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ORIGINAL ARTICLE

IMPACT OF VITAMIN D IN THE PREVENTION OF PULMONARY AND BRONCHICAL CANCER
IMPACTO DA VITAMINA D NA PREVENÇÃO DO CÂNCER PULMONAR E BRÔNQUICO
IMPACTO DE LA VITAMINA D EN LA PREVENCIÓN DEL CÁNCER PULMONAR Y BRONQUIAL

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ABSTRACT

Objective: to identify evidence of preventive action of vitamin D on the mortality rate of lung and bronchial cancer in the Brazilian population. **Method:** quantitative, epidemiological, descriptive study, developed from data collection from INCA and IBGE sources. The INCA data revealed mortality rates for both cancers, while the IBGE provided specific latitudes of all the capitals of the country. After the data collection, the data was entered in the Microsoft Excel program, later transferred to the program of construction of maps of the Target Map and analyzed by means of descriptive statistics. **Results:** it was observed that the Five most distant federative units of the Equator line represent the highest mortality rates of Brazil, common in both sexes. **Conclusion:** the results show the preventive action of vitamin D in the sunniest regions of the country and that this substance can be a transformative resource of public health. However, there is a great need for multicenter studies for greater scientific support. **Descriptors**: Vitamin D; Lung Neoplasms; Bronchial Neoplasms; Disease Prevention; Uses of Epidemiology; Mortality Registries.

RESUMO

Objetivo: identificar evidências de ação preventiva da vitamina D sobre a taxa de mortalidade de câncer de pulmão e de brônquios da população brasileira. **Método:** estudo quantitativo, epidemiológico, descritivo, desenvolvido a partir da coleta de dados das fontes INCA e IBGE. Os dados do INCA revelavam taxas de mortalidade para os dois cânceres, enquanto que o IBGE disponibilizava latitudes específicas de todas as capitais do país. Após a coleta, os dados foram digitados no programa *Microsoft Excel*, posteriormente, transferidos para o programa de construção de mapas *Target Map* e analisados por meio de estatística descritiva. **Resultados:** observou-se que as cinco unidades federativas mais distantes da linha do Equador representam as maiores taxas de mortalidade do Brasil comum em ambos os sexos. **Conclusão**: os resultados evidenciam uma ação preventiva da vitamina D nas regiões mais ensolaradas do país e que esta substância pode ser um recurso transformador de saúde pública. Contudo, há grande necessidade de estudos multicêntricos para maior respaldo científico. **Descritores**: Vitamina D; Neoplasias Pulmonares; Neoplasias Brônquicas; Prevenção de Doenças; Aplicações da Epidemiologia; Registros de Mortalidade.

RESUMEN

Objetivo: identificar evidencias de acción preventiva de la vitamina D sobre la tasa de mortalidad de cáncer de pulmón y de bronquios de la población brasileña. **Método:** estudio cuantitativo, epidemiológico, descriptivo, desarrollado a partir de la recolección de datos de las fuentes Inca e IBGE. Los datos del INCA revelaban tasas de mortalidad para los dos cánceres, mientras que el IBGE disponía de latitudes específicas de todas las capitales del país. Después de la recolección, los datos fueron digitados en el programa *Microsoft Excel*, posteriormente, transferidos al programa de construcción de mapas *Target Map* y siendo analizados por medio de estadística descriptiva. **Resultados:** se observó que las cinco unidades federativas más distantes de la línea del Ecuador representan las mayores tasas de mortalidad de Brasil, siendo común en ambos sexos. **Conclusión:** los resultados evidencian una acción preventiva de la vitamina D en las regiones más soleadas del país y que esta sustancia puede ser un recurso transformador de salud pública. Sin embargo, hay gran necesidad de estudios multicéntricos para mayor respaldo científico. **Descriptores:** Vitamina D; Neoplasias Pulmonares; Neoplasias de los Bronquios; Prevención de Enfermedades; Usos de la Epidemiología; Registros de Mortalidad.

