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Tese

Distribuição espaço-temporal e determinantes da emergência de dengue no Rio Grande do Sul – 2007 a 2023

Sergiane Baes Pereira

Pelotas, 2025

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Distribuição espaço-temporal de determinantes da emergência de dengue no Rio Grande do Sul, 2007 a 2023

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Dedico esta tese à memória do meu avô Mario Baes (1934-2025).

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"(...) tua palavra, tua história, tua verdade fazendo escola, e tua ausência fazendo silêncio em todo lugar (...)" (O Teatro Mágico)

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A saúde é direito de todos e dever do Estado, garantida mediante políticas sociais e econômicas que visem a redução do risco de doenças e de outros agravos e ao acesso universal e igualitário às ações e serviços para a sua promoção, proteção e recuperação. (Constituição da República Federativa do Brasil – Art. 196, 1988)

Resumo

PEREIRA, Sergiane Baes. **Distribuição espaço-temporal e determinantes da emergência de dengue no Rio Grande do Sul, 2007 a 2023.** 2025. 85f. Tese (Doutorado em Ciências) - Programa de Pós-Graduação em Veterinária, Faculdade de Veterinária, Universidade Federal de Pelotas, Pelotas, 2025.

As doenças negligenciadas compõem um grupo de doenças que ainda representam um problema persistente de saúde pública. Dentre essas enfermidades, estima-se que a dengue – arbovirose transmitida por mosquitos do gênero *Aedes* - exponha a risco de infecção mais de quatro bilhões de pessoas globalmente, sendo considera uma das dez principais ameaças à saúde pública mundial. É considerado que no Brasil, desde a primeira epidemia de dengue registrada em 1986, a doença se encontre em situação de hiperendemicidade com sucessivos períodos de epidemias, gerando relevantes impactos sociais e econômicos. No Rio Grande do Sul, o primeiro caso autóctone da doença foi registrado em 2007 e, embora fosse o estado anteriormente considerado uma área protegida, pode-se observar expansão da doença em seu território, com notificações de casos em 91,15% dos municípios em 2022. Assim, o objetivo geral desta tese foi realizar a análise epidemiológica de dados gerados na rotina de vigilância e controle de dengue no Rio Grande do Sul, a partir de dados da distribuição da doença no estado e seus determinantes disponibilizados nos sistemas de informação nacionais e estaduais. Como objetivos específicos, cita-se a análise da expansão temporal e geográfica da dengue no Rio Grande do Sul no período de 2007 a 2023; a identificação de fatores socioambientais associados à incidência de dengue no Rio Grande do Sul, e o fornecimento de informações para auxílio nas estratégias de prevenção primária mais eficazes. Para isso foi construído um estudo que resultou em dois artigos com utilização de dados secundários de vigilância epidemiológica. O primeiro artigo constituiu-se em um estudo ecológico dos casos de dengue no Rio Grande do Sul no período de 2007 a setembro de 2023, com objetivo que avaliar a expansão geográfica e temporal da dengue no estado durante esse período. Para a descrição espacial foram construídos mapas anuais de taxas de incidência por município; a autocorrelação espacial foi avaliada por meio de Índice Global de Moran e os Indicadores Locais de Associação Espacial (LISA) e a identificação clusters espaços-temporais foi realizada por meio do modelo discreto de Poisson e Modelos Aditivos Generalizados. As análises foram realizadas utilizando o software SatCan e R. Foi observado que no período analisado, o Rio Grande do Sul notificou 126.067 casos de dengue, que resultaram em 142 óbitos, sendo 80,5% do total de casos notificados apenas no biênio 2022-2023. As maiores taxas de incidência e mortalidade foram observadas na mesorregião Noroeste, seguida pela mesorregião Centro-Oriental, observando-se escalada acentuada no risco de dengue a partir de 2019 e intensificação pronunciada a partir de 2022 – indicando uma epidemia em andamento. Já o segundo artigo objetivou identificar fatores ambientais e socioeconômicos associados à incidência de dengue no estado no período de 2013 a dezembro de 2023. Para isso foi avaliada a influência do índice de urbanização e da densidade rural – durante os anos de 2010 e 2022 - e da qualidade ambiental (por meio do Índice de Performance Socioambiental) sobre a taxa média de incidência de dengue nas diferentes mesorregiões do estado por meio da análise de regressão geograficamente ponderada (GWR) utilizando o *software* R. Observou-se que durante o período analisado foram notificados 127.945 casos de dengue no estado, sendo 82,74% desses notificados entre 2022 e 2023 e que as variáveis avaliadas aturam de forma heterogênea sobre a expansão da doença nas diferente mesorregiões do estado, com destaque para a variável densidade rural que em 2022 demonstrou expansão da influência para mesorregião Sudoeste e consolidação nas mesorregiões Nordeste e Metropolitana. Os resultados observados nesta tese demonstram a situação epidemiológica alarmante da dengue no Rio Grande do Sul, com expansão por suas mesorregiões e com diferentes fatores socioambientais influenciando a incidência da doença e sua expansão. Espera-se, assim, que tais resultados possam orientar a tomada de medidas de controle e prevenção eficazes e direcionadas para as populações de risco.

Palavras-chave: arboviroses; dengue; epidemia; expansão geográfica; vigilância epidemiológica.

Abstract

PEREIRA, Sergiane Baes. **Spatiotemporal distribution and determinants of dengue emergence in Rio Grande do Sul, 2007 to 2023.** 2025. 85f. Thesis (Doctor degree in Sciences) - Programa de Pós-Graduação em Veterinária, Faculdade de Veterinária, Universidade Federal de Pelotas, Pelotas, 2025.

Neglected diseases comprise a group of diseases that still represent a persistent public health problem. Among these diseases, dengue—an arbovirus transmitted by mosquitoes of the Aedes genus—is estimated to put more than four billion people globally at risk of infection, and is considered one of the ten main threats to global public health. Since the first dengue epidemic in 1986, Brazil has been considered hyperendemic, with successive periods of epidemics generating significant social and economic impacts. In Rio Grande do Sul, the first indigenous case of the disease was recorded in 2007. Although the state was previously considered a protected area, the disease is expanding within its territory, with cases reported in 91.15% of municipalities in 2022. Therefore, the general objective of this thesis was to conduct an epidemiological analysis of data generated by routine dengue surveillance and control in Rio Grande do Sul, based on data on the distribution of the disease in the state and its determinants available in national and state information systems. Specific objectives include analyzing the temporal and geographic spread of dengue in Rio Grande do Sul from 2007 to 2023; identifying socio-environmental factors associated with dengue incidence in Rio Grande do Sul; and providing information to support more effective primary prevention strategies. To this end, a study was constructed resulting in two articles were developed using secondary epidemiological surveillance data. The first article was an ecological study of dengue cases in Rio Grande do Sul from 2007 to September 2023, aiming to assess the geographic and temporal expansion of dengue in the state during this period. For spatial description, annual maps of incidence rates by municipality were constructed; spatial autocorrelation was assessed using the Global Moran Index and Local Indicators of Spatial Association (LISA), and spatiotemporal cluster identification was performed using the discrete Poisson model and Generalized Additive Models. The analyses were performed using SatCan and R software. It was observed that during the analyzed period, Rio Grande do Sul reported 126,067 dengue cases, resulting in 142 deaths, with 80.5% of the total cases reported in the 2022-2023 biennium alone. The highest incidence and mortality rates were observed in the Northwest mesoregion, followed by the Central-Eastern mesoregion, with a sharp increase in the risk of dengue fever from 2019 onwards and a pronounced intensification from 2022 onwards – indicating an ongoing epidemic. The second article aimed to identify environmental and socioeconomic factors associated with the incidence of dengue in the state from 2013 to December 2023. To this end, the influence of the urbanization index and rural density - during the years 2010 and 2022 - and environmental quality (through the Socio-Environmental Performance Index) on the average incidence rate of dengue in the different mesoregions of the state were evaluated through geographically weighted regression (GWR) analysis using the R software. It was observed that during the analyzed period, 127,945 cases of dengue were reported in the state, with 82.74% of these reported between 2022 and 2023. The variables evaluated act heterogeneously on the expansion of the disease in the different mesoregions of the state, with emphasis on the rural density variable, which in 2022 demonstrated an expansion of influence to the Southwest mesoregion and consolidation. in the Northeast and Metropolitan mesoregions. The results observed in this thesis demonstrate the alarming epidemiological situation of dengue in Rio Grande do Sul, with expansion throughout its mesoregions and with various socio-environmental factors influencing the incidence of the disease and its spread. It is hoped, therefore, that these results can guide the adoption of effective control and prevention measures targeted at at-risk populations.

