



Lung cancer associated with natural vegetation cover: spatial analysis in the state of Pará, eastern Brazil

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Abstract

Lung cancer represents the second-highest incidence of cancer worldwide and the leading cause of cancer-related deaths. Smoking is still the main risk factor, but other factors are also important, such as those associated with the large-scale exploitation of natural resources. This ecological study aimed to analyse the potential association between the spatial distribution of lung cancer and the natural vegetation cover in the state of Pará, Brazil. The study included 700 new cases of lung cancer taken from the Integrador Hospital Cancer Registries, a web-based system consolidating cancer data across Brazil. Spatial exploratory techniques were estimated by global and local spatial correlation coefficients and presented as thematic maps. The independent variables were socio-economic and environmental indicators. A significant variation was identified between different geographical areas and the distribution pattern of lung cancer incidence, with a negative correlation ($I = -0.12$, $p\text{-value} = < 0.001$) between cancer rates and natural vegetation cover. The findings provide insights into the role of environmental factors that influence public health, ratifying the need for environmental conservation policies to promote health and prevent disease.

Introduction

According to estimates by the Global Cancer Observatory (GCO), an interactive web platform developed by the International Agency for Research on Cancer (IARC), lung cancer represents the second-highest cancer incidence worldwide, *i.e.*, 2,206,771 new cases, which is equivalent to 28.3% of the total global cancer incidence in 2020. It is also considered the leading cause of cancer-related deaths, accounting for 1,796,144 deaths and a crude rate of 23 per 100,000 inhabitants (IARC, 2022). It is estimated that there will be an increase of approximately 75% new cases of tracheal, bronchial and lung cancer in Latin America by 2040, and in Brazil, where lung cancer ranks third in age-standardised incidence rates, this increase is expected to be 82% on average (IARC, 2022).

Smoking is still the main risk factor for lung cancer. However, other factors are important for respiratory tract cancers, such as those associated with the unsustainable exploitation of natural resources (Huang *et al.*, 2022). According to the Global Burden of Disease (GBD), environmental exposure to household air pollution from solid fuels and microscopic particulate matter (classified by size, with PM_{2.5} referring to particles smaller than 2.5 microm-



eters and PM₁₀ to those smaller than 10 micrometers) as well as occupational carcinogens, such as asbestos is a major risk (GBD 2019 Respiratory Tract Cancers Collaborators, 2021).

In Brazil, the Brazilian Ministry of Health (MoH) records all hospital data on patients with a confirmed cancer diagnosis through the Integrador Hospital Cancer Registries (RHC), a web-based system developed by the National Cancer Institute (INCA), which guarantees the quality of the data based on strict guidelines and procedures for collecting, storing and analysing the data. Completeness of the system depends on the participation of Brazilian hospitals, which are responsible for regularly sending in their databases (MoH, 2022). The estimated number of new cases of trachea, bronchus and lung cancer in Brazil for each year of the three-year period from 2023 to 2025 is 32,560 (MoH, 2022). According to the MoH, the southern region has the highest incidence rates for both sexes. Among men, it is the second most common malignant neoplasm in the South and Northeast; and the third in the Southeast; Centre-West and North. Among women, it is the third most common cancer in the South; the fourth in the Southeast; Centre-West and North; and the fifth in the Northeast (MoH, 2022).

Environmental impact

As a member of the United Nations (UN), Brazil has signed up to the 2030 Agenda, committing to the Sustainable Development Goals (SDGs), especially its target 3.4, with a view to reducing premature mortality from non-communicable diseases by one third through prevention and treatment, and promoting mental health and well-being (UN Brazil, 2024). However, despite the investments in public policies made in Brazil, there is no evidence of satisfactory progress towards achieving this target (Brazil's Chamber of Deputies, 2024). It should particularly be noted that the state of Pará has undergone numerous transformations related to land use and land cover (LULC), especially since the 1970s. Considering the different economic cycles, the policies and projects established have altered the natural landscape, with the destruction of forests by the construction of important stretches of road, which contribute to the process of transforming LULC through logging, cattle ranching, mining and the introduction of digital agriculture (Araújo *et al.*, 2023; Correa *et al.*, 2023).