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INTRODUCTION

The process of health education of the Brazilian population is very structured in the biomedical and clinical model and this historical framework contributes negatively to the value and social status of prophylactic programs. With this, the importance of prevention is seen as a priority, since this understanding represents the starting point for the emergence of positive health outcomes in a more lasting way.

Vitamin D (1,25-dihydroxyvitamin D3) is one of the great examples that perfectly portrays this historical reality. Insufficient or deficient serum levels of this substance have been considered a public health problem that impacts worldwide due to its implications for the development of various diseases such as osteoporosis, type 2 diabetes mellitus (T2DM), obesity, arterial hypertension and even cancer. [1]

In recent years, there has been a very strong interest in research into the effects of vitamin D on human health with the publication of a large number of studies. However, it is not possible to issue clear and well-founded recommendations about the benefits and risks of its administration as a preventive measure for chronic diseases.[2] In addition, there is growing evidence that more cases of lung cancer occur in individuals with low levels of vitamin D, [3-4] although its importance is not confirmed effectively after diagnosis by lung and bronchial neoplasia, by the specific type of tumor called non-small cell, found in 85% of the cases. [5]

In the formation of lung tumors, natural lung defense mechanisms are lost through the progressive and disorganized growth of malignant cells. The anatomical structures affected are regions such as the lower part of the trachea to the periphery of the entire lung. The disease is considered as one of the main causes of death due to neoplasia in Brazil and in the world. According to the World Health Organization (WHO), the frequency is higher among males, however, the incidence in males stabilized, while for females the effect was reversed, with a considerable increase in the last decades. All this change in the mortality burden shows the origin of a phenomenon called "feminization" of the disease, which is also similar for mortality records in individuals with human immunodeficiency virus (HIV). [6-7]

When considering risk factors, smoking is the main etiological agent of both cancers. Approximately 90% of cases occur in smokers and the risk is proportional to the daily smoking load, type and duration. The risk is reduced after the feeling of the smoking habit reaching only the non-smoker level after ten years. Smokers who consume 20 cigarettes a day for many years have a tenfold greater risk than non-smokers. Also, other factors are considered as etiological as is the case of industrial risks, air pollution, genetic inheritance and precursor lesions. [8]

The risk of the two neoplastic formations is also highlighted within the context of passive smoking. People who are married to smokers are 20% to 30% more likely to develop lung cancer than spouses of nonsmokers. In addition, more and more studies support vitamin D deficiency as the main risk factor for many cancers and may negatively influence the incidence of lung or bronchial cancer. [8-9]

The incidence of autoimmune or chronic diseases is less common in regions near the Equator, where the sun shines most of the year. Increasingly, epidemiologists realize that the prevalence of lethal diseases is lower in individuals living in more sunny regions than in individuals living in regions with limited amounts of sunlight. A geographic study of breast cancer throughout Mexico showed that as it moved away from the Equator, the country's death rates were higher. [10]

It is observed that the studies with this profile are more efficient in countries that have a large population and a greater territorial extension, as is the case of Brazil, the United States and China. Increasingly, the literature shows vitamin D deficiency as a risk factor for lung cancer, but the major challenge is to turn this hypothesis into a conclusive finding. With this new openness to research, clinical and geographic studies could define the causal relationship of vitamin D with lung and bronchial neoplasia. [11]

OBJECTIVE

● To identify evidence of the preventive action of vitamin D on the mortality rate of lung and bronchial cancer in the Brazilian population.

METHOD

Quantitative, epidemiological, descriptive study, performed from secondary data through the National Cancer Institute (INCA) and the Brazilian Institute of Geography and Statistics (IBGE). Data are reported in the Mortality Information System (MIS) and were collected in January and February of 2017, however, they refer to the period from 2010 to 2014. The choice occurred because they are the five most recent years available by INCA.

The INCA data refers to mortality from the option of International Statistical Classification of Diseases and Related Health Problems - Malignant Neoplasms of the Bronchi and Lungs (ICD 10 - C34) and include comparative elements such as sex, age and mortality rate by capital and its respective Federative Unit. IBGE provided support for INCA data by identifying latitudes of each capital and its population in each year from 2010 to 2014.