Keywords: arboviruses; dengue; epidemic; epidemiological surveillance; geographic expansion.

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Sumário

1 Introdução

As arboviroses são causadas por vírus que se mantêm em ciclos de transmissão entre hospedeiros vertebrados e artrópodes hematófagos, como mosquitos, flebotomíneos, moscas e carrapatos (MAYER et al., 2017.) Dentre essas, a dengue é transmitida por mosquitos do gênero *Aedes*, altamente prevalente em regiões tropicais e subtropicais e estima-se que exponha ao risco de infecção mais de quatro bilhões de indivíduos globalmente (SIRISENA et al., 2021; PARVENN et al., 2023). A doença se configura como uma das dez principais ameaças à saúde pública mundial, com incidência anual estimada entre 100 e 400 milhões de novas infecções (LEE et al., 2021; KULARATNE; DALUGAMA, 2022). A dinâmica de transmissão da dengue está fundamentada na interação estável entre o vírus, o vetor, o ser humano e o espaço geográfico (MARTINS et al., 2020).

Dados epidemiológicos demonstram que aproximadamente dois quintos da população mundial residem em áreas de risco para a infecção por dengue, com uma estimativa de 390 milhões de infecções anuais, das quais cerca de 500 mil resultam em hospitalizações e 20 mil em óbitos, principalmente em países como Brasil, Vietnã e Filipinas (KULARATNE; DALUGAMA, 2022; PARVEEN et al., 2023; KHAN et al., 2023). Em regiões tropicais e subtropicais, observa-se um cenário de hiperendemicidade intercalado por epidemias, predominantemente em áreas urbanas e semiurbanas, resultando na sobrecarga de sistemas de saúde frequentemente já fragilizados (KULARATNE; DALUGAMA, 2022; PARVEEN et al., 2023).

O vírus da dengue pertence ao gênero *Orthoflavivirus*, da família *Flaviviridae*, a qual abrange mais de 70 agentes patogênicos conhecidos. A transmissão ocorre, majoritariamente, por meio da picada de mosquitos *Aedes aegypti* – principal vetor no Brasil – e, em menor frequência, por *Aedes albopictus* (LEE et al., 2021; KHAN et al., 2023; SEIXAS et al., 2024). Esses vetores apresentam hábitos diurnos, desenvolvem-se em criadouros contendo água estagnada e têm predileção por áreas urbanas densamente povoadas, possuindo o *A. aegypti* tendência a repousar em ambientes intradomiciliares (KHAN et al., 2023; WITTE et al., 2024).

O vírus apresenta genoma constituído por RNA de fita simples, com polaridade positiva e aproximadamente 11 kb de comprimento, e estrutura icosaédrica, envolta por um envelope lipídico com proteínas estruturais (KHAN et al., 2023). Esse vírus é composto por três proteínas estruturais e sete não estruturais e, com base em variações nessas proteínas, são reconhecidos quatro sorotipos principais: DENV-1, DENV-2, DENV-3 e DENV-4, os quais compartilham cerca de 65% de identidade genômica (SIRISENA et al., 2021; KULARATNE; DALUGAMA, 2022). Em 2013, foi descrito um quinto sorotipo, o DENV-5 - isolado de um paciente hospitalizado na Malásia em 2007 - que apresenta ciclo silvestre e infecta predominantemente primatas não humanos (SIRISENA et al., 2021).

A circulação simultânea de múltiplos sorotipos em uma mesma região endêmica favorece a ocorrência de infecções concomitantes, as quais podem ser decorrentes de uma única picada de mosquito coinfectado ou múltiplas picadas por diferentes vetores infectados com sorotipos distintos. Tais infecções concomitantes podem atingir prevalência de até 50% em áreas hiperendêmicas (SIRISENA et al., 2021). A imunidade adquirida após infecção por um sorotipo é específica e duradoura (imunidade homóloga), enquanto a imunidade contra outro sorotipo (imunidade heteróloga) confere proteção transitória, podendo estar implicada no agravamento da infecção subsequente (WONG et al., 2022; SEIXAS et al., 2024).

Após a exposição ao vírus por meio da picada do vetor, o período de incubação varia entre três a sete dias, podendo os sintomas se estender por até quatorze dias (PAJOR et al., 2024). A gravidade da doença está associada aos sorotipos circulantes, à carga viral e à ocorrência de reinfecções por sorotipos distintos (SIRISENA et al., 2021). A infecção primária tende a ser assintomática em até 80% dos casos ou se manifestar como um quadro febril autolimitado (KHAN et al., 2023). A doença apresenta, caracteristicamente, um curso trifásico (fase febril, fase crítica e fase de recuperação), embora também sejam possíveis cursos monofásicos, principalmente em áreas não endêmicas (WITTE et al., 2024).

Em casos de reinfecção, anticorpos heterólogos em níveis subneutralizantes podem facilitar a entrada do vírus em células fagocíticas, como macrófagos e células dendríticas, por meio do fenômeno de amplificação dependente de anticorpos (ADE), agravando o quadro clínico (PARVEEN et al., 2023; WITTE et al., 2024). A taxa de letalidade da forma grave da doença varia entre 2% e 5% com tratamento adequado, podendo atingir 20% nos casos não tratados, sendo estimados 17.000 óbitos em um período de 25 anos no Brasil (KHAN et al., 2023; GURGEL-GONÇALVES et al., 2024). De acordo com a classificação da Organização Mundial da Saúde, os casos são categorizados em dengue não grave - sem sinais de alarme e com sinais de alarme - e dengue grave - incluindo choque, comprometimento de órgãos e, ocasionalmente, hemorragias -, sendo esta última frequentemente associada aos sorotipos DENV-2 e DENV-3 (KULARATNE; DALUGAMA, 2022; WONG et al., 2022; SEIXAS et al., 2024).

Fatores não diretamente relacionados à doença, como gravidez, idade inferior a 12 anos ou superior a 70 anos, e comorbidades, como doenças hemolíticas ou insuficiência renal crônica, também configuram risco aumentado para formas graves ou óbito (WITTE et al., 2024). Sinais clínicos como dengue prévia, trombocitopenia com hemoconcentração e vômitos recorrentes constituem marcadores importantes de mau prognóstico (WITTE et al., 2024). Diante disso, a identificação precoce de fatores preditivos é fundamental para a redução da mortalidade e otimização dos recursos hospitalares (YUAN et al., 2022).

O diagnóstico laboratorial da dengue pode ser realizado por métodos diretos, como a detecção do RNA viral via RT-PCR ou da proteína NS1 por ELISA, preferencialmente durante a fase febril. Métodos indiretos, como a sorologia para IgM e IgG, são indicados a partir do quinto dia de sintomas e permitem a distinção entre infecção primária e secundária, sendo que títulos elevados de anticorpos anti-hemaglutinina são sugestivos de infecção secundária (KULARATNE; DALUGAMA, 2022).

Não há evidência de transmissão direta entre os mosquitos, contudo, indivíduos assintomáticos podem atuar como reservatórios virais, infectando vetores inicialmente não infectados (SIRISENA et al., 2021). A transmissão do vírus de humano para mosquito depende da magnitude da viremia humana necessária para infectar os mosquitos e de sua competência vetorial (MAYER et al., 2017). A variabilidade genética tanto do vírus quanto do hospedeiro, incluindo fatores imunológicos e predisposição genética, influencia diretamente na virulência viral e nas manifestações clínicas (POURZANGIABADI et al., 2025).

Quanto aos ciclos de transmissão, três ciclos distintos são reconhecidos: (1) silvestre/enzoótico, envolvendo mosquitos e primatas em florestas tropicais; (2) rural/endêmico, com transmissão localizada e imunidade de rebanho; e (3) urbano/epidêmico, caracterizado por surtos periódicos com múltiplos sorotipos, em ambientes densamente povoados (KULARATNE; DALUGAMA, 2022).

A adaptação do *Aedes aegypti* ao ambiente domiciliar urbano e a presença simultânea dos quatro sorotipos virais explicam, em parte, o aumento da incidência da dengue nas últimas décadas, potencializado por mudanças ambientais, ecológicas e climáticas – acompanhadas por padrões de precipitação alterados, inundações e maior probabilidade de eventos climáticos extremos (WHITEHORN; YACOUB, 2019; SEIXAS et al., 2024; POURZANGIABADI et al., 2025). As primeiras evidências de doenças semelhantes à dengue datam de 992 d.C., na Enciclopédia Médica Chinesa, e de 1699 nas Américas, sendo seu caráter epidêmico amplamente reconhecido após a Segunda Guerra Mundial devido à urbanização, uma vez que as áreas urbanas apresentam condições ambientais e socioeconômicas heterogêneas e complexas, diferindo das áreas rurais (KHAN et al., 2023; BOHM et al., 2024). Em um período de 50 anos, a incidência de dengue aumentou 30 vezes, com ampliação da expansão geográfica para novos países, pequenas cidades e áreas rurais (SILVA et al., 2020).