In this context, considering the growing economy of the state of Pará, the municipalities of Belém, Ananindeua, Marituba and Benevides are characterised as having seen the greatest growth in the urban area since the 1980s. This is because, from the 1980s onwards, the natural environment of the Belém Metropolitan Region has undergone radical changes, such as the transformation of the entire length of the BR-316 and Augusto Montenegro highways into new spaces for urban residences, reflecting intense LULC changes, with pastoral and forest areas being converted into urban and 'verticalised' landscapes (Gusmão *et al.*, 2021).

Further, construction companies are competing for Belém's urban fabric, investing in new housing concepts for the population (Costa *et al.*, 2022). Studies carried out in Bengbu, China on the impact of the natural and built environment on the incidence of lung cancer, found that urban construction sites can have an impact on air quality in cities (Wang *et al.*, 2022) and that high residential density is detrimental to ventilation and increases exposure to pollutants (Gu *et al.*, 2023). The same happened in Santarém, a municipality in the Baixo Lower Amazonas Mesoregion of Pará. The city attracts a large number of students from nearby towns because it has become a university centre, as well as being consid-

ered an important financial, commercial and cultural urban centre. As a result, the urban area has become an alternative for people who used to work in rural areas, and the vegetation cover has increasingly been replaced by construction and road paving. Furthermore, small areas of pasture or subsistence farming in the rural areas have been transformed into large tracts of land with mechanised agriculture (Santos *et al.*, 2019).

In the North-east of Pará, given that the current landscape is characterised by a high degree of anthropisation, For example, the municipality of Capitão Poço, as in Asia (Beale *et al.*, 2022), has had its natural vegetation greatly modified by land use for agricultural practices and, more recently, also for the mineral exploitation of sand and pebbles (Piedade da Silva *et al.*, 2023; da Silva Prestes *et al.*, 2023). Similarly, in addition to mining and logging, cattle ranching was the activity that contributed to the deforestation process most in the Southeast of Pará, as in the municipality of Xinguara (Parente *et al.*, 2021). Through its extensive nature of production, which seeks to incorporate new areas of forest or secondary vegetation, without the any technological increment to increase productivity, cattle farming contributes to the loss of forest cover (Amorim *et al.*, 2022). Furthermore, in the Amazon biome, the conversion of natural vegetation cover to other land use has been taking place, especially in the 'Arc of Deforestation', where the municipality of Anapu and a Sustainable Development Project (PDS) are located (Watrin *et al.*, 2020). The latter is a type of settlement that is not based on a title, but on the issue of Real Right of Use Concession Contracts, often issued in the name of family associations. Although it is based on low environmental impact activities, there is criticism of the lack of effective control over the use of natural resources, which can jeopardise environmental conservation in the long term (Porro *et al.*, 2018).

Finally, it has been found that total deforestation in Anapu reached a significant rate seven years after the creation of the PDS. This was attributed to the advance of farming activities, which tend to deplete the forest reserves on the plots (Watrin *et al.*, 2020).

Approach

The analysis of the spatial distribution of diseases and health problems is an important tool for supporting decision-making in planning and policy formulation (Aceng *et al.*, 2024). By adopting an ecological approach with a multiple-group design, using data on new cases of lung cancer and environmental variables, as well as identifying spatial patterns of the disease, it is hoped to determine potential environmental factors that modulate incidence, contributing to a methodological improvement in the application of advanced geospatial analysis techniques. In this way, the contribution of this study lies in the possibility of subsidising policies to mitigate environmental impacts on respiratory health, promoting interventions that are specific to the regional reality. The methodological approach also makes it possible to improve epidemiological models based on spatial data, contributing to lung cancer prevention and control strategies that are more precise and adapted to the particularities of the territory studied.