The mortality load variable was classified into two distinct categories: capital and federative unit, according to the classification system employed by IBGE. The samples in this study are two: the first includes only Brazilian men and the second only women. The separate analysis according to the sex of the population is justified by characteristic differences in the mortality burden for both samples throughout the period 2010-2014.

The data was entered into the spreadsheet software Microsoft Excel for Windows 2010, then transferred to the mapping program for the construction of geographical maps Target Map and analyzed using descriptive statistics. The program also helps in the definition of standardized colors that identify the degree of mortality in all the federal units of the country and, therefore, facilitates the analysis of the epidemiological panorama.

After the statistical survey of the data in the Target Map, the charts were tabulated and assembled, and the use of tables was adopted to observe similarities in the mortality rates between the capitals and their federative units due to contingent capital population in its Federative Unit. The most significant findings were presented in graphs obeying the following order: gross rate, latitude, year and sex. This sequence occurred for a better understanding of the quality of data provision.

The imaginary line of the Equator was chosen as a parameter for the discussion of the results by identifying the influence of the sun on the mortality rates of lung and bronchial neoplasms. The samples of men and women, as the two portions of the Brazilian population for the analyzes, benefit the criterion of greater biostatistical control over the limitations of this study, such as smoking, air pollution, genetic inheritance and nutritional factors. Considering that the research was done from data in the public domain, it was not necessary to submit to a Research Ethics Committee.

RESULTS

The mean number of cases reported for bronchial and lung cancer mortality in all Brazilian capitals from 2010 to 2014 has increased over the years. Although male individuals represent the largest number of cases, with a gross rate variation of 17.71, in the year of 2010, at 18.22, in 2014, in the analyzed period, there is always an increase progression for women over the years (Table 1).

Table 1. Gross mortality rates for bronchial and lung cancer considering the average of all Brazilian capitals. Crato (CE), Brazil, 2017.

Year of notification	Men	Women	All the population
2010	17.71	10.88	14.11
2011	18.22	11.45	14.65
2012	17.84	12.12	14.82
2013	18.59	12.13	15.19
2014	18.22	12.93	15.43
Total (2010-2014)	18.11	11.9	14.84

Source: INCA. Consolidated data as of 06/30/2016.

Taking the average gross rate of all capitals as the standard for the mortality rate of each city in its respective year, one can trace the epidemiological profile comparing all of them from the latitudes of each geographic area. The most critical capital cities are those with a mortality rate higher than the average rate of all capitals (Table 01). The table below presents the highest mortality capitals, with their specific rates and latitudes for each year (Table 02).

Table 2. Largest mortality rates from lung and bronchial cancer for each year, from 2010 to 2014, considering the average of all Brazilian capitals. Crato (CE), Brazil, 2017.

Capitol	2010	2011	2012	2013	2014	Latitude
Curitiba	14.78	15.87	_	15.93	_	25° 25' 40" S
Florianópolis	23.98	22.7	22.86	23.78	23.78	27° 35' 48" S
Porto Alegre	32.71	33.47	35.36	33.03	32.82	30° 01' 59" S
Recife	15.93	14.94	_	15.95	15.76	08° 03' 14" S
Rio de Janeiro	19.9	18.88	19.67	19.83	19.7	21° 56' 01" S
São Paulo	14.88	15.44	15.41	16.09	16.07	24° 29' 15" S
Vitória	16.47	17.55	18.91	17.71	_	20° 19' 10" S
Campo Grande	_	15.7	_	_	_	20° 26' 34" S
Cuiabá	_	14.74	_	_	_	15° 35' 46" S
Fortaleza	_	_	15.16	_	15.84	03° 43' 02" S
Goiânia	_	_	15.74	15.52	15.89	16° 40' 43" S
Total (2010-2014)	14.11	14.65	14.82	15.19	15.43	

Source: INCA. Consolidated data as of 06/30/2016. Note: unidentified values mean that the respective capitals did not belong to the group with the highest mortality rates.

