysis; This inclusion does not prevent that variables from the same block are also included as "adjustment variables", regardless of their association. 3) Inclusion of variables which once in partial correlation, controlled by modeled variables, showed significant correlation with the dependent variable. The final model exclusion criteria for variables were the p value ≥ 0.05 .

Graphical analyzes were performed between standardized residues in the verification of linear regression assumptions, observed and predicted values, and the diagnosis of normality using Q-Q plot plots. The post-tests of Breusch-Pagan and Koenker-Bassett for verification of heteroscedasticity were also applied. The non-spatial autocorrelation of residues was also verified in obtaining final models. The software used was Stata 11.0, SPSS 18.0 and GeoDa 0.95-i.

Results

Figure 1 shows the spatial distribution of OC mortality rates to age ≥ 40 years. It is observed that the highest rates occurred in the South and Southeast region, followed by the Northeast and Midwest regions of Brazil, with the lowest rates being identified in the Northern region.

The spatial distribution of this rate was not random, with high spatial autocorrelation ($I = 0,648$; p-value = 0.001 for 999 permutations). It was possible to observe the occurrence of spatial autocorrelations of the "high-high" type, indicating the grouping of Brazilian UF with higher mortality rates due to OC located in the following regions: South (SC and PR), Southeast (SP and MG), Central-West (MS and GO) and Northeast (AL). It was also observed the occurrence of "low-low" spatial autocorrelations, considered as a group with the lowest rate, represented by the States of AC, AM, RR and PA (Northern region) and MA (Northeast region) (Figure 2).

Moran Local Statistics I, shown in Figure 3, is also of great importance for the analysis, since it shows the degree of significance of certain groups. By the Local

Spatial Association Indicator (LISA), the states with the highest death rates for OC for age ≥ 40 years were MS, MG and AL. The analysis identified significant sectoral clusters from the LISA. The significance of this indicator in the period under consideration implies that there are positive multidirectional externalities of mortality rates due to OC in some UF of Brazil.

In the bivariate analysis (Table 1), the consumption of pesticides and similar registered, the proportion of the population that consulted in the last year, the proportion of the population that dentist visited last year, the proportion of the population with a health plan coverage, the average of performance index of the single health system, the percentage of physically inactive adults, the HPV contamination rate, the percentage of consumption of oils and fats, the percentage of soft drink, the percentage of alcohol consumption, the percentage of consumption of ready-to-eat foods and industrial mixtures and the percentage of overweight adults were positively correlated ($p < 0.05$) with mortality rates from OC. There were also negative significant correlations among the proportion of the population who have never been in any dental appointment, the proportion of the population with per capita household income below $\frac{1}{2}$ salary, the HDI mean and the percentage of fish consumption and the mortality rates for OC ($p < 0.05$).

Table 2 shows the results of the final spatial multiple regression analysis model. The HDI presented a significant inverse association with mortality rates from OC in the study period ($p < 0.05$). Besides, the proportion of the population who did dental appointment within the last year, the percentage of consumption of oils and fats, the percentage of ready-to-eat foods and industrial mixtures consumption and the percentage of overweight adults were positively associated with mortality rates of t OC ($p < 0.05$).

Discussion

The results of the present study show a fairly unequal distribution of mortality rates due to OC (Figure 1). In order to adjust the differences in the age distribution of the population and consequently a possible confounding effect of the age structure on the mortality rates due to OC in the UF of Brazil, the direct method of standardization of these rates was used¹⁸. Since the incidence of this cancer has increased in young adults (< 45 years) in countries with high incidence of this neoplasm in the world².

There was a predominance of significant spatial groupings of mortality rates

due to OC for age-standardized in the Central-South region of the country (Figure 2) that it was confirmed by the LISA (Figure 3). Brazil is a country with continental dimensions, divided into five geographic regions with different demographic, economic, cultural and health conditions and generalized internal inequalities¹⁹. Considering this context, it is important to highlight that although genetic factors play an important role in carcinogenesis, environmental, behavioral and occupational risk factors play a strong role in this process²⁰.

The HDI was negatively associated with mortality rates for OC for age-standardized in multiple spatial regression. It has been observed that socially disadvantaged groups tend to have greater contact with several risk factors, as well as poor oral health conditions, nutritional deficiencies and access to health services²¹. Ferlay et al.²² report that both the crude rate and the age-standardized incidence rate of the OC in the world population are higher in more developed regions, but mortality is higher in less developed areas, which shows social inequality. Significant spatial groupings in the Brazilian UF that have medium and high human development index were observed (Figure 2), corroborating with the findings of Borges et al.²³ which reported higher mortality rates in Brazilian capitals with high HDI. It is important to note that both survival and quality of life related to OC depend mainly on its clinical stage at the time of diagnosis and also on access to evidence-based multidisciplinary treatments²⁴. This has not been a reality for most of the developing world, since health education and early diagnosis are rare in these countries and most of these tumors are diagnosed late²⁵.

The proportion of the population who did dental appointment in the last year was positively associated with death rates from OC in the final spatial model. It is evident that this type of cancer has one of the lowest rates of survival over 5 years when compared to the most prevalent carcinomas, among which are included breast cancer, skin, testicles, prostate, uterus and urinary bladder²⁶. Besides, early diagnosis and immediate treatment can significantly reduce the morbidity associated with its therapy and consequently improve overall long-term survival²⁷, since in most cases its evolution is slow²⁸. However, the early stage of OC is usually asymptomatic²⁹. Approximately 50% of the patients with this pathology make a first appointment with a health professional within 2 months after identifying some sign or symptom, while 20-30% of the patients delay seeking professional help for more than 3 months³⁰. This delay of the patient in consulting a health professional can be attributed to the patient's delay in

identifying the signs or symptoms of these cancer or to difficulties in accessing professional care³¹. There is a shortage of trained or specialized professionals in oral diagnosis or stomatology acting in the primary and secondary care of the public health system of Brazil, limiting the offer of services of this nature³². In addition, access to private and supplementary health services in Brazil is dependent on the individual's economic status³².