Given the epidemiological magnitude of lung cancer and the environmental scenario in Pará State, this study sought to fill the gap in the literature by integrating spatial analysis of the distribution of the disease with ecological characteristics, especially related to natural vegetation cover and territorial transformations. Although previous studies (Mathias *et al.*, 2020) have addressed environmental factors in the development of lung cancer, the geospatial relationship between the degradation of vegetation

cover and the incidence of the disease still needs further investigation. The overall aim of this study was to analyse the spatial distribution of lung cancer associated with natural vegetation cover in the state of Pará using an ecological, exploratory, multiple-group approach (Rothman *et al.*, 2009).

Materials and Methods

Study site

The state of Pará, located in the Lower Amazon in eastern Brazil, is geographically divided into 144 municipalities (the unit of the investigation), which are part of six political mesoregions: the Lower Amazon, Southwest, Marajó, Northeast, Belém Metropolitan and Southeast (Figure 1).

Data

Secondary data included were the total number of Integrador RHC cancer case records, diagnosed between January 2017 and December 2021, defined by primary location in the lung (code C34 of the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems - ICD-10) catalogued by the RHC. We used the average annual incidence rates of cancer adjusted per 100,000 population for each municipality using the direct method (Rothman *et al.*, 2009) and the population information from the 2022 demographic census (IBGE, 2023). In order to

standardise incidence rates by the structure proposed by Integrador RHC was adopted taking into account 5-year age groups from 0 - 4 years to 80 - 84 years followed by a ≥ 85 years group. Microsoft® Excel® for Microsoft 365 MSO was used to calculate the standardised rates, and a map of their quintile distribution was constructed.

Since peaks or falls over time could distort the analysis, the average annual incidence rate was used as the dependent variable as this made it possible to eliminate annual variations and make more accurate and fair comparisons. The independent variables were percentage of natural vegetation cover and hotspot concentrations plus a set of socio-economic indicators: the Municipal Human Development Index (MHDI), the Social Vulnerability Index (SVI), the Gini Index, the Gross Domestic Product (GDP), the per capita income, the primary care coverage, the percentage of those employed in the agricultural sector, the percentage of those employed in the mineral extraction sector, the percentage of those employed in the manufacturing industry, the percentage of those employed in the public utility industrial services sectors, the percentage of those employed in the construction sector, the percentage of those employed in the commerce sector and the percentage of those employed in the services sector. These latter independent variables were collected from the Atlas of Human Development in Brazil (UNDP, 2013), the Atlas of Social Vulnerability (IAER, 2015) and MoH's e-Gestor AB portal.

The existence of spatial autocorrelation was checked using uni- and bivariate global Moran's *I* followed by Local Indicators of Spatial Association (LISA) maps. The global Moran's indices indicate spatial dependence, considering values from -1 to +1, where values close to 0 indicate none or very low spatial dependence.