Among the capitals of the country, Porto Alegre-RS and Florianópolis-SC correspond to the two largest latitudes and always with the two highest mortality rates of bronchial and lung cancer in the whole period. Porto Alegre-RS leads with a percentage of 231.82% higher than the average mortality rate of all capitals for the year 2010 and continues in this way in all years until 2014, with a rate of 212.7%.

When checking mortality rates in each state, the influence of latitude for bronchial and pulmonary cancers is perceived more comprehensively because it includes, as a sample, the entire Brazilian population. With this, the search limitation is much lower. However, the difficulty arises in determining a specific latitude by geographical area. In this sense, the distance of each State from the Equator line was considered. The table below represents the five highest mortality rates for the sexes, including, as a sample, all Brazilian states plus the Federal District (Table 3).

Table 3. Five higher mortality rates of bronchial and lung cancer by sex, for each year, from 2010 to 2014, considering all federative units, including the Federal District. Crato (CE), Brazil, 2017.

Federative Units	2010-2012		2012-2014	
	MEN	WOMEN	MEN	WOMEN
Rio Grande do Sul	37.22	19.39	38,21	20,93
Santa Catarina	24.47	10.85	23,85	12,32
Paraná	18	11.14	18,73	11,86
São Paulo	16.92	10.42	17,82	11,29
Rio de Janeiro	20.31	11.97	20,06	13,01
Average Total Rate	23.38	12.75	23.73	13.88

Source: INCA. Consolidated data as of 06/30/2016.

The Five most distant federative units of the Ecuadorian line represent the highest mortality rates of lung and bronchial cancer, and this situation occurs for both sexes. The State of Rio de Janeiro always has a higher mortality rate than São Paulo. It is observed that this situation is repeated when comparing its Brazilian capitals, since it represents a greater percentage of the population.

A great similarity of tables two and three is that the most critical capital cities were Porto Alegre, Florianópolis, Rio de Janeiro and São Paulo, and these cities coincide with their respective states when observing the highest mortality rates. The exception is Curitiba, which is not mentioned in every year. However, Paraná always appears as one of the five states with higher mortality.

When considering the average mortality rate of the period 2010-2014, one can also see an increase as the State distances itself from the Equator, except in some exceptions, as in the case of Bahia, in relation to Ceará, for males and the state of Espírito Santo, also compared to Ceará, for females (Figure 1).

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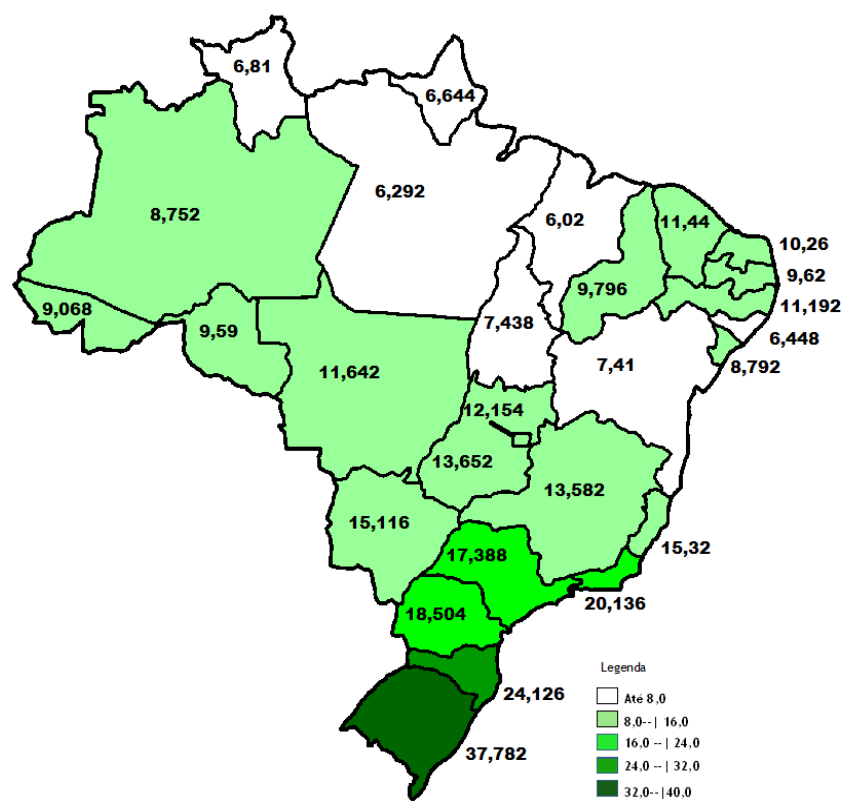Cruz KAO, Silva ML da, Silva TS.   Impact of vitamin d in the prevention...