The percentage of overweight adults remained positively associated with death rates from OC in this study. Overweight seems to have a mutual relationship with oxidative stress³³. This in turn is able to fragment DNA, RNA, lipids and protein and consequently interfere in the DNA repair system, contributing to the development of diseases, such as cancer³⁴.

In these study, the percentage of consumption of oils and fats remained positively associated with mortality rates due to OC³⁵. The usual presence of saturated animal fat in the Brazilian diet has been identified as a risk factor for OC and some mechanisms have been proposed to explain the influence of fatty acids on carcinogenesis and include the peroxidation of polyunsaturated fatty acids and subsequent DNA damage; effects on estrogen concentrations and their availability; effects on membrane-bound enzymes that regulate xenobiotic metabolism; changes in cell membranes, resulting in changes in hormone receptors and growth factor; regulation of fatty acids from the production of eicosanoids and subsequent modulation of the immune response; activation of fatty acids from nuclear transcription factors, leading to cell differentiation; modulation of signal transduction pathways by fatty acids, leading to altered gene expression and effects on cell proliferation and apoptosis and inhibition of translation initiation, leading to a decrease in cell proliferation due to the reduction of G1 cyclin synthesis and expression and G1 cell cycle arrest³⁶.

The percentage of ready-to-eat foods and industrial mixtures consumption has remained positively associated with mortality rates due to OC in the multiple spatial model. The consumption of ready-to-eat foods or fast foods have been associated with increased risk of OC³⁵. Furthermore, the consumption of foods, fried, baked or cooked in the microwave should be avoided by increasing the risk of this type of cancer, due to the formation of heterocyclic amines³⁷. Other aspects that should be studied in order to prevent this malignant neoplasm are the methods of preparation and conservation of foods because they can collaborate directly or indirectly in the development of certain types of cancer³⁸.

This study has some limitations inherent to the methodology used, and the possibility of ecological fallacy cannot be excluded since an association observed between aggregates does not necessarily mean that the same association occurs at the individual level³⁹. The low construct validity is another possibility that cannot be discarded, since not all outcome explaining variables of the may have been included in the methodology used⁴⁰. In order to reduce some of these limitations, this study has worked with variables available in several national databases and may present differences in quality that are inherent to the use of indirect estimates⁴¹.

Conclusion

This is the first study that analyzed the factors associated to the spatial clusters of mortality due to oral cancer in the Brazilian Federative Units and their results bring important contributions to the understanding of the spatial epidemiological aspects involved in this process. Although public policies to combat OC have been introduced since the beginning of the 21st century in Brazil, this study show a fairly unequal distribution of OC mortality rates that presented inverse association with HDI and direct association dental appointment in the last year, consumption of oils and fats, ready-to-eat foods and industrial mixtures consumption and overweight these rates. It suggests the need to redirect Brazilian public policies aimed at combating them so that they cease to be temporary and become permanent.

References

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011;61: 69-90.
2. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* 2009;45: 309-16.
3. Petersen PE. Oral cancer prevention and control--the approach of the world health organization. *Oral Oncol* 2009;45: 454-60.
4. Wünsch-Filho V. The epidemiology of oral and pharynx cancer in brazil. *Oral Oncol* 2002;38: 737-46.
5. Bravi F, Bosetti C, Filomeno M, Levi F, Garavello W, Galimberti S, et al. Foods, nutrients and the risk of oral and pharyngeal cancer. *Br J Cancer* 2013;109: 2904-10.
6. Pelucchi C, Talamini R, Negri E, Levi F, Conti E, Franceschi S, et al. Folate intake and risk of oral and pharyngeal cancer. *Ann Oncol* 2003;14: 1677-81.
7. Tarvainen L, Kyyronen P, Kauppinen T, Pukkala E. Cancer of the mouth and pharynx, occupation and exposure to chemical agents in finland [in 1971-95]. *Int J Cancer* 2008;123: 653-9.
8. Olsen AH, Parkin DM, Sasieni P. Cancer mortality in the united kingdom: Projections to the year 2025. *British Journal of Cancer* 2008;99: 1549-54.
9. Bray F, Moller B. Predicting the future burden of cancer. *Nat Rev Cancer* 2006;6: 63-74.
10. Shibuya K, Mathers CD, Boschi-Pinto C, Lopez AD, Murray CJL. Global and regional estimates of cancer mortality and incidence by site: Ii. Results for the global burden of disease 2000. *BMC Cancer* 2002; 2:37.
11. Philander SG. *Encyclopedia of global warming and climate change, second edition*: SAGE Publications; 2012.
12. Instituto Brasileiro de Geografia e Estatística [Brazilian Institute for Geography and Statistics] - IBGE. States@. Available at: <http://www.ibge.gov.br/english/> [last accessed 07 january 2017].
13. International Classification of Diseases (ICD). The international classification of diseases for oncology Available at: <http://www.who.int/classifications/en/> [last accessed 07 january 2017].