Na década de 1950 o Brasil chegou a eliminar o *Aedes aegypti*, porém a persistência da infestação em países vizinhos e o relaxamento na vigilância brasileira acabaram permitindo a recolonização pelo vetor (LUZA et al., 2021). Assim, desde a primeira epidemia registrada no Brasil, em 1986, o país tornou-se considerado hiperendêmico, com sucessivos períodos de epidemias e crescente impacto social e econômico, apresentando o maior custo associado à dengue nas Américas (MARTINS et al., 2020; LEE et al., 2021; GURGEL-GONÇALVES et al., 2024). A notificação da doença tornou-se obrigatória em 1961 (Decreto Nº 49.974-A) e passou a ser registrada eletronicamente no Sistema de Informação de Agravos de Notificação (SINAN) a partir de 1993 (GURGEL-CONÇALVES et al., 2024).

As epidemias de dengue têm apresentado um padrão cíclico, com períodos epidêmicos intensos intercalados com períodos interepidêmicos de três a quatro anos, que apresentaram diminuição em sua duração nos últimos anos (ANDRIOLI et al., 2020). Tais picos sazonais podem sobrecarregar os sistemas de saúde e impactar negativamente o manejo e os desfechos de outras doenças durante períodos cruciais (SIQUEIRA JUNIOR et al., 2022).

Para que uma doença surja em uma população vários fatores são necessários, incluindo a introdução do patógeno e sua disseminação na população humana, seguida por sua capacidade de se manter na natureza (MAYER et al., 2017). O aumento da prevalência de dengue é atribuído, além da urbanização acelerada, à mobilidade populacional, mudanças climáticas, vulnerabilidade social, falta de investimentos em saúde pública, e à expansão dos vetores para novas áreas geográficas, incluindo zonas periurbanas e rurais e regiões com clima temperado (LEE et al., 2021; WONG et al., 2022; ROBERT et al., 2023 BOHM et al., 2024).

Uma vez que é sabido que os níveis de temperatura e precipitação influenciam os padrões sazonais de transmissão da dengue, a literatura demonstra que além de umidade extrema, a escassez de água em áreas altamente urbanizadas, observadas durante períodos de seca extrema, também exacerbam o risco de transmissão da doença (LOWE et al., 2021). Assim, a previsão é de que essas tendências se intensifiquem, ampliando a população em risco de infecção, inclusive em zonas climáticas antes não favoráveis à presença dos vetores (WITTE et al., 2024).

Nesse contexto, ainda que anteriormente fossem identificadas barreiras geográficas à transmissão da dengue no Brasil e considerado que certas áreas, como o Sul do Brasil, estavam relativamente protegidas de surtos, atualmente são poucas as áreas brasileiras que permanecem protegidas (LEE et al., 2021). No Rio Grande do Sul, o mosquito *Aedes aegypti* foi identificado pela primeira vez em 1995, no município de Caxias do Sul e o primeiro caso autóctone foi registrado 12 anos após, em 2007, no município de Giruá (CES, 2010; TUMIOTO et al., 2014).Desde o registro do primeiro caso autóctone no estado, a doença se espalhou rapidamente, expandindo-se de 58 municípios em 2008 para 391 municípios em 2020, e sendo notificada em 453 dos 497 municípios em 2022, tornando-se um significativo problema de saúde pública (RIO GRANDE DO SUL, 2020; AL et al., 2021).

Além dos fatores socioambientais que favorecem a expansão da doença, o controle do vetor é dificultado pela localização intradomiciliar dos criadouros, sobrevivência dos ovos do mosquito por até 120 dias em condições de seca e sombra, resistência a inseticidas e baixa adesão comunitária às ações de controle, o que reforça a necessidade de políticas públicas integradas de vigilância, mobilização social e educação em saúde (TRPIS, 1972; GURGEL-GONÇALVES et al., 2024).

Condições de vida locais, como a densidade populacional, mobilidade humana e saneamento básico são fatores importantes de risco coletivo para a dengue, uma vez que abastecimento de água e serviços de coleta de lixo inadequados são promotores para criadouros de mosquitos (LOWE et al., 2021). A estratificação de risco com base em dados epidemiológicos e ambientais, a vigilância antecipada e a previsão sazonal de casos são fundamentais para uma resposta oportuna e eficaz (GURGEL-GONÇALVES et al., 2021; POURZANGIABADI et al., 2025).

Embora a dengue apresente alta prevalência no Brasil, sua real magnitude e taxas de hospitalizações podem estar subestimadas devido a limitações dos sistemas de vigilância, elevada taxa de infecções assintomáticas, autogestão de sintomas e diagnósticos subnotificados ou incorretos (KULARATNE; DALUGAMA, 2022; SIQUEIRA JUNIOR et al., 2022). O enfrentamento efetivo da dengue requer sistemas abrangentes de vigilância em áreas identificadas como de risco, planejamento territorial, estratégias de controle baseadas em evidências, e compreensão profunda dos fatores que impulsionam sua expansão, de modo a antecipar surtos e mitigar seus impactos nas regiões mais vulneráveis (WHITEHORN; YACOUB, 2019; LEE et al., 2021). O reconhecimento dos fatores associados possibilita o conhecimento de áreas e períodos com maior risco, a fim de produzir alertar para as vigilâncias epidemiológica e ambiental, tanto para o controle do vetor quanto na organização da assistência necessária ao atendimento dos casos (SILVA et al., 2020).

2 Objetivo

2.1 Objetivo Geral

Realizar a análise epidemiológica de dados gerados na rotina de vigilância e controle de dengue no Rio Grande do Sul – Brasil, a partir dos dados sobre a distribuição da doença no estado e de seus determinantes disponibilizados nos sistemas de informação nacionais e estaduais.

2.2 Objetivos Específicos

- Analisar a expansão temporal e geográfica de dengue no período de 2007 a 2023 no Rio Grande do Sul;
- Identificar fatores socioambientais associados à incidência e distribuição geográfica de dengue no Rio Grande do Sul;
- Fornecer informações para auxiliar nas estratégias de prevenção primária mais eficazes e mitigar o impacto da dengue na saúde pública do Rio Grande do Sul.

3 Artigos

3.1 Artigo 1

Emergence and spatiotemporal incidence of dengue in Rio Grande do Sul, Brazil

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Emergence and Spatiotemporal incidence of Dengue in Rio Grande do Sul, Brazil

Abstract

This ecological study used surveillance data to examine the spatiotemporal dynamics of dengue in RS from 2007 to 2023. The temporal progression and geographic distribution of the cases were analyzed using generalized additive models (GAM), Local Indicators of Spatial Association (LISA), and spatiotemporal scan statistics. During the study period, 126,067 dengue cases and 142 deaths were reported, with 80.5% of cases and 85.2% of deaths occurring between 2022 and 2023. The mean incidence rate was 65.3 per 100,000 inhabitants, and the mortality rate was 0.11 per 100,000. The GAM analysis demonstrated a marked escalation in dengue risk beginning in 2019, with pronounced intensification from 2022 onward, indicating an ongoing epidemic. Most cases and fatalities were concentrated in the Northwest Rio Grande and Metropolitan Porto Alegre mesoregions. Significant spatial clusters were detected in the Central Eastern and Central Western mesoregions between 2021 and 2023, encompassing approximately 2.8 million individuals. These findings underscore the critical need to enhance surveillance and implement robust primary-prevention measures. Such measures are vital for curbing the current epidemic and mitigating the risk of future outbreaks. This study provides a detailed epidemiological assessment of dengue expansion in RS, highlighting priority areas for intervention and resource distribution to effectively manage evolving public health threats.

Keywords: Dengue, Spatiotemporal Analysis, Generalized Additive Models, Rio Grande do Sul, Public Health, Climate Change

Introduction

The global geographic range of dengue has expanded significantly in recent decades, posing an emerging threat to public health worldwide. [1–3] In this context, despite Brazil's long-standing battle with dengue, until recently, the southern regions of the country were largely unaffected by their subtropical and temperate climates, which were historically unfavorable to the vector's survival and reproduction.