Figure 1. Magnitude and variation of the lung and bronchial cancer mortality rate in men in Brazil and in Federative Units, in the period 2010-2014. Crato (CE, Brazil, 2017. Source: INCA. Consolidated data as of 07/30/2016.

From the Brazilian regions, it is considered that the North region has a mortality rate of 16.3%; Northeast, with 24.17%; Central West, with the inclusion of the Federal District, has 15.7%; Southeast, 19.83% and South, with 24%. Only Rio Grande do Sul, the state farthest from the Equator, has a rate of 11.27%, equivalent to almost one tenth of the Brazilian population (Figure 1).

In the female population, the North region had a 16% mortality rate, while the Northeast, South, Central West and Southeast regions had 28.64%, 20.77%, 15.67% and 18.91%, respectively (Figure 2). It can be seen that 61.57% of the cases of bronchial and lung cancer occur in men and 38.43% in the female population. In addition, there was no state in which the mortality rate was higher in the female population than in the male population. However, the State of Alagoas stood out as the one with the lowest disparity for both sexes (Figures 1 and 2).

The Brazilian states with the greatest disparity between men and women were Rio Grande do Sul and Santa Catarina. The two units are also among the most critical for both sexes. However, Rio de Janeiro is the second state with the highest mortality burden among women, even surpassing Santa Catarina by a slight difference of 0.37% (Figures 1 and 2).
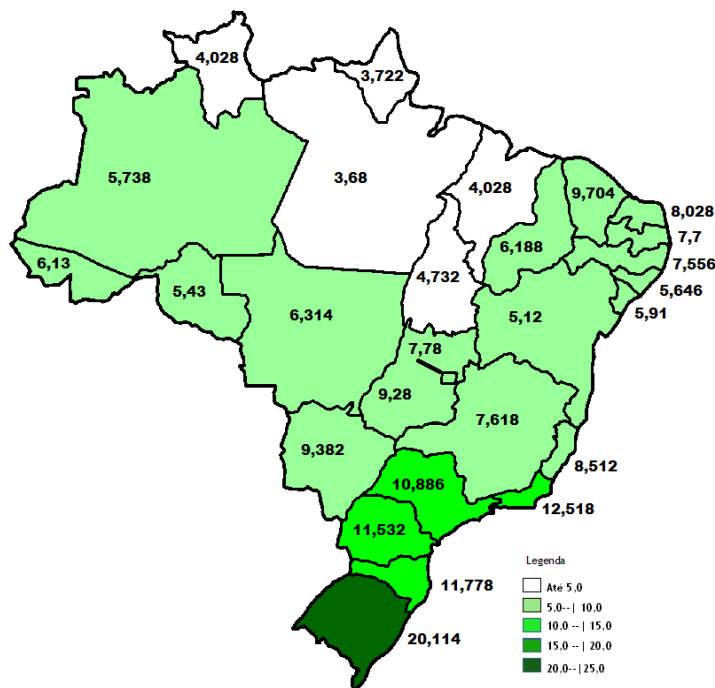

Figure 2. Magnitude and variation of the lung and bronchial cancer mortality rate in women in Brazil and in Federative Units, in the period 2010-2014. Crato (CE), Brazil, 2017. Source: INCA. Consolidated data as of 07/30/2016.