14. Departamento de Informática do Sistema Único de Saúde [Department of informatics of the Unified Health System] DATASUS. Available at: <http://datasus.saude.gov.br/informacoes-de-saude> [last accessed 07 january 2017].
15. Instituto Brasileiro do Meio Ambiente e dos Recursos Renováveis [Brazilian Institute of Environment and Natural Renewable Resources]-IBAMA. Agrochemicals trading reports. http://ibama.gov.br/index.php?option=com_content&view=article&id=594&Itemid=546 (last accessed 07 january 2017).
16. Druck S, Carvalho MS, Câmara G, Monteiro AMV. Spatial analysis and geoprocessing. In: Druck S, Carvalho MS, Câmara G, Monteiro AMV, editors: *Spatial analysis of geographic data*. Brasília, Distrito Federal (Brazil): EMBRAPA; 2004.
17. Anselin L. *Exploring spatial data with geodatm: A workbook*. Illinois, USA: University of Illinois, Urbana-Champaign 2005: 226.
18. Bonita R, Beaglehole R, Kjellström T, World Health O. *Basic epidemiology*: World Health Organization; 2006.
19. Paim J, Travassos C, Almeida C, Bahia L, Macinko J. The brazilian health system: History, advances, and challenges. *The Lancet*;377: 1778-97.
20. Perera FP, Weinstein IB. Molecular epidemiology: Recent advances and future directions. *Carcinogenesis* 2000;21: 517-24.
21. Boing AF, Peres MA, Antunes JLF. Mortality from oral and pharyngeal cancer in brazil: Trends and regional patterns, 1979-2002. *Revista Panamericana de Salud Pública* 2006;20: 1-8.
22. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in globocan 2012. *Inter J Cancer* 2015;36: E359 - 86.
23. Borges D, Sena M, Ferreira M, Roncalli A. Mortality for oral cancer and socioeconomic status in brazil. *Cadernos de Saúde Pública* 2009;25: 321-27.
24. Johnson NW, Warnakulasuriya S, Gupta PC, Dimba E, Chindia M, Otoh EC, et al. Global oral health inequalities in incidence and outcomes for oral cancer: Causes and solutions. *Adv Dent Res* 2011;23: 237-46.
25. Carvalho A, Pintos J, Schlecht N, Oliveira B, Fava A, Curado M, et al. Predictive factors for diagnosis of advanced-stage squamous cell carcinoma of the head and neck. *Arc Otolaryngol Head Neck Surg* 2002;128: 313 - 8.

26. Onizawa K, Nishihara K, Yamagata K, Yusa H, Yanagawa T, Yoshida H. Factors associated with diagnostic delay of oral squamous cell carcinoma. *Oral Oncol* 2003;39: 781-8.
27. Peacock ZS, Pogrel MA, Schmidt BL. Exploring the reasons for delay in treatment of oral cancer. *J Am Dent Assoc* 2008;139: 1346-52.
28. Kirita T, Kajihara A, Choudhury CR, Inoue M, Maeda M, Yasumoto J, et al. A patient with untreated tongue carcinoma surviving for 15 years. *International Journal of Oral and Maxillofacial Surgery* 2005;34: 324-27.
29. Yu T, Wood RE, Tenenbaum HC. Delays in diagnosis of head and neck cancers. *J Can Dent Assoc* 2008;74: 61.
30. Jafari A, Najafi SH, Moradi F, Kharazifard MJ, Khami MR. Delay in the diagnosis and treatment of oral cancer. *Journal of Dentistry* 2013;14: 146-50.
31. Carvalho AL, Pintos J, Schlecht NF, Oliveira BV, Fava AS, Curado MP, et al. Predictive factors for diagnosis of advanced-stage squamous cell carcinoma of the head and neck. *Arch Otolaryngol Head Neck Surg* 2002;128: 313-8.
32. Martins RC, Reis CM, Matta Machado AT, Amaral JH, Werneck MA, Abreu MH. Relationship between primary and secondary dental care in public health services in Brazil. *PLoS One* 2016;11: e0164986.
33. Lubrano C, Genovesi G, Specchia P, Costantini D, Mariani S, Petrangeli E, et al. Obesity and metabolic comorbidities: Environmental diseases? *Oxid Med Cell Longev* 2013;2013: 640673.
34. Sosa V, Moline T, Somoza R, Paciucci R, Kondoh H, ME LL. Oxidative stress and cancer: An overview. *Ageing Res Rev* 2013;12: 376-90.
35. Toporcov TN, Antunes JL, Tavares MR. Fat food habitual intake and risk of oral cancer. *Oral Oncol* 2004;40: 925-31.
36. Blackburn GL, Go VLW, Milner J, Heber D. *Nutritional oncology*: Elsevier Science; 2011.
37. Taghavi N, Yazdi I. Type of food and risk of oral cancer. *Arch Iran Med* 2007;10: 227-32.
38. Garófolo A, Avesani CM, Camargo KG, Barros ME, Silva SRJ, Taddei JAdAC, et al. Dieta e câncer: Um enfoque epidemiológico. *Revista de Nutrição* 2004;17: 491-505.
39. Szklo M, Nieto J. *Epidemiology: Beyond the basics*: Jones & Bartlett Learning; 2007.

40. Schwartz S. The fallacy of the ecological fallacy: The potential misuse of a concept and the consequences. *Am J Public Health* 1994;84: 819-24.
41. Frias PGd, Pereira PMH, Andrade CLTd, Szwarcwald CL. Sistema de informações sobre mortalidade: Estudo de caso em municípios com precariedade dos dados. *Cadernos de Saúde Pública* 2008;24: 2257-66.