However, in recent years, climate change and the adaptation of *Aedes aegypti* to new urban environments have facilitated the spread of dengue into previously unaffected regions, including southern Brazil.[4,5] Shifting environmental conditions, such as increased temperatures and altered precipitation patterns, have allowed mosquitoes to establish themselves in areas previously too cold for their survival. Combined with human-driven factors, these environmental changes have contributed to the establishment of dengue transmission in regions that were historically unsuitable for the vector.[6,7] Consequently, southern states, such as Rio Grande do Sul, are now experiencing dengue outbreaks, a phenomenon that would have been considered improbable a few decades ago.

In Rio Grande do Sul, *Aedes aegypti* was first identified in Caxias do Sul in 1995 and the first autochthonous dengue case was recorded in April 2007 in the municipality of Giruá, located in the northwestern region.[8,9] Since then, the disease has spread rapidly across the state, expanding from 58 municipalities in 2008 to 391 municipalities by 2020, reaching 453 out of 497 municipalities by 2022.[10,11] The rapid increase in the number of affected areas underscores the growing vulnerability of the state to dengue outbreaks, largely driven by the adaptation of the mosquito to a colder climate and the expansion of favorable environmental conditions for its proliferation.

The ongoing expansion of dengue in Rio Grande do Sul has raised significant public health concerns, with over 65,000 cases reported by October 2022.[12] Understanding the spatiotemporal dynamics of dengue transmission within this diverse region is critical for the development of targeted prevention strategies. Therefore, this study aimed to analyze the temporal and geographic expansion of dengue from 2007 to 2023. By providing insights into these patterns, this study seeks to inform more effective primary prevention strategies and mitigate the public health impact of dengue in Rio Grande do Sul, particularly in the context of ongoing climate change and increasing vector adaptation.

Methods

Study design

This ecological study used data collected during routine dengue surveillance in Rio Grande do Sul, Brazil between 2007 and 2023. The dynamics of this disease in the state were analyzed using temporal, spatial, and spatiotemporal statistical analyses.

Study location

Rio Grande do Sul is located at latitude 27˚03042@ and 33˚45009@ South and longitude 49˚42041@ and 57˚40057@ West and is the southernmost state in Brazil (Figure 1), bordering Argentina and Uruguay. The state covers an area of 281,707.151 km², and is divided into 497 municipalities. In 2021, the population was 11,466,630, representing a density of 39.79 inhabitants/km2, of which 85.1% lived in urban areas, and the HDI was 0.746.[13] In 2015, 93.7% of the population was served directly or indirectly through garbage collection, and 40% was served through a sewage collection network.[13] The climate of Rio Grande do Sul is subtropical temperate, classified as humid mesothermal (Köppen classification). Because of its geographical position, it presents significant differences from the rest of Brazil. Temperatures show great seasonal variation, with hot summers and rigorous winters, including frost and occasional snowfall. Average temperatures range between 15°C and 18°C, with minimum temperatures dropping to -10°C and maximum temperatures reaching 40°C.[14]

There are three major economic regions in Rio Grande do Sul: (1) the southern region, with a large concentration of land, large livestock farms, and mechanized planting of rice, soybeans, and wheat. This area also has a greater income inequality. (2) The northeastern region, which includes the state capital, has more industries and smaller properties. (3) The northern region, which European immigrants mostly colonize, has forest cover, valleys, and plains with small agricultural lands (Figure 1).[15] In addition, the state is divided into seven mesoregions: Metropolitana de Porto Alegre, Centro Oeste Rio Grandense, Centro Oriental Rio Grandense, Nordeste Rio Grandense, Noroeste Rio Grandense, Sudeste Rio Grandense, and Sudoeste Rio Grandense (Figure 1).

Data collection

Since 1996, the reporting of dengue cases has been mandatory in Brazil through the Notifiable Diseases Information System (SINAN), coordinated by the Ministry of Health using a passive surveillance system[16]. In 2007, the system was updated and fully implemented nationwide. That same year, the state of Rio Grande do Sul reported its first autochthonous dengue case[9]. Data on the number of confirmed cases, deaths, and municipalities with dengue occurrences in Rio Grande do Sul between 2007 and September 2023 were obtained from SINAN, provided by the Brazilian Ministry of Health[17-18]. Cases included in this study were confirmed based on clinical-epidemiological or laboratory criteria, as outlined in the Ministry of Health's Epidemiological Surveillance Guide[19].

Laboratory confirmation of dengue involves the detection of viral RNA using molecular techniques such as reverse transcription-polymerase chain reaction (RT-PCR), the identification of the NS1 antigen through immunochromatographic testing or enzyme-linked immunosorbent assay (ELISA), or serological testing to detect specific IgM antibodies. Serological testing is recommended from the sixth day after symptom onset to minimize the risk of false-negative results. Additionally, cases can be confirmed using clinical-epidemiological criteria, which require identifying a suspected case in an individual residing in or having traveled to an area with confirmed dengue transmission and presenting symptoms consistent with the disease[19]. Once confirmed, whether by laboratory or clinical-epidemiological criteria, cases are recorded in SINAN, ensuring comprehensive monitoring and surveillance of dengue cases across the country.

Statistical analysis

Using data collected over a 17-year observation period, the incidence and mortality rates (per 100,000 inhabitants) and lethality (%) were calculated based on population projections from the Brazilian Institute of Geography and Statistics (IBGE). The 17-year period was chosen to encompass long-term trends and minimize the influence of short-term fluctuations. Data were analyzed on an annual basis to preserve the temporal resolution necessary for capturing year-to-year variations and trends, which are critical for understanding the dynamics of dengue transmission and the impact of interannual factors. Trends in incidence rates were analyzed using generalized additive models (GAM). Furthermore, the incidence rates were mapped to confirm the existence of spatial and spatiotemporal clusters, thereby identifying priority municipalities for dengue surveillance and control in the state.[20,21]

Spatial descriptive analyses

For spatial description, we constructed annual maps of incidence rates (cases per 100,000 inhabitants) by municipality. In all descriptive maps created in the present study, the Jenks natural break classification method was used to determine the class intervals used for visual representation.[22]

Spatial autocorrelation

For each 3-year period, a spatial pattern analysis of dengue cases was performed using Moran's Global Index and Local Indicators of Spatial Association (LISA) to analyze the association and clustering in the areas.[23] The triennial interval was chosen to reduce the influence of short-term variability, ensuring sufficient data aggregation to detect stable spatial patterns and trends. To perform Moran's Global and LISA, we created a first-order neighborhood matrix (Queen) that considers neighbors as shared border areas or vertices.

The Global Moran's Index was calculated to analyze the spatial autocorrelation for the entire dataset (the entire study region), which provides a single measure for the set of all municipalities characterizing the entire study region. LISA was used to analyze the spatial distribution pattern and intensity of clusters at the municipality level, with a significance level of $p < 0.05$. The LISA index must meet the following criteria: (i) have, for each municipality, an indication of significant spatial clusters of similar values around the municipality and (ii) the sum of the LISAs for all municipalities should be proportional to the Global Moran's I.[23]

The results of the LISA test can be interpreted as follows: positive values (between 0 and +1) indicate positive autocorrelation, suggesting that the values in municipalities tend to be similar to the values of neighboring areas (High-High or Low-Low). Negative values (between 0 and -1) suggest an inversely proportional correlation, meaning that if a particular municipality shows values above average, the surrounding municipalities tend to be below average (High-Low and Low-High). The results found for the LISA are presented in the form of thematic maps, where: (i) high–high correlations identify municipalities with high dengue incidence surrounded by other municipalities with high dengue incidence; (ii) low–low correlations identify municipalities with low dengue incidence surrounded by municipalities with low dengue incidence; (iii) high–low correlations represent municipalities with high dengue incidence surrounded by municipalities with low dengue incidence; and (iv) low–high correlations identify municipalities with low dengue incidence surrounded by municipalities with high dengue incidence. The municipalities identified as high-high in the results of LISA were considered high-priority areas.[24]

In this study, Global Moran and LISA were created using GeoDa software, version 1.22.

Spatiotemporal analysis

A space-time scan cluster analysis was performed to identify high- and low-risk spatiotemporal clusters of dengue occurrence in Rio Grande do Sul.[25] This technique is used to identify clusters of events in time and space, thus allowing recording of the number of expected and estimated cases at each location.[21] Spatiotemporal clusters for the dengue incidence were created using the following information: population, number of cases, expected cases, annual cases, observed/expected cases, and location. To perform the tests, information regarding each municipality was inserted into the software: 1) number of cases, 2) year of infection, 3) population average of the 3 years that make up the 3-year period studied, and 4) geocode of each municipality. This information was entered for the entire period (2007-september/2023).