DISCUSSION

Despite the drop in cigarette production at a rate of 25.2%, from 2010 to 2014, the mortality burden from pulmonary and bronchial neoplasia increased by 7.34%. Although Brazil is considered a worldwide reference in the control of smoking, this statistical data reflects the need to develop new preventive strategies that do not aim only at the control of smoking. [12]

The states with the highest number of daily smokers are Rio Grande do Norte (17%), Acre (14.4%), Ceará (14.3%), Maranhão (13.8%), Tocantins 3%) and Roraima (12.9%). Rio Grande do Norte is considered the most critical in this regard, however, it has one of the lowest mortality burdens in the country for both sexes. The situation is one of the examples that show how the daily smoke does not present negative influence of effective form for many Federative Units near the line of the Equator.

The southern region was considered the most critical for both sexes. However, in the Midwest, there was a greater increase in the period from 2010 to 2014 for women (0.47%), while for men the situation occurred in the North (0.33%). In addition, in the male population, there is a greater stability in the mortality burden, different for women, with a continuous increase in all regions. The difference in these two standards is also confirmed by the estimate created by annual monitoring of the Non-Communicable Chronic Disease Surveillance System (Vigitel) from 2006 to 2015. [13]

The epidemiological evidence identified by the influence of latitude does not suppress the harmful effects caused by smoking, since cigarette smoke is still considered the main risk factor. The States with the highest number of smokers had no reduction in the mortality burden in more than 95% of the time. In the case of Federative Units with a lower percentage of smokers, the trend for mortality was more visible (65%). The damage caused by the cigarette is very consistent, with more than fifty carcinogenic substances such as arsenic, asbestos and cadmium. This whole malignant picture represents the real reason why 90% of lung tumors are due to smoking. [12-14]

In addition to smoking, cases of tuberculosis (TB) and Chronic Obstructive Pulmonary Disease (COPD), family history of lung and bronchial tumors or poor nutrition in fruits and vegetables are also risk factors for both types of cancer. In this sense, because they contributed to the morbidity and mortality rates, they were defined as limiting for this study. [15]

It is also considered the underreporting of deaths as another form of research restriction during data collection. Within this context, there is a high proportion of registered mortality rates with ill-defined causes, although MIS is well established in the country. [13] Another challenge is in relation to epidemiological studies on lung cancer, since many of them do not depict the specific histological type of the neoplasm and this represents a change in the lifetime of the individual depending on the type of tissue reached by the malignant tumor. [15]

The country's territorial extension contributes significantly to the collection of results. According to IBGE, the distance between the north and south ends of Brazil is 4398 kilometers (latitude range from 05 ° 16 'N to 33 ° 45' S). It appears that if the same method were applied in a country with a minimum territorial extension from north to south, as is the case in Japan or Portugal, sampling that determines latitude variations would have a considerable statistical bias.

The Equator line is the most sun-oriented parallel due to the inclination of the Earth's rotational axis at 23o 27`30``. The influence of ultraviolet radiation more focused on Federative Units, such as Roraima, Amapá, Pará, Maranhão and Amazonas, shows a low mortality rate when compared to southern states, such as Rio Grande do Sul, Santa Catarina, Paraná, São Paulo and Rio de Janeiro.

The importance of the geographical location for these regions is observed, considering that sun exposure, in an intelligent way, is the main resource to improve levels of vitamin D. This substance has a malignant effect and even triples when added to smoking. Thus, the lack of exposure to the sun does not exclude the most relevant etiologic agent for lung and bronchial neoplasia. Therefore, there is a growing need for studies that include as many risk factors as possible. [16-17]

Researchers from China conducted a comprehensive review of the literature and a meta-analysis to assess the association between serum levels and dietary intake of vitamin D with the risk of lung cancer. As a result, they found that those with higher serum vitamin D levels had a 16% lower risk of developing lung cancer. Among studies evaluating the relationship between serum vitamin D levels and the risk of lung cancer, the highest levels were associated with a reduced risk of 17%. Already the risk of lung

cancer for those with higher dietary intake was reduced by 11%. [18]