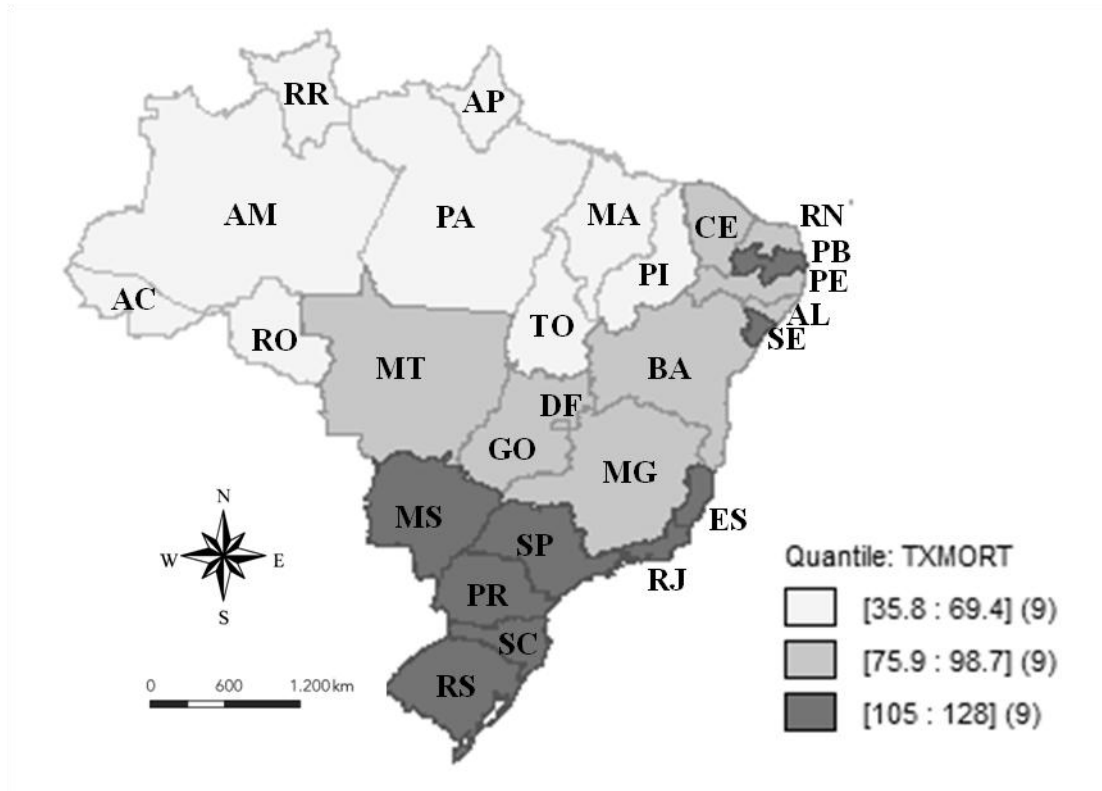


Figure 1. Mortality rates for mouth cancer standardized for the age of 40 years or over per 100,000 inhabitants, in the Brazilian Federative Units, in the period from 2005-2014, according to tertile.

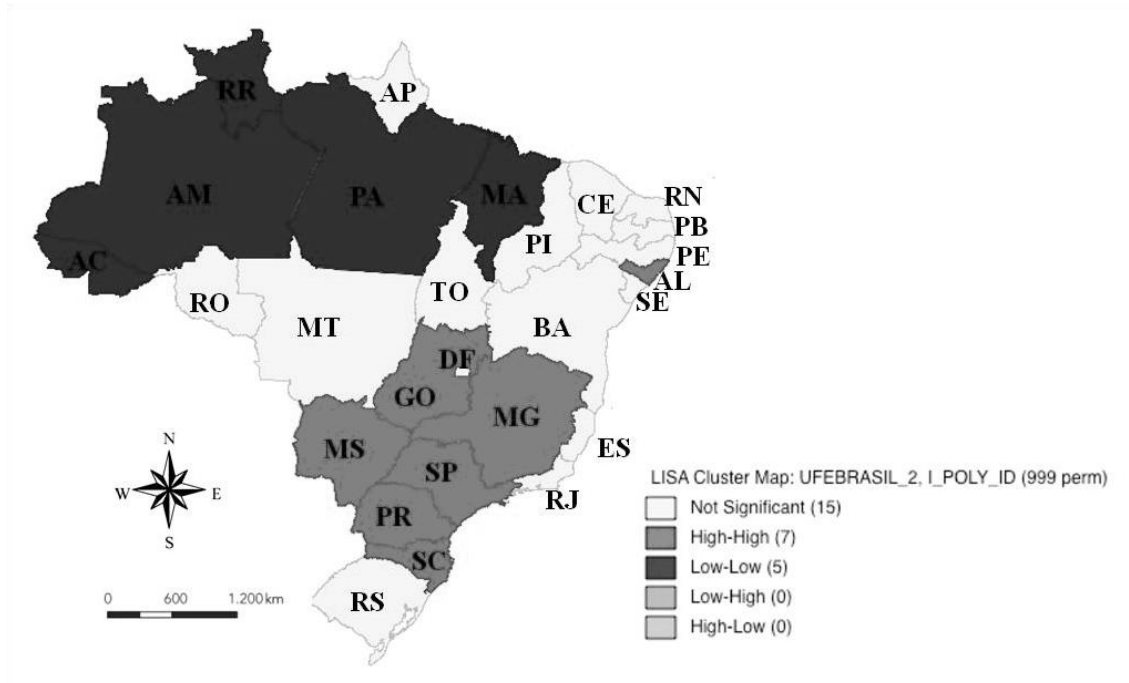


Figure 2. Moran dispersion map for mortality rates from mouth cancer standardized for the age of 40 years or over per 100,000 inhabitants, in the Brazilian Federative Units, in the period from 2005-2014.