The discrete Poisson model was used to identify spatiotemporal clusters and to perform the scan statistic, with the following settings: 2007-2023 study period, no geographic overlap of clusters, clusters of maximum size equal to 50% of the exposed population, circular sets, 999 repetitions, and time accuracy standardized at 1.[26,27] This model considers the space and time in which cases occur.[26–28] The significance test of the identified clusters was based on a comparison of the null distribution obtained by Monte Carlo simulation. To compare different areas, the program presents the relative risk (RR) and likelihood ratio of each cluster, which represents the relationship between the risk of occurrence of the injury within the cluster and that outside it.[26] The analyses were carried out using SatCan software version 10.2.1..

Generalized additive models

Generalized Additive Models (GAM) represent an extension of the generalized linear model and are alternatives for modeling nonlinear relationships that do not have a defined shape.[29] They are based on non-parametric functions called smoothing curves, in which the data defines the association shape.[29,30]

The general formula for the GAM with Poisson likelihood is as follows:

$$y_i \sim Poisson\ (\mathrm{Z}_i)$$
$$\log(\mathrm{Z}_i) = b_0 + \sum s_j\left(x_{ij}k\right),$$

where y_i is the observation *I* and i = 1,..., T (last observed time period), Z_i is the mean number of cases observed at the time i, b_0 is the intercept term, s_j is the spline function applied to the predictor x_{ij}, and k is the number of knots, a parameter that defines the number of windows into which the dataset will be broken, defined by the users.[31]

The response variable was the number of confirmed dengue cases in the year i with a Poisson distribution, with the population as the offset term and a spline function as the continuous time variable (Cota et al., 2021).[32] A Poisson distribution with a log link was used.[32–34] Smooth terms were used to select a GAM regression model. We considered the following smoothing terms to select the best model fit: (i) thin-plate regression splines, (ii) uchon splines, (iii) cubic regression splines, (iv) B-splines, and (v) P-splines.[34] The knot-based penalized cubic regression splines exhibited the best performance. The unbiased risk estimator (UBRE) was scaled according to Akaike's information criterion (AIC) (generalized case) (R, 2010). The UBRE and percentage of deviance explained were used to identify the appropriate smoothness and select the best model fit.[34] (S1 Table and S1 Figure).

Analyses were performed using the R packages mgcv and ggplot2.[36]

Results

Between 2007 and 2023, Rio Grande do Sul reported 126,067 dengue cases, resulting in 142 deaths. From 2007 to 2021, the average incidence and mortality rates were 14.92 cases and 0.02 deaths per 100,000 inhabitants. In 2022-2023, these rates surged to 443.35 cases and 0.81 deaths per 100,000 inhabitants. The fatality rate has increased from 0.09% (2017-2021) to 0.12% (2022-2023). In the biennium 2022-2023 alone, there were 101,481 cases (80.5% of the total) and 121 deaths (85.2% of the total). The mean incidence rate over this period was 65.30 cases per 100,000 inhabitants, and the mean mortality rate was 0.11 deaths per 100,000 inhabitants, with a case fatality rate of 0.11% (Table 1).

The majority of dengue cases in the target period occurred in Northwest Rio Grande do Sul (52,785 cases; 41.9%) and Metropolitan Porto Alegre (43,393 cases; 34.2%) mesoregions, accounting for 76.1% of all cases. The Northwest Rio Grande mesoregion also recorded more than half of all deaths (73 deaths; 51.4%), followed by Metropolitan Porto Alegre (34 deaths; 23.9%), totaling 75.3% of dengue-related fatalities. The highest incidence and mortality rates were observed in the Northwest Rio Grande mesoregion (95.1 cases and 0.19

deaths per 100,000 inhabitants), followed by the Central Eastern Rio Grande mesoregion (70.8 cases and 0.09 deaths per 100,000 inhabitants), which had the highest mortality rate (0.15%) (Table 1).

Generalized Additive Models (GAM) were used to analyze trends (Figure 2, S1 Table and S2 Figure), indicating a rapid increase in dengue risk across the seven mesoregions. In the Central Western and Southwest mesoregions, significant growth began in 2016, and in other mesoregions from 2019 onwards, suggesting an epidemic that rapidly spread throughout Rio Grande do Sul, particularly between 2022 and 2023.

The dengue incidence maps demonstrated substantial variability across the mesoregions of Rio Grande do Sul (Figure 3, S3 Table). The majority of municipalities exhibited a heterogeneous spatial distribution of incidence rates. Despite this variability, the maps, similar to the Generalized Additive Models (GAM), highlighted an explosive increase in dengue epidemics starting in 2019, particularly from 2022 to 2023. During this period, the disease spread to previously unaffected mesoregions and municipalities.

The median percentage of municipalities reporting dengue cases has increased significantly from 9.5% (2007-2018) to 17.9% in 2019 and 65.8% in 2023. Between 2007 and 2009, 404 municipalities reported no dengue cases. This number decreased slightly to 360 municipalities from 2010 to 2012 and to 354 municipalities from 2013 to 2019. However, from 2019 to 2021, the number of municipalities without cases dropped to 247 and plummeted to 81 between 2022 and 2023. During the 17 year study period, only 60 of 497 municipalities reported no dengue cases.

Among the mesoregions, the Northwest and Metropolitan regions of Porto Alegre exhibited the most significant increase in the number of municipalities with dengue cases, from eight to 72 and 141 municipalities, respectively. The Central-Western mesoregion experienced the most significant percentage growth in positive municipalities, increasing from a median of 1.6% (2007-2018) to 69.4% in 2023. This was followed by the central-eastern mesoregion, which increased from 6.5% to 69.4%, and the southwestern mesoregion, which increased from 5.3% to 57.9%.

During the first four analyzed triennia (2007-2009, 2010-2012, 2013-2015, 2016-2018), the Moran Global Index values, very close to 0 (0.0232, 0.012, 0.026, and 0.003, respectively), indicated a potential random distribution of dengue cases, although it can be a limited analysis due to the small number of occurrences. In contrast, significantly positive Moran Global Index values were observed in the triennia 2019-2021 (0.188) and 2022-2023 (0.354) triennia (Figure 4). LISA maps identified priority municipalities for dengue control (high-high clusters) in the Northwest (2007-2023), Central-Eastern Rio Grande (2019-2023), and Metropolitan Porto Alegre (2022-2023) mesoregions. Within these regions, a 600% increase in the number of priority municipalities was noted from the to 2016-2018 triennium (five municipalities) to the 2022-2023 biennium (30 municipalities). Additionally, the number of municipalities identified as low incidence clusters (low-low clusters) significantly increased in the 2019-2021 triennium (84 municipalities) and the 2022-2023 biennium (100 municipalities), compared to the total observed from 2007 to 2018 (three municipalities). This increase was particularly prominent in the Southwestern, Southeastern, Metropolitan Porto Alegre, and Northeastern mesoregions (Figure 4).

Similar to the LISA maps, SatScan models also indicated that the dengue epidemic in the state primarily spread to the Central-Western, Central-Eastern, Metropolitan Porto Alegre, and Northwestern mesoregions. Eight clusters with significant relative risks (RRs) were identified, including four high-risk (RR > 1) and four low-risk (RR < 1) dengue clusters (Table 2, Figure 4). The risk clusters were distributed between 2021 and 2023, encompassing 159 municipalities (32% of the total), which together account for approximately 2.8 million people (24.6% of the population), spread across four of the seven mesoregions of Rio Grande do Sul (Table 2, S3 Table).

High-risk areas were observed in the Metropolitan Porto Alegre mesoregion (Cluster 1; population = 1,056,485; RR = 53.9), Northwestern Rio Grande (Cluster 2; population = 1,006,233; RR = 21.9), Central-Eastern Rio Grande (Cluster 3; population = 439,963; RR = 22.6), and Central-Western Rio Grande (Cluster 4; population = 324,114; RR = 31.0) (Figure 3). The emergence of high-risk areas for dengue in Rio Grande do Sul began in 2021 in the central-western mesoregion, followed by the Metropolitan Porto Alegre and Northwestern mesoregions in 2022, and by the central-eastern mesoregion in 2023. Among these high-risk clusters, only one located in the Metropolitan Porto Alegre mesoregion ended in 2022, while the others remained in high-risk areas for dengue in Rio Grande do Sul by 2023 (Figure 5, Table 2).