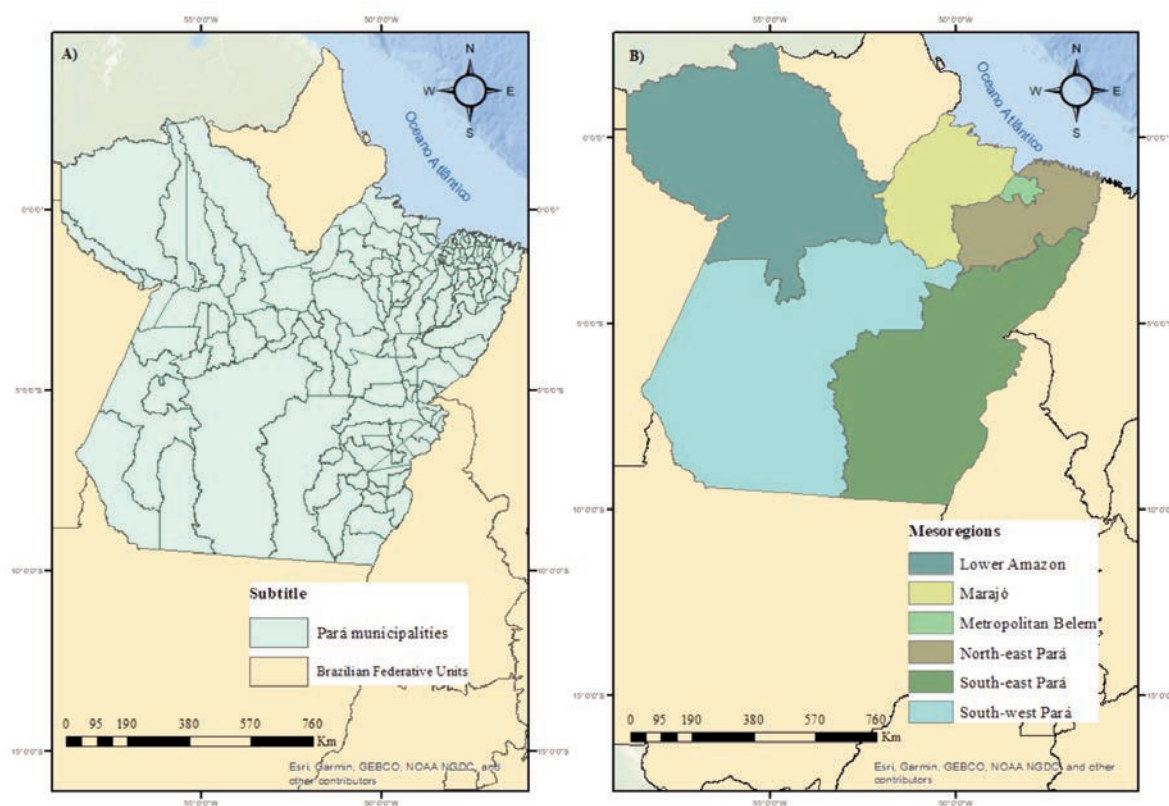


Figure 1. Map of the state of Pará, Brazil: the study area. **A)** Municipalities; **B)** Mesoregions

Values close to -1 represent negative or inverse spatial dependence, and values close to +1 represent no or very low spatial dependence. The local tests, in addition, make it possible to check for the presence of clusters and their intensity (Arcêncio *et al.*, 2022). The degree of neighbourliness was determined by the weight matrix, using queen contiguity as the criterion. The pseudo-significance test was used to estimate the significance of the indices using 999 permutations. All spatial autocorrelation analyses and map construction were carried out using GeoDa software, version 1.14.0, and ArcGIS, version 10.8 using $p \leq 0.05$ as indication of statistical significance.

Results

According to the annual rate adjusted per 100,000 population lung cancer incidence, there was significant variation of the distribution between areas. The five municipalities with the highest average annual rates in the period were Sapucaia at 1.03, Barcarena at 1.02, Curuá at 0.98, Primavera at 0.97 and Xinguara at 0.92 (Figure 2).

Univariate global Moran's I showed the existence of positive spatial autocorrelation of the standardised lung cancer incidence rate ($I = 0.09$, $p = 0.023$) and with regard to the local associations, the regions with significant LISA values are shown in Figure 3. High incidence rates, where the neighbouring municipalities also have a high incidence rates were found in five municipalities: Abaetetuba, Mãe do Rio, Ponta de Pedras, São Domingos do Capim and Sapucaia that belong to the three mesoregions of Marajó, Northeast and Southeast Para. Low incidence rate, neigh-

bouring municipalities with the same characteristics Were found in five other municipalities: Breves, Curralinho, Melgaço, Oriximiná and Porto de Moz that belong to the two mesoregions of Marajó and the Lower Amazon. The municipalities shown in white represent areas that were not influenced by the incidence rates of their neighbours, i.e. no spatial autocorrelation was detected.

By applying the bivariate global Moran's Index, it was possible to detect spatial autocorrelations between the incidence rate of lung cancer and the percentage of natural vegetation cover ($I = -0.12$, $p < 0.001$). The negative correlation index indicated that high incidence rates were spatially autocorrelated with low percentages of natural vegetation cover.