An example that demonstrates the benefit of vitamin D for lung and bronchial neoplasms in this study can be identified by the following chart, in radar format, for the year 2013. In it, the proportionality ratio in the male population is shown from three aspects: (1) mortality burden of lung and bronchial tumors; (2) individuals who make daily tobacco use and (3) distance from the state to the Equator line with a hypothetical value proportional to the real latitude of their capitals (Figure 3).
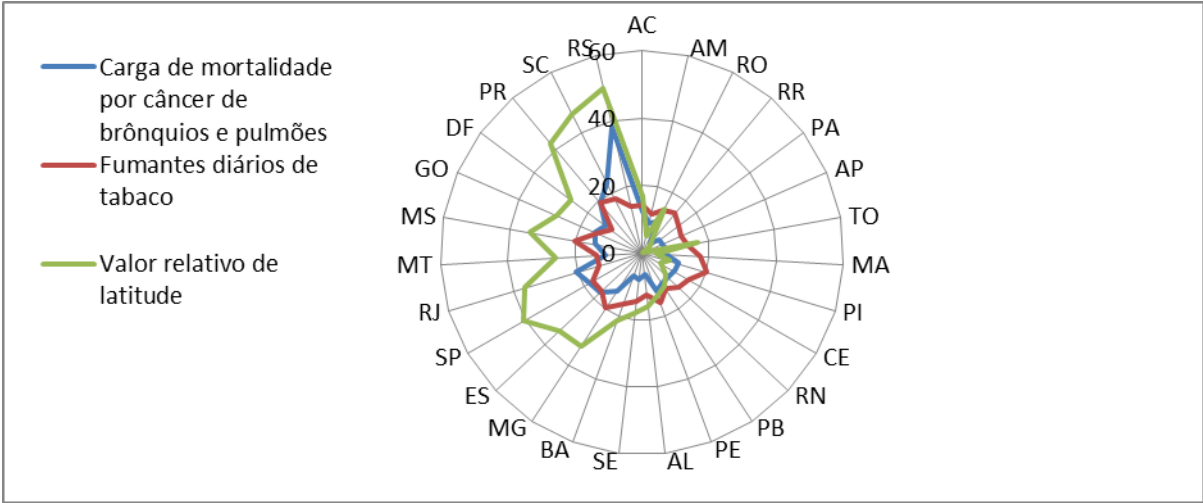

Figure 3. Proportionality ratio between the Ecuadorian line, the smoking practice and the mortality rates of each Federative Unit in men, in the year 2013. Crato (CE), Brazil, 2017. Sources: INCA and IBGE. Consolidated data as of 07/30/2016.

It is noted that the area occupied by the mortality burden is more symmetrical with latitude than smoking. From this picture, the importance of examining the low sun exposure as a new risk factor is perceived. However, more studies are needed to support this evidence, such as epidemiological studies in countries with a large territorial or clinical extent, from hemograms that identify vitamin D levels in patients with lung or bronchial cancer, observing the histological type reached by the tumor (bFigure 3).

from lung and bronchial cancer increased more and more. With this, the existence of other risk factors is evident, as is the case of insufficiency or deficiency of vitamin D in part of the Brazilian population. This whole picture brings the importance of new studies that quantify the influence of this substance in relation to the daily smoke for the indices of bronchial and pulmonary neoplasias as a way of identifying if the insufficiency of vitamin D is defined as a new risk factor or not for literature.

CONCLUSION

The study revealed the need for multicentric research to offer greater scientific resolve on the influence of vitamin D in cases of lung and bronchial neoplasms. There is a huge lack of clinical approach within the epidemiological field, as occurs when the subtypes of the two cancers occur, to better understand the mortality indicators.

Through various scientific evidence, it can be seen that vitamin D can be a transformative resource for public health. Most of the expenditures advocated by the Ministry of Health would decrease if health education had a permanent and prophylactic rather than purely clinical direction. The mortality indicators of the Brazilian population represent the results of a sum of risk factors throughout the life of each individual and, therefore, the need for a continuous health care.

Although Brazil is considered a worldwide reference in smoking control, mortality rates

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