Discussion

The recent expansion of dengue in Rio Grande do Sul highlights a concerning and growing risk for the population. Between 2007 and 2023, the state reported over 126,000 cases and 142 deaths, with a significant increase in incidence and mortality rates between 2022 and 2023. This rise was particularly pronounced in the Northwest and Metropolitan Porto Alegre mesoregions, which together accounted for the majority of cases and deaths. The period from 2022 to 2023 was particularly notable, representing 80.5% of the cases and 85.2% of the deaths, reflecting the rapid spread of the virus across the state. This expansion, coupled with the observed explosive increase in incidence, suggests an ongoing epidemic in the Rio Grande do Sul since 2019, particularly between 2022 and 2023. Furthermore, by quantifying the spatiotemporal distribution of the disease, we reinforced that Rio Grande do Sul is one of the main frontiers in the expansion of dengue in Brazil .[35]

Between 1986 and 2015, 11,084,755 suspected dengue cases were reported in Brazil, with 5,399 confirmed deaths. In 2015, an explosive epidemic resulted in 1,649,008 cases and 986 fatalities.[36] Between 1990 and 2017, an increasing trend in dengue cases was observed in all regions of the country, with the highest incidence rates per 100,000 inhabitants observed in the Midwest (448.0), followed by the southeast (272.7), northeast (246.7), north (198.6), and south (46.7).[37]

This high incidence of dengue in Brazil contrasts with the historically low incidence in Rio Grande do Sul, which until 2007 had not reported autochthonous case of the disease.

Nevertheless, we observed a geographical expansion of dengue cases in Rio Grande do Sul in recent years, especially in municipalities previously free of the disease. We believe that this expansion is related to the ongoing climate changes in the region,[6,35] favoring the reproduction and adaptation of *A. aegypti* in one of the states with the coldest winter in Brazil. [7,38]

It is also important to highlight that although dengue transmission still mainly occurs in tropical and subtropical climates worldwide over the last decade, the distribution of dengue has been expanding into temperate regions due to rapid unplanned urbanization, increased human movement, trade, and changes in land use and climate.[39–41] In this context, the recent catastrophic floods in September 2023 and May 2024 devastated parts of Rio Grande do Sul, potentially exacerbating the dengue epidemic. These extreme weather events have the potential to change mosquito infestation patterns, leading to increased incidence and mortality rates of vector-borne diseases such as dengue and leptopirosis.[42,43] The floods damaged infrastructure, creating stagnant water and compromising sanitation systems, ideal conditions for mosquito breeding. Consequently, the dengue crisis in Rio Grande do Sul is projected to worsen, underscoring the urgent need for comprehensive public health interventions.

Regarding deaths from dengue, lethality is low compared to other infectious diseases endemic in Brazil, such as visceral leishmaniasis and leptospirosis.[34,44] However, the mortality related to the disease is relatively high in the country, due to the high incidence of the disease, especially in epidemic years.[36,37] In this context, our study revealed a substantial rise in dengue cases and fatalities in Rio Grande do Sul, especially from 2019 onwards, with 80.5% of total cases and 85.2% of deaths occurring in 2022-2023. The fatality rate also increased from 0.09% between 2017 and 2021 to 0.12% between 2022 and 2023, which is much higher than that observed in Brazil as a whole; up to epidemiological week 20 of 2022, the lethality rate was 0.04%.[45] This highlights that dengue is a serious public health problem and a high-risk disease in the state's population.

Brazil's experience in dengue surveillance and control is widely recognized, but its implementation varies unevenly across the country. Even in Rio Grande do Sul, municipalities that historically have not reported cases are now experiencing sudden outbreaks of dengue. This unpredictability is particularly evident in the state, where increasing trends in dengue incidence rates have been observed across all mesoregions. The majority of dengue cases and deaths between 2007 and 2023 were concentrated in the Northwest Region and the Metropolitan Porto Alegre Area. However, the largest increase in the number of municipalities with reported cases occurred in the Centro-oriental and Centro-occidental mesoregions. These four mesoregions, home to approximately 2.8 million people, are now at high risk for the spread of the disease, further emphasizing the urgent need for effective control measures and preparedness.

Despite their economic prosperity, the metropolitan mesoregion faces significant public health challenges. High population density, extensive human movement, and inadequate infrastructure are critical factors contributing to the spread of vector-borne diseases such as dengue.[46,47] Additionally, the climatic characteristics of this low-altitude area, such as periodic flooding, contribute to mosquito vector proliferation.[42] Furthermore, the state has extensive border areas with Santa Catarina, Argentina, and Uruguay, facilitating the movement of people and the propagation of diseases.[35]

With the greatest border extension, the southwestern mesoregion showed a significant increase in dengue cases. The number of affected municipalities has increased from 5.3% in 2007 and 2018 to 57.9% in 2023. The northwestern mesoregion, which shares extensive borders with Santa Catarina and Argentina, faces a substantial risk of dengue expansion. The lack of integration between Brazil and Argentina's national surveillance systems exacerbates this situation, facilitating cross-border transmission.[35] To manage and mitigate dengue outbreaks, Brazil and Argentina should enhance their cooperation by establishing standard control programs and harmonizing epidemiological surveillance systems. Strengthening cross-border collaboration will be crucial in reducing the spread of dengue and protecting public health.

Analysis of LISA maps also revealed an increase in high-incidence dengue clusters in Northwest, Metropolitan of Porto Alegre, Centro-oriental and Centro-occidental mesoregions after 2019, particularly in 2022-2023. It is essential to note that LISA considers the spatial distribution of the disease rather than just the overall incidence rate.[22] Furthermore, the increase in cases observed in the last three years is responsible for the increase in the statistical power of the Moran Global Index, as it leads to an increase in the identification of municipalities with statistical differences (low-low and high-high clusters). Thus, many new municipalities have been considered priority areas in recent years. However, many new low-case clustering areas emerged in the state, even though the dengue incidence in the municipalities of the Southwestern, Southeastern, and Northeastern mesoregions also increased after 2019. This variability underscores the complexity of identifying priority areas and controlling dengue in Rio Grande do Sul.

Using secondary data from surveillance systems has inherent limitations.[48] Despite dengue being subject to immediate compulsory notification, it remains underreported. This underreporting is due to a lack of access to medical care, incorrect diagnoses, incomplete reporting, and difficulty in identifying the affected individuals.[49]

Despite potential notification biases, data from routine surveillance remain a valuable tool for planning control measures, as they help identify priority areas and guide the implementation of more effective strategies.[50,51,52]

This study analyzed the spatiotemporal dynamics of dengue in Rio Grande do Sul between 2007 and 2023, revealing significant expansion patterns throughout the state.

The findings of this study contribute to the growing body of evidence indicating the expansion of dengue in southern Brazil. Since 2019—and especially after 2022—there has been a notable rise in dengue incidence across all regions of the state, accompanied by an increasing number of affected municipalities. This trend points to an ongoing epidemic scenario that calls for strengthened and adaptive surveillance strategies.

Furthermore, recent extreme weather events—such as the catastrophic floods of 2023 and 2024—have exacerbated public health risks by promoting mosquito breeding and facilitating disease transmission. In this context, reinforcing surveillance and control actions becomes even more urgent.

Some limitations must be acknowledged. This analysis did not include a quantitative assessment of key determinants of dengue transmission—such as temperature variation, vector surveillance, socioeconomic disparities, and economic activities—due to constraints in accessing and integrating high-resolution, time-consistent datasets. Consequently, these factors remain theoretical assumptions rather than empirically tested components in the present study.

Future research should aim to explore these drivers more thoroughly, particularly those linked to environmental and social vulnerability, regional connectivity, population mobility, and climate change. Special attention should be given to mesoregions and border areas, where distinct transmission dynamics may occur. Incorporating these variables into spatial risk models can improve the identification of high-risk areas and guide more targeted and equitable public health strategies.

Conclusion

A significant increase in incidence and mortality rates of dengue in Rio Grande do Sul between 2022 and 2023 was observed. This rise was particularly pronounced in the Northwest and Metropolitan Porto Alegre mesoregions, which together accounted for the majority of cases and deaths, especially between 2022 and 2023, reflecting the rapid spread of the virus across the state.

Analytical models, such as GAM and risk analyses with SatScan, revealed a swift expansion of the epidemic, especially from 2019 onwards, with a remarkable growth of high-risk areas. In particular, the Central-Western, Central-Eastern, Northwest, and Metropolitan Porto Alegre mesoregions emerged as hotspots of high incidence. The risk cluster analyses also showed a significant shift in the spatial distribution of the disease, with the number of affected municipalities increasing substantially in recent years.

These findings underscore the urgent need for more effective control measures and enhanced preparedness to deal with the disease, given its rapid spread and increasing fatality. Surveillance strategies, mosquito control, and public education must be strengthened, particularly in high-risk areas, to mitigate the impact of the disease. Continuous monitoring and the use of advanced modeling technologies, such as GAM and SatScan, are essential for predicting and responding swiftly to new outbreaks, safeguarding public health in Rio Grande do Sul.