Thus, the bivariate Local Moran's I enabled municipalities to either be identified as low cancer incidence rates, surrounded by municipalities with high percentages of natural vegetation cover and thus be classified as Low-High (LH) clusters, or high cancer incidence rates, surrounded by municipalities with low percentages of natural vegetation cover and thus be classified as High-Low (HL) clusters. As seen in Figure 4, the former included the following municipalities: Afuá, Aveiro, Bagre, Breves, Curralinho, Gurupá, Itaituba, Jacareacanga, Juruti, Limoeiro do Ajuru, Melgaço, Monte Alegre, Muaná, Óbidos, Oriximiná, Portel, Porto de Moz, Prainha, Rurópolis, São Sebastião da Boa Vista, Senador José Porfírio, Terra Santa, Trairão and Vitória do Xingu belonging to the mesoregions of Baixo Lower Amazona, Marajó and Sudoeste Paraense. The latter, on the other hand, included Aurora do Pará, Capitão Poço, Castanhal, Conceição do Araguaia, Irituia, Mãe do Rio, Marabá, Palestina do Pará, Redenção, Santa Maria do Pará, São Domingos do Araguaia, São Domingos do Capim, São Geraldo do Araguaia, São Miguel do Guamá, Sapucaia and Xinguara, belonging to the mesoregions of Northeast and

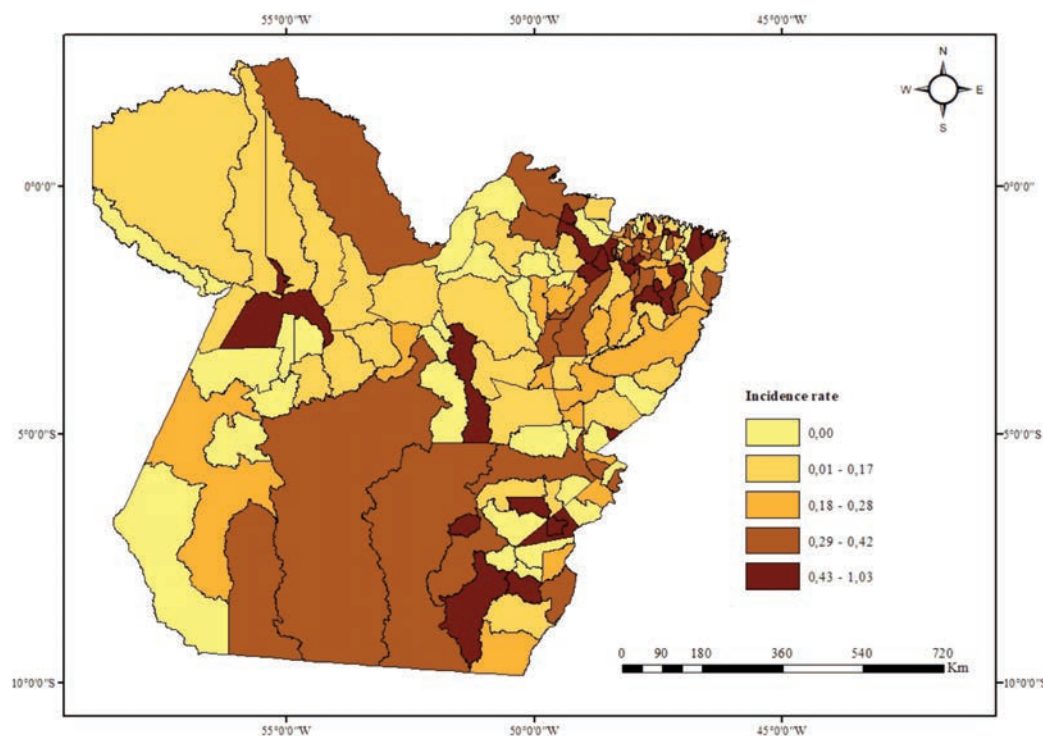


Figure 2. Distribution of the average annual lung cancer incidence in Pará, Brazil 2017-2021.