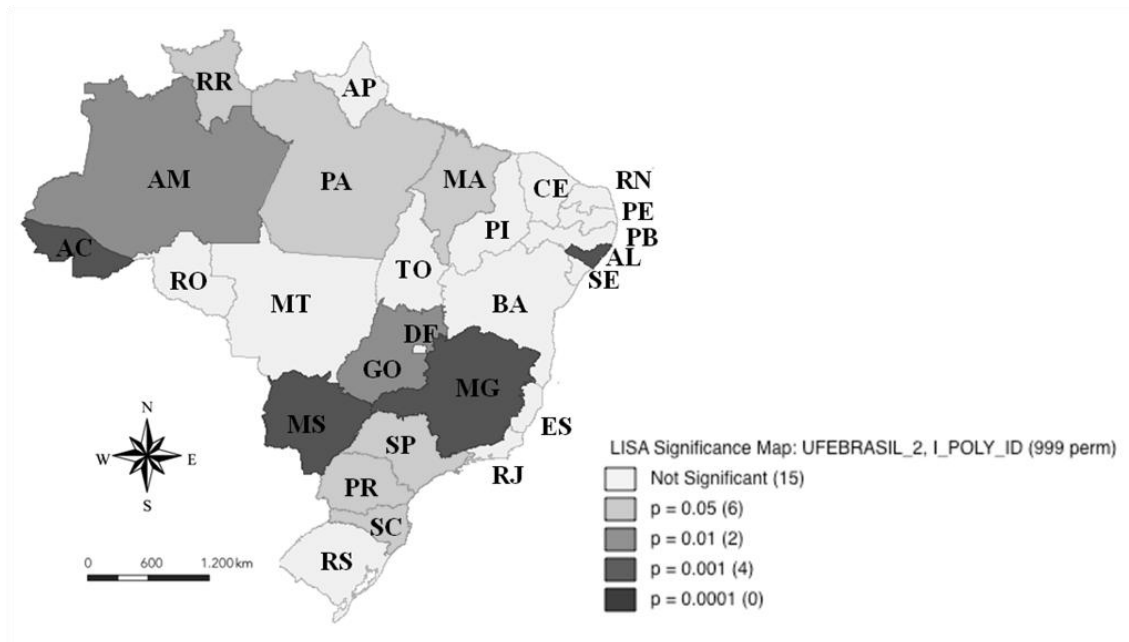


Figure 3. Identification of the occurrence of significant clusters, based on the analysis of the Local Moran index, for mortality rates for mouth cancer for the age of 40 years or over per 100,000 inhabitants, in the Brazilian Federative Units, in the period from 2005-2014.

Table 1. Correlation matrix among standardized mouth cancer mortality rates for the age group of ≥ 40 years per 100,000 inhabitants in the Brazilian Federative Units, in the period 2005-2014, and the variables selected in the different blocks of analysis .

	ZMC	ZP	ZMA	ZDA	ZNDA	ZHIC	ZISHS	ZPIA	Z1/2S	ZHDI	ZFC	ZFC	ZOFC	ZRC	ZAC	ZRFIMC	ZOW
ZMC	1																
ZP	.630**	1															
ZMA	.468*	.273	1														
ZDA	.339*	.419*	.754**	1													
ZNDA	-.522**	-.515**	-.714**	-.844**	1												
ZHIC	.763**	.612**	.658**	.629**	-.871**	1											
ZISHS	.588**	.520**	.693**	.636**	-.734**	.779**	1										
ZPIA	.389*	.095	.173	-.135	-.034	.200	.150	1									
Z1/2S	-.486*	-.612**	-.525**	-.653**	.887**	-.874**	-.747**	.029	1								
ZHDI	-.582**	.579**	.596**	.709**	-.882**	.879**	.750**	.066	-.935**	1							
ZHPV	.859**	.519**	.377	.178	-.300	.538**	.406*	.255	-.280	.335	1						
ZFC	-.311*	-.378	-.425*	-.277	.452*	-.443*	-.678**	.079	.556**	-.394*	-.284	1					
ZOFC	.210*	.509**	.182	.055	-.205	.251	.242	-.003	-.344	.233	.261	-.368	1				
ZCR	.644**	.580**	.344	.544**	-.749**	.856**	.542**	.045	-.825**	.838**	.373	-.228	.144	1			
ZAC	.564**	.497**	.374	.445*	-.696**	.763**	.623**	.148	-.738**	.690**	.306	-.434*	.026	.700**	1		
ZRFIMC	.581**	.500**	.526**	.735**	-.867**	.846**	.728**	-.030	-.841**	.833**	.324	-.406*	-.045	.837**	.807**	1	
ZOW	.106*	.211	-.066	.221	-.260	.262	.065	.166	-.301	.284	-.123	.121	.009	.460*	.390*	.299	1

** p<0,01

* p<0,05

ZMC: age-standardized oral cancer mortality rate; ZP: consumption of pesticides and similar products (tons of active ingredient); ZMA: proportion of the population who did medical appointment in the last year; ZDA: proportion of the population who did dental appointment in the last year; ZNDA: proportion of the population who have never been in any dental appointment; ZHIC: proportion of the population with health insurance coverage; ZISHS: average performance index of the single health system; ZPIA: percentage of physically inactive adults; Z1/2S: proportion of population with per capita household income below 1/2 salary; ZHDI: average human development index; ZHPV: HPV contamination rate; ZFC: percentage of fish consumption kcal / day per capita; ZOFC: percentage of oils and fats consumption kcal / day per capita; ZRC: percentage of refrigerant consumption kcal / day per capita; ZAC: percentage of alcohol consumption kcal / day per capita; ZRFIMC: percentage of ready-to-eat foods and industrial consumption mixtures kcal / day per capita and ZOW: percentage of overweight adults (IMC \geq 25kg/m²).

Table 2. Spatial Multiple Regression Model of mortality rates for mouth cancer standardized for age ≥ 40 years, per 100,000 inhabitants and associated factors in the Brazilian Federative Units in the period of 2005-2014.

Variables	Coefficients	Standard Deviation	t	p-value
Percentage of oils and fats consumption*	1.690	0.767	2.198	0.039
Percentage of ready-to-eat food and industrial consumption mixtures*	9.233	3.754	2.459	0.023
HDI	-15.591	4.602	-3.229	0.004
Percentage of overweight adults**	2.598	0.732	3.547	0.002
Proportion of the population who dental appointment within last year	1.339	0.504	2.659	0.015

* kcal / day per capita

** IMC ≥ 25 kg/m²

3 CONCLUSÃO

Os resultados do presente estudo evidenciam uma distribuição bastante desigual das taxas de mortalidade por câncer de lábio, cavidade oral e faringe padronizada para a idade igual ou superior a 40 anos por 100 mil habitantes nas unidades federativas brasileiras mortalidade, em 2005-2014, cujas taxas transformadas variaram entre 35,82/100.000 habitantes e 127,94/100.000 habitantes.