Author Contributions:

Sergiane Baes Pereira: Writing – review & editing. Bianca Conrad Bohm: Writing – review & editing, original draft, validation, software, methodology. Angelita dos Reis Gomes: Writing – review & editing, validation. Glênio Aguiar Gonçalves: Methodology, formal analysis, data curation. Nádia Campos Pereira Bruhn: Software, methodology, formal analysis, data curation. Vinicius Silva Belo: Writing – review & editing, methodology. Francisco Aguilera-Benavente: Writing – review & editing, methodology, formal analysis, data curation, conceptualization. Fabio Raphael Pascoti Bruhn: Writing – review & editing, original draft, supervision, methodology, formal analysis, data curation, conceptualization.

Ethical statement

This study employed aggregated, secondary data that is non-identifiable and publicly available. Therefore, ethical approval and informed consent were not required for this research.

Data availability statement

The dengue surveillance data used is publicly available on https://portalsinan.saude.gov.br/dados-epidemiologicos-sinan.

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Competing interests

The authors declare no competing interests.

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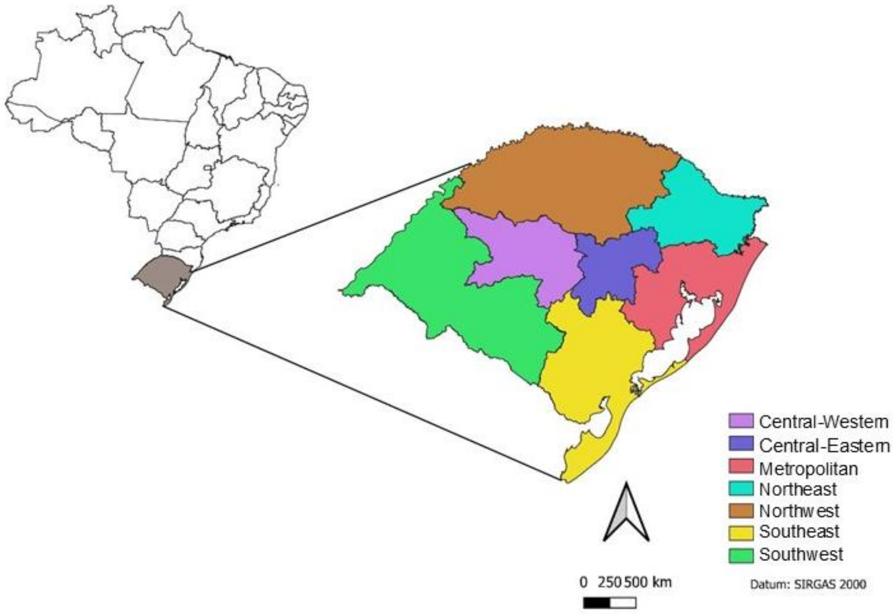


Figure 1. Division of the macro-regions of Rio Grande do Sul, Brazil, according to SIRGAS 2000, highlighting the regions Centro Ocidental, Centro Oriental, Metropolitan Porto Alegre, Northeast, Northwest, Southeast, and Southwest Rio-grandense.

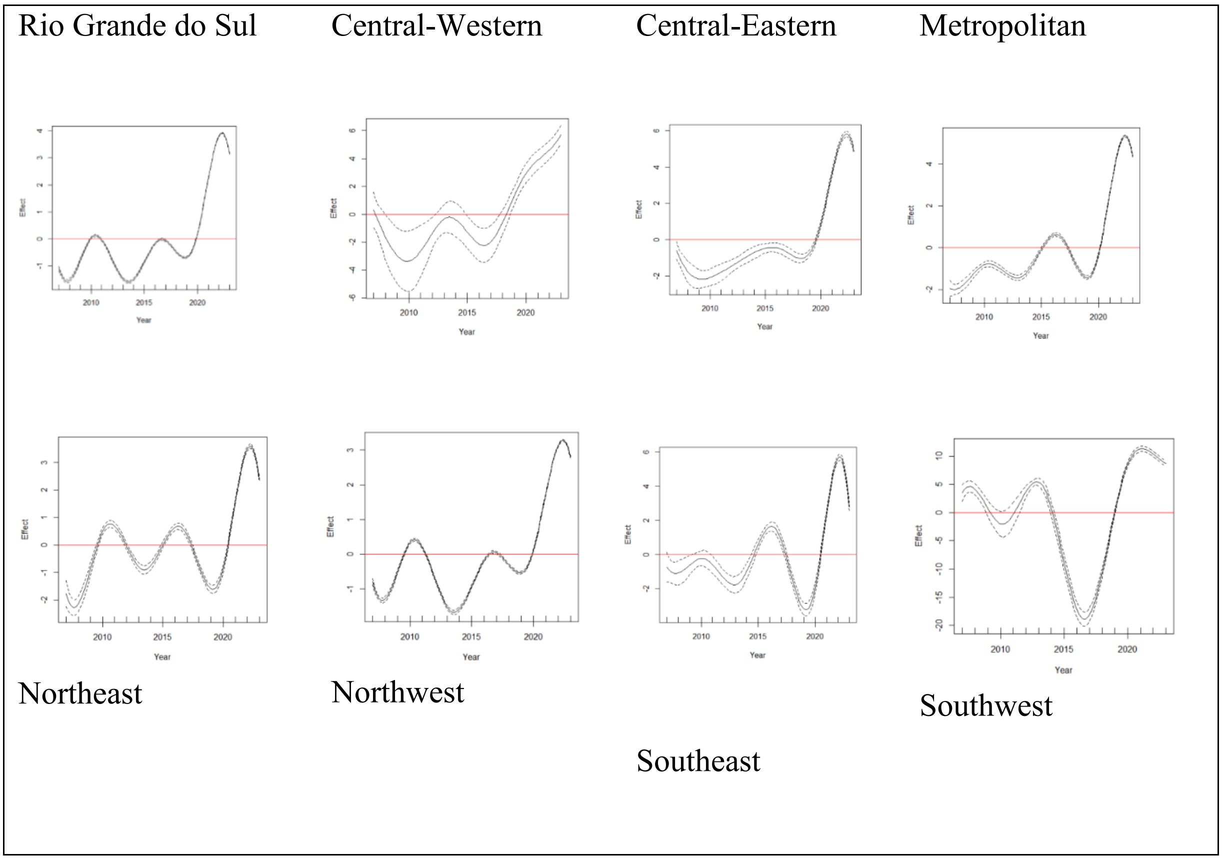


Figure 2. Figure X. Trend analysis of dengue incidence in Rio Grande do Sul (2007-2023) using Generalized Additive Models (GAM). The solid line represents the smoothed trend of dengue incidence, while the dotted lines indicate the 95% confidence intervals of the model, reflecting the uncertainty in the estimated trend over time.