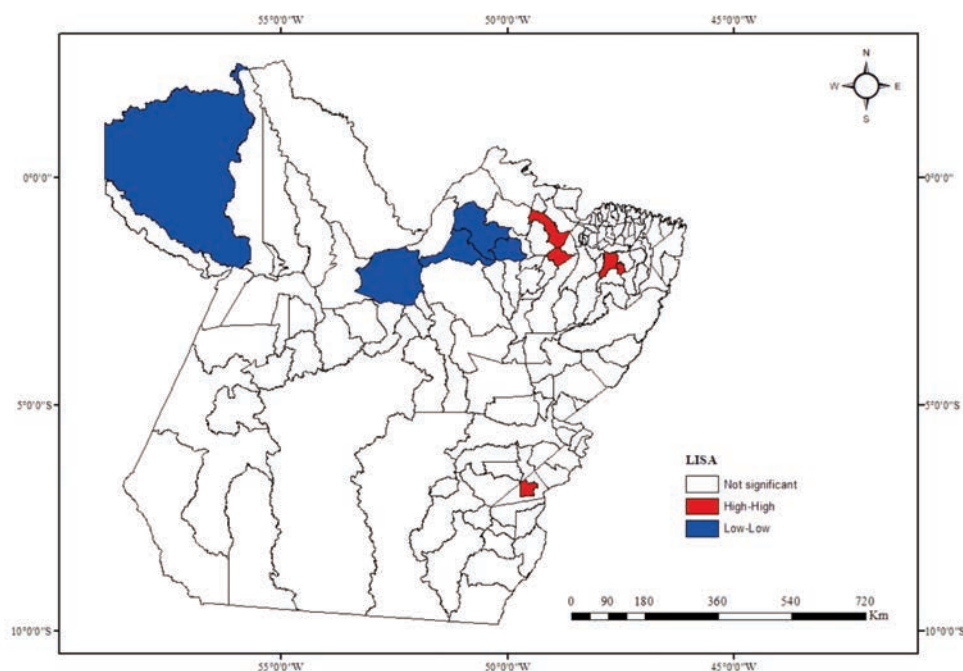


Figure 3. Levels of clustering of the average annual lung cancer incidence in Pará, Brazil 2017-2021. Statistic: univariate local indicator of spatial association (LISA). Areas shaded in red: high incidence rates, where the neighbouring municipalities also have a high incidence rates (HH clusters). Areas shaded in blue: low incidence rates, where the neighbouring municipalities also have a low incidence rates (LL clusters).

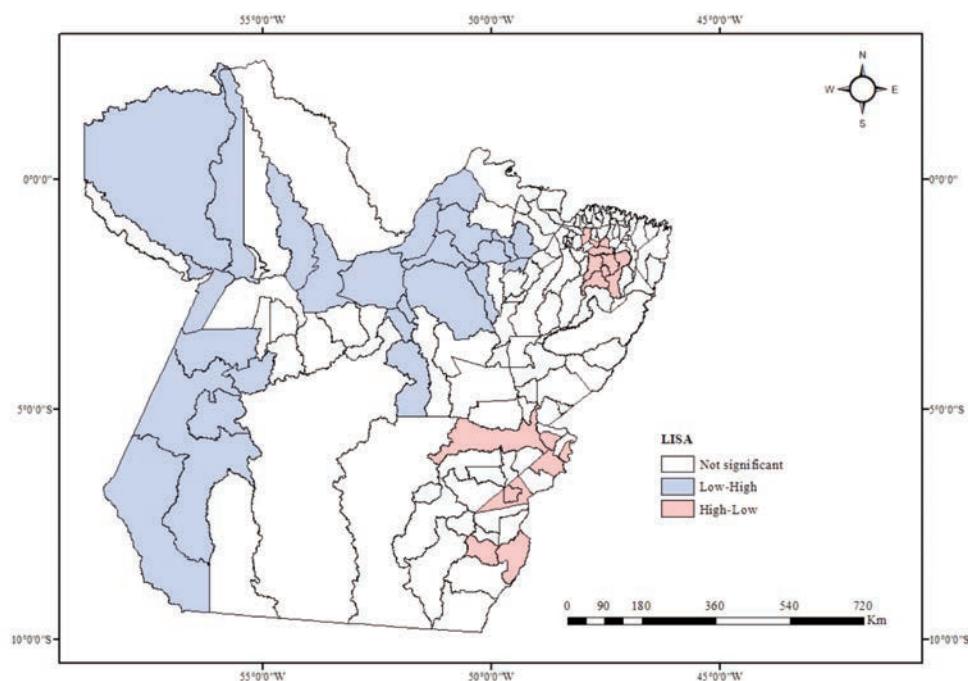


Figure 4. Clustered association of average annual lung cancer incidence rates and percentage of natural vegetation cover in Pará, Brazil 2017-2021. Statistic: bivariate local indicator of spatial association (LISA). Areas shaded in blue: municipalities with low lung cancer incidence rates surrounded by municipalities with high percentages of natural vegetation cover (LH clusters). Areas shaded in pink: municipalities with high incidence rates, neighbouring areas with low percentages of natural vegetation cover (HL clusters).