Houve uma distribuição aleatória desta taxa, com elevada autocorrelação espacial. Sendo possível observar a ocorrência de autocorrelações espaciais do tipo "alto-alto", indicando agrupamento de unidades federativas brasileiras com maiores taxas de mortalidade por esta patologia localizadas nas regiões sul (Santa Catarina e Paraná), sudeste (São Paulo e Minas Gerais), Centro-Oeste (Mato Grosso do Sul e Goiás) e Nordeste (Alagoas) e do tipo "baixo-baixo", considerado agrupamento com a menor taxa, representado pelos estados do Acre, Amazonas, Roraima e Pará (região norte) e Maranhão (região nordeste).

Existem externalidades positivas multidirecionais da taxas de mortalidade por câncer de lábio, cavidade oral e faringe para a idade igual ou superior a 40 anos representadas pelos estados de Mato Grosso do Sul, Minas Gerais e Alagoas.

O índice de desenvolvimento humano, a proporção da população que realizou consulta dentista no último ano, o percentual de consumo de óleos e gorduras kcal/dia per capita, o percentual de consumo de alimentos preparados e misturas industriais kcal/dia per capita e o percentual de adultos com sobrepeso ($IMC \geq 25 \text{kg/m}^2$) permaneceram correlacionadas às taxas de mortalidade por câncer de lábio, cavidade oral e faringe padronizada por idade no período estudado no modelo final da análise de regressão múltipla espacial.

Este é o primeiro estudo que analisou os fatores associados aos clusters espaciais da mortalidade por câncer de lábio, cavidade oral e faringe nas unidades federativas brasileiras e seus resultados trazem importantes contribuições para a compreensão dos aspectos epidemiológicos espaciais envolvidos neste processo. Sugerindo a necessidade de redirecionamento das políticas públicas brasileiras destinadas ao combate do câncer bucal para que deixem de ser temporárias e se tornem permanentes.

REFERÊNCIAS²

Antunes JLF, Borrell C, Pérez G, Boing AF, Wunsch-Filho V. Inequalities in mortality of men by oral and pharyngeal cancer in Barcelona, Spain and São Paulo, Brazil, 1995-2003. *Int. J. Equity Health* [Internet]. 2008;7:14. Available from: <http://www.scopus.com/inward/record.url?eid=2-s2.0-47249102479&partnerID=tZOtx3y1>

Bravi F. B, Bosetti C., Filomeno M. B, Levi F., Garavello W., Galimberti S., et al. Foods, nutrients and the risk of oral and pharyngeal cancer. *Br. J. Cancer* [Internet]. 2013;109(11):2904–10. Available from: <http://www.scopus.com/inward/record.url?eid=2-s2.0-84888866190&partnerID=40&md5=513898797a6364b07cd2a713a2db43aa>

Bray F, Moller B, Møller B. Predicting the future burden of cancer. *Nat.Rev.Cancer* [Internet]. 2006;6(1474–175X (Print)):63–74. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16372017>

Brown LM, Check DP, Devesa SS. Oropharyngeal cancer incidence trends: diminishing racial disparities. *Cancer Causes Control*. 2011;22(5):753–63.

de Camargo Cancela M, Voti L, Guerra-Yi M, Chapuis F, Mazuir M, Curado MP. Oral cavity cancer in developed and in developing countries: population-based incidence. *Head Neck*. 2010;32(3):357–67.

Canto MT, Devesa SS. Oral cavity and pharynx cancer incidence rates in the United States, 1975-1998. *Oral Oncol*. 2002;38(6):610–7.

Coleman MP, Babb P, Sloggett A, Quinn M, De Stavola B. Socioeconomic inequalities in cancer survival in England and Wales. *Cancer*. 2001;91:208–16.

D'Souza G, Kreimer AR, Viscidi R, Pawlita M, Fakhry C, Koch WM, et al. Case-control study of human papillomavirus and oropharyngeal cancer. *N. Engl. J. Med.* [Internet]. 2007;356(19):1944–56. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17494927>

Dayama A, Srivastava V, Shukla M, Singh R, Pandey M. *Helicobacter pylori* and oral cancer: possible association in a preliminary case control study. *Asian Pac. J. Cancer Prev*. 2011;12(5):1333–6.

Irani S, Monsef Esfahani A, Bidari Zerehpoush F. Detection of *Helicobacter pylori* in Oral Lesions. *J. Dent. Res. Dent. Clin. Dent. Prospects* [Internet]. 2013;7(4):230–7. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3935555&tool=pmcentrez&rendertype=ab>

² De acordo com Ceccotti, Heloisa Maria. *Elaboração e normalização de teses e dissertações da FOP/UNICAMP.* / Heloisa Maria Ceccotti – Piracicaba, SP : UNICAMP/FOP, 2015. 92 f.

stract

J. Ferlay, HR. Shin, F. Bray, D. Forman, C. Mathers DMP. Estimates of worldwide burden of cancer in 2008:GLOBOCAN 2008. *Int J Cancer.* ; 2010;127:2893–917.

Jemal A, Bray F, Center MM, Ferlay J, Ward E FD. Global cancer statistics. *Cancer J Clin.* 2011;61:69–90.

Kingsley K, O'Malley S, Ditmyer M, Chino M. Analysis of oral cancer epidemiology in the US reveals state-specific trends: implications for oral cancer prevention. *BMC Public Health [Internet].* 2008;8:87. Available from:

<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2287178&tool=pmcentrez&rendertype=abstract>

Listl S, Jansen L, Stenzinger A, Freier K, Emrich K, Holleczeck B, et al. Survival of Patients with Oral Cavity Cancer in Germany. *PLoS One.* 2013;8(1).

Llewellyn CD, Johnson NW, Warnakulasuriya KAAS. Risk factors for squamous cell carcinoma of the oral cavity in young people - A comprehensive literature review. *Oral Oncol.* 2001. p. 401–18.