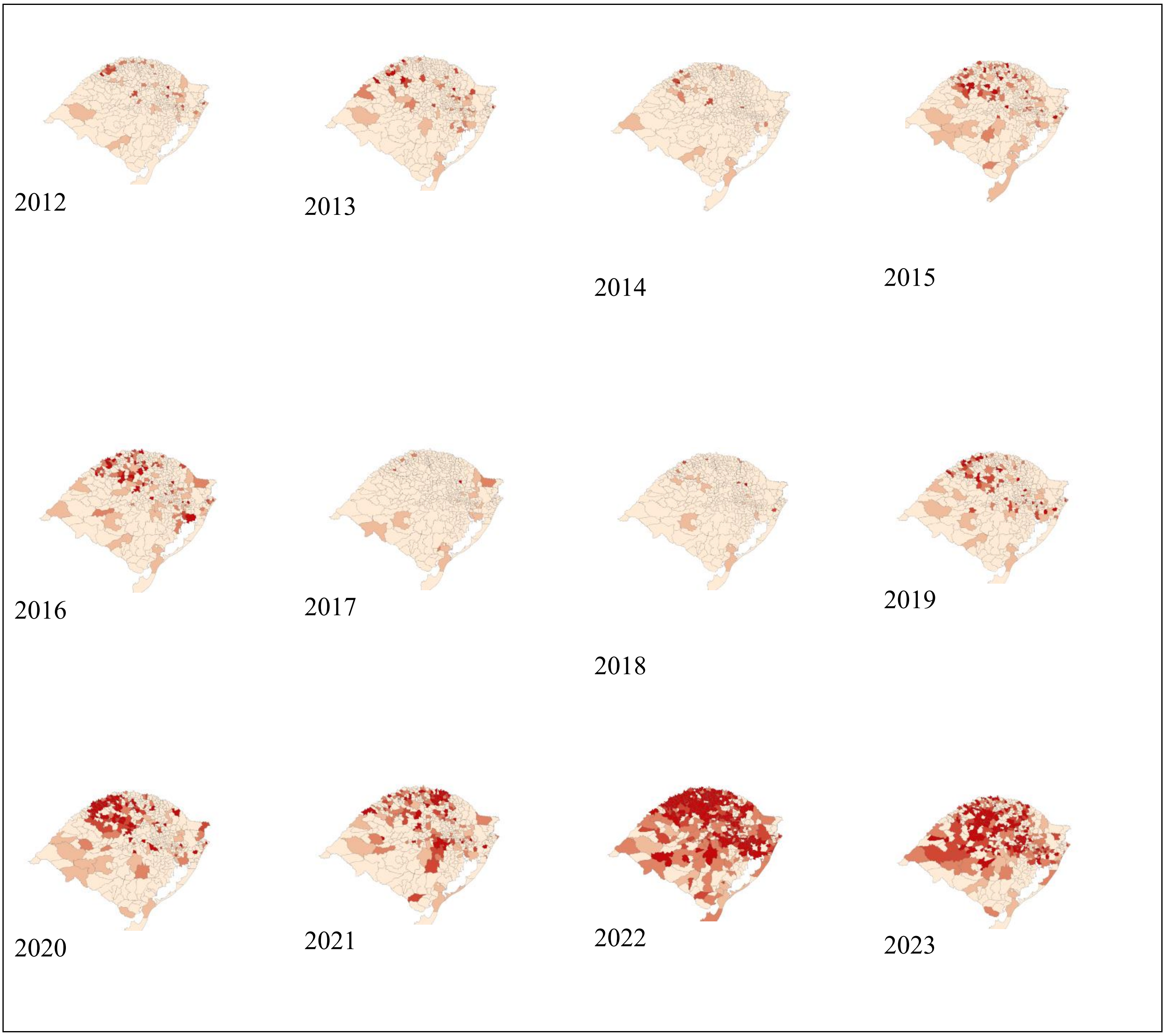


Figure 3. Spatial distribution of crude dengue incidence rate in Rio Grande do Sul municipalities, Brazil, from 2012 to September/2023 (incidence rate: cases/100,000 inhabitants).

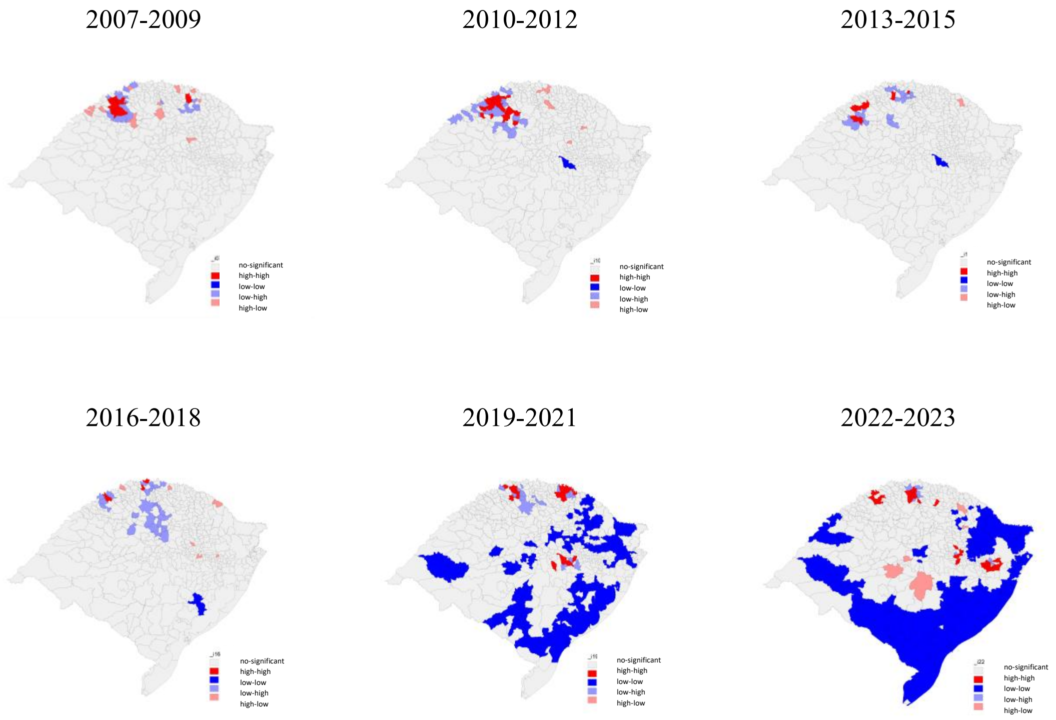


Figure 4. Spatial distribution of Moran's Local Index for dengue cases in Brazilian municipalities from 2007 to September 2023. The color scheme represents the degree of spatial autocorrelation between municipalities and their neighbors, indicating high and low dengue incidence clusters.

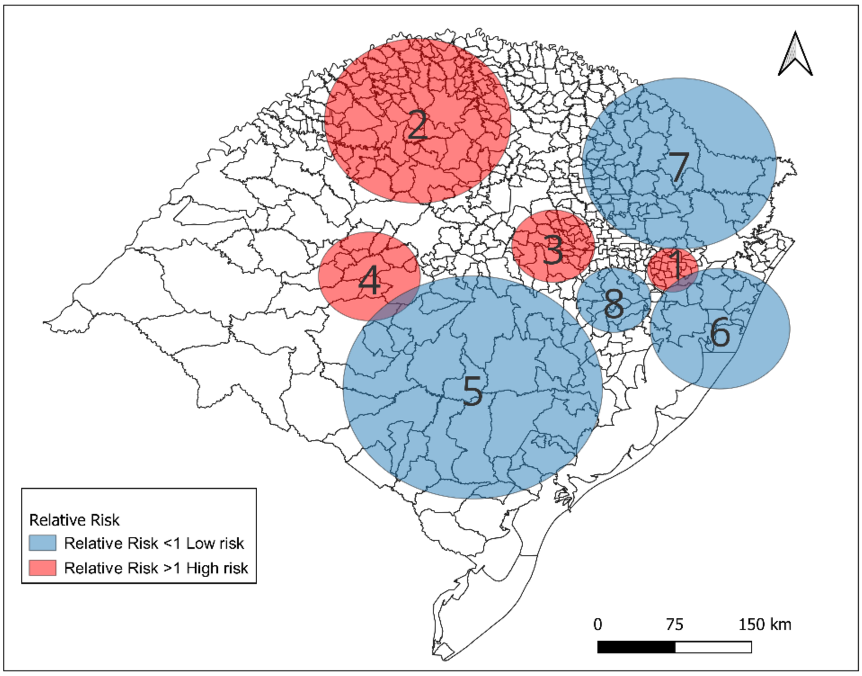


Figure 5. Spatial distribution of relative risk for dengue in municipalities of Rio Grande do Sul, Brazil, from 2007 to September 2023. Red-shaded areas represent regions with a relative risk > 1 (high risk), while blue-shaded areas indicate regions with a relative risk < 1 (low risk). Numbered circles highlight key clusters identified based on the relative risk of the disease. The geographical scale is shown at the bottom of the figure.

Mesoregion	Cases (% of total)	Deaths (% of total)	Mean incidence rate (x 100,000)	Mean mortality rate (x 100,000)	Lethality rate (%)
Central-Western	984 (0.8)	1 (0.7)	25.9	0.02	0.11
Central-Eastern	13420 (10.6)	20 (14.1)	70.8	0.09	0.15
Metropolitan	43393 (34.4)	34 (23.9)	54.6	0.05	0.08
Northeast	5247 (4.1)	4 (2.1)	19.5	0.04	0.08
Northwest	52785 (41.9)	73 (51.4)	95.1	0.19	0.14
Southeast	3072 (2.4)	4 (2.8)	17.2	0.01	0.13
Southwest	7166 (5.7)	6 (4.22)	25.4	0.09	0.08
Rio Grande do Sul	126067	142	65.3	0.11	0.11

Table 1. Epidemiological analysis of dengue cases, deaths, incidence, and mortality rates in Rio Grande do Sul and its mesoregions, Brazil (2007–September/2023)

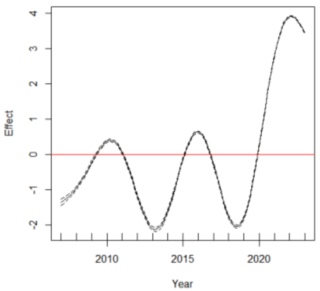
Cluster	Time Frame	Population	