Southeast Para mesoregions.

Discussion

The spatial distribution of lung cancer incidence was found to be considerably affected by the environment in the areas studied. We found increased levels of this disease in all the municipalities targeted for environmental management as mentioned in the Introduction section. Space is thus relevant and there is a need to investigate and understand the occurrence and distribution of its incidence in Para in relation to LULC and the presence of road traffic, spatial form, green and open spaces, air pollution, and service facilities as pointed out by Gu *et al.* (2023). High incidence rates were found in all of the state's mesoregions, particularly in those municipalities recognised by profound transformations in their form and content, contributing to the space and landscape being modified by social, political and economic elements (Amorim *et al.*, 2022; Furtado *et al.*, 2023).

The vegetation cover indicator has been pointed out as a determining factor for high and very high socio-environmental vulnerability to climate change, and it is also believed that tourism, cattle and buffalo farming, and plant extraction have a hand in increasing local deforestation (Santos *et al.*, 2021). Not surprisingly, this study identified high incidence rates of lung cancer in some municipalities in the Marajó Mesoregion, which is not only the largest river and sea archipelago in the world, but also targeted by large-scale environmental management.

The results of the bivariate analysis in this study are in line with those identified in India, Germany and megacities in the United States, where it was found that the increase in concentrations of environmental, in particular $PM_{2.5}$, was accompanied by an apparent decrease in vegetation, resulting in a negative correlation (Lim *et al.*, 2020). In this regard, it is worth mentioning that in the UK, a significant association was found between $PM_{2.5}$ levels and the incidence of lung cancer in people, who had never smoked or in light smokers. This has been shown to be related to the influx of macrophages into the lung and the release of interleukin-1 β , caused by atmospheric pollutants, resulting in cellular states that nurture carcinogenesis (Hill *et al.*, 2023).

In this context, among the numerous ways of mitigating air pollution, in addition to policies and technological methods focused on reducing emissions (De Pascali *et al.*, 2019), programmes employing mass planting of trees and shrubs are recommended, as they are considered inexpensive and environmentally friendly (Lee *et al.*, 2020). Furthermore, $PM_{2.5}$ can be absorbed by plant stomata and undergoes different processes to protect the organism against the toxicity of the contaminant: excretion and conjugation followed by compartmentalisation or degradation to simple cellular metabolites (Wróblewska *et al.*, 2021).

Potential limitations

As a time-series ecological study, the main limitation lies in the ecological fallacy (Silva *et al.*, 2024), since the findings reflect population patterns. This characteristic prevents robust causal inferences and requires caution when interpreting the results. Furthermore, the use of secondary data can introduce information bias due to the quality of the records, compromising the accuracy of the analyses. Another potential bias is the heterogeneity of environmental data sources, which may vary in their methodological approach to capturing and processing information.

These limitations suggest that possible future studies employ

longitudinal cohorts and advanced spatial modelling, incorporating individual monitoring data and multivariate analyses for a more refined understanding of environmental impacts on lung cancer incidence. The results of this study reinforce the relevance of environmental preservation as a key determinant of public health and support the development of sustainable territorial planning strategies.

Conclusions

There is evidence of a heterogeneous distribution of lung cancer incidence in the state of Pará Brazil. The detailed spatial analysis suggests that areas with greater environmental preservation may play a protective role against the development of lung cancer, as well as reinforcing the need for environmental conservation policies as means of promoting health and preventing disease. Overall, the study paves the way for future research that can explore the complex interactions between the environment and human health in regions of great ecological diversity, such as in the Amazon biome.

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