Lorant V, Boland B, Humblet P, Deliege D, V. L. B. B, et al. Equity in prevention and health care. *J. Epidemiol. Community Health [Internet].* 2002;56(7):510–6. Available from:

<http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=12080158%5Cnhttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed5&NEWS=N&AN=2002236333>

Macfarlane GJ, Macfarlane T V, Lowenfels AB. The influence of alcohol consumption on worldwide trends in mortality from upper aerodigestive tract cancers in men. *J. Epidemiol. Community Health [Internet].* 1996;50(6):636–9. Available from:

<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1060380&tool=pmcentrez&rendertype=abstract>

Mehanna H, Paleri V, West CML, Nutting C. Head and neck cancer-Part 1: Epidemiology, presentation, and preservation. *Clin. Otolaryngol.* 2011. p. 65–8.

Meng X, Wang Q, He C, Chen M, Liu J, Liu W, et al. An inverse association of *Helicobacter pylori* infection with oral squamous cell carcinoma. *J. Oral Pathol. Med. [Internet].* 2016;45(1):17–22. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25899621>

Morse DE, Kerr AR. Disparities in oral and pharyngeal cancer incidence, mortality and survival among black and white Americans. *J. Am. Dent. Assoc.* 2006;137(2):203–12.

Negri E, La Vecchia C, Franceschi S, Tavani A. Attributable risk for oral cancer in northern Italy. *Cancer Epidemiol. Biomarkers Prev.* 1993;2(3):189–93.

Olsen AH, Parkin DM, Sasieni P. Cancer mortality in the United Kingdom: projections to the year 2025. *Br.J.Cancer* [Internet]. 2008;99(9):1549–54. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2579704/pdf/6604710a.pdf>

Östman J, Anneroth G, Gustafsson H, Tavelin B. Malignant oral tumours in Sweden 1960-1989-An epidemiological study. *Eur. J. Cancer. Part B Oral Oncol.* 1995;31(2):106–12.

Pelucchi C, Talamini R, Negri E, Levi F, Conti E, Franceschi S, et al. Folate intake and risk of oral and pharyngeal cancer. *Ann. Oncol.* [Internet]. 2003;14(11):1677–81. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/14581278>

Perera FP. Environment and cancer: who are susceptible? *Science* (80-.). [Internet]. Washington; 1997;278(5340):1068–73. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/9353182>

Perera FP, Weinstein IB. Molecular epidemiology: recent advances and future directions. *Carcinogenesis* [Internet]. 2000;21(3):517–24. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10688872

Peñié S, Meyers M, Mazzaschi O, De Chanel OC, Baujat B, Lacau St Guily J. Épidémiologie et anatomie des cancers ORL. *Bull. Cancer.* 2014. p. 404–10.

Petti S, Scully C. Oral cancer: The association between nation-based alcohol-drinking profiles and oral cancer mortality. *Oral Oncol.* 2005;41(8):828–34.

Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. *Int. J. Cancer.* 1999;83(1):18–29.

Rivera C. Essentials of oral cancer. *Int. J. Clin. Exp. Pathol.* [Internet]. 2015;8(9):11884–94. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4637760&tool=pmcentrez&rendertype=abstract>

Rodriguez T, Altieri A, Chatenoud L, Gallus S, Bosetti C, Negri E, et al. Risk factors for oral and pharyngeal cancer in young adults. *Oral Oncol.* 2004;40(2):207–13.

Rodu B, Cole P. Oral cavity and pharynx-throat cancer in the United States, 1973-2003. *Oral Surgery, Oral Med. Oral Pathol. Oral Radiol. Endodontology.* 2007;104(5):653–8.

Rubin P. *Clinical oncology: a multidisciplinary approach to physicians and students*. 7th ed. Philadelphia: Saunders; 1993.

Saman D. A review of the epidemiology of oral and pharyngeal carcinoma: update. *Head Neck Oncol*. 2012;4(1).

Shiboski CH, Schmidt BL, Jordan RCK. Tongue and tonsil carcinoma: increasing trends in the U.S. population ages 20-44 years. *Cancer* [Internet]. 2005 May 1;103(9):1843–9. Available from: <http://doi.wiley.com/10.1002/cncr.20998>

Shibuya K, Mathers CD, Boschi-Pinto C, Lopez AD, Murray CJL. Global and regional estimates of cancer mortality and incidence by site: II. Results for the global burden of disease 2000. *BMC Cancer* [Internet]. 2002;2:37. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=149364&tool=pmcentrez&rendertype=abstract>

Siegel R, Naishadham D, Jemal A. *Cancer Statistics*, 2012. *CA Cancer J Clin*. 2012;62:10–29.

Smith EM, Ritchie JM, Summersgill KF, Klussmann JP, Lee JH, Wang D, et al. Age, sexual behavior and human papillomavirus infection in oral cavity and oropharyngeal cancers. *Int. J. Cancer*. 2004;108(5):766–72.

Swaminathan R, Rama R, Shanta V. Lack of active follow-up of cancer patients in Chennai, India: Implications for population-based survival estimates. *Bull. World Health Organ*. 2008;86(7):509–15.

Swango PA. Cancers of the oral cavity and pharynx in the United States: an epidemiologic overview. [Review]. *J. Public Health Dent*. 1996;56(6):309–18.

Tapia JL, Goldberg LJ. The Challenges of Defining Oral Cancer: Analysis of an Ontological Approach. *Head Neck Pathol*. 2011;5(4):376–84.

Tarvainen L, Kyyrönen P, Kauppinen T, Pukkala E. Cancer of the mouth and pharynx, occupation and exposure to chemical agents in Finland [in 1971-95]. *Int. J. Cancer*. 2008;123(3):653–9.

Tramacere I, Negri E, Bagnardi V, Garavello W, Rota M, Scotti L, et al. A meta-analysis of alcohol drinking and oral and pharyngeal cancers. Part 1: Overall results and dose-risk relation. *Oral Oncol*. 2010;46(7):497–503.

Umeda M, Kobayashi H, Takeuchi Y, Hayashi J, Morotome-Hayashi Y, Yano K, et al. High Prevalence of *Helicobacter pylori* Detected by PCR in the Oral Cavities of Periodontitis Patients. *J. Periodontol*. 2003;74(1):129–34.

Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol.* 2009. p. 309–16.

Westra WH. The changing face of head and neck cancer in the 21st century: The impact of hpv on the epidemiology and pathology of oral cancer. *Head Neck Pathol.* 2009;3(1):78–81.

World Health Organization (WHO). Malignant neoplasms of lip, oral cavity and pharynx (C00-C14)International Classification of Diseases (ICD) 10. [Internet]. Geneva; 2010 [cited 2016 Jun 1]. Available from: <http://apps.who.int/classifications/icd10/browse/2010/en#/C00-C14>

Wunsch-Filho V, Moncau JE. Mortalidade Por Câncer No Brasil 1980-1995 : Padroes Regionais E Tendencias Temporais. *Rev. Assoc. Med. Bras.* 2002;48(3):250–7.

Zini A, Czerninski R, Sgan-Cohen HD. Oral cancer over four decades: Epidemiology, trends, histology, and survival by anatomical sites. *J. Oral Pathol. Med.* 2010;39(4):299–305.

Zini A, Czerninski R, Vered Y, Livny A, Sgan-Cohen HD. Trends of oral and pharyngeal cancer in Israel, by gender, age, ethnic group, and country of origin: 1970-2006. *Community Dent. Oral Epidemiol.* 2009;37(6):547–54.

APÊNDICE 1



PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: ANÁLISE ESPACIAL DOS ASPECTOS EPIDEMIOLÓGICOS ASSOCIADOS À MORTALIDADE POR NEOPLASIAS MALIGNAS DE LÁBIO, CAVIDADE ORAL E FARINGE NOS ESTADOS BRASILEIROS

Pesquisador: Gisele Pedroso Moi

Área Temática:

Versão: 1

CAAE: 62746616.1.0000.5692

Instituição Proponente: INSTITUICAO EDUCACIONAL MATOGROSSENSE-IEMAT

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.879.889

Apresentação do Projeto:

Estudo ecológico de caráter exploratório sobre as taxas de mortalidade por neoplasias malignas que acometem o lábio, a cavidade oral e a faringe no período 2005-2014.

Objetivo da Pesquisa:

Analisar a distribuição espacial conjunta e explorar possíveis associações dos aspectos epidemiológicos com as taxas de mortalidade por neoplasias malignas que acometem o lábio, a cavidade oral e a faringe no período 2005-2014 nos estados brasileiros.

Adequado!

Avaliação dos Riscos e Benefícios:

A pesquisa apresenta riscos mínimos, de acordo com a Resolução CNS 466/12, uma vez que se constitui em um estudo ecológico de coleta de dados secundários agregados de domínio público, não permitindo a identificação individual dos participantes e portanto a preservação da privacidade dos pacientes, garantindo que as informações coletadas serão utilizadas única e exclusivamente para execução do projeto em questão.

Endereço: Av. Dom Orlando Chaves nº 2655
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UF: MT **Município:** VARZEA GRANDE
Telefone: (65)3688-6111 **E-mail:** cep@univag.edu.br



Continuação do Parecer: 1.879.889

Adequado!

Comentários e Considerações sobre a Pesquisa:

Pesquisa relevante para a área.

Considerações sobre os Termos de apresentação obrigatória:

Adequado!

Recomendações:

Projeto considerado apto para execução, podendo ser iniciado após a publicação do parecer!

Conclusões ou Pendências e Lista de Inadequações:

Não se aplica!

Considerações Finais a critério do CEP:

Projeto aprovado, apto para início de execução!

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Projeto Detalhado / Brochura Investigador	CANCER_LABIO_CAVIDADE_ORAL_E_OROFARINGE_final.doc	22/12/2016 13:03:04	Rosa Maria Elias	Aceito
Outros	Folha_de_rosto_assinado.pdf	06/12/2016 18:12:15	Ana Paula dos Santos	Aceito
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_836364.pdf	06/12/2016 00:18:28		Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Solicitacao_de_dispenza_do_TCLE.pdf	06/12/2016 00:17:29	Gisele Pedroso Moi	Aceito
Folha de Rosto	Folha_de_rosto.pdf	06/12/2016 00:07:50	Gisele Pedroso Moi	Aceito
Projeto Detalhado / Brochura Investigador	CANCER_LABIO_CAVIDADE_ORAL_E_OROFARINGE.doc	02/12/2016 17:51:38	Gisele Pedroso Moi	Aceito
Outros	Curriculo.pdf	01/12/2016 20:10:10	Gisele Pedroso Moi	Aceito
Outros	formulario_de_encaminhamento_do_projeto_ao_CEP_UNIVAG.docx	01/12/2016 20:05:56	Gisele Pedroso Moi	Aceito
Outros	declaracao_participacao_dos_pesquisadores_em_projeto_de_pesquisa.docx	01/12/2016 20:05:22	Gisele Pedroso Moi	Aceito

Situação do Parecer:

Endereço: Av. Dom Orlando Chaves nº 2655
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Telefone: (65)3688-6111 **E-mail:** cep@univag.edu.br



Continuação do Parecer: 1.879.889

Aprovado

Necessita Apreciação da CONEP:

Não


VARZEA GRANDE, 22 de Dezembro de 2016

Assinado por:
Rosa Maria Elias
(Coordenador)

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APÊNDICE 2

22/03/2017 ScholarOne Manuscripts

 Community Dentistry and Oral Epidemiology

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Submission Confirmation

Thank you for your submission

Submitted to
Community Dentistry and Oral Epidemiology

Manuscript ID
CDOE-17-129

Title
SPATIAL ANALYSIS OF THE DEATH ASSOCIATED FACTORS DUE ORAL CANCER IN BRAZIL: AN ECOLOGICAL STUDY

Authors
Moi, Gisele
Meneghim, Marcelo
Silva, Ageo
Pereira, Antonio

Date Submitted
22-Mar-2017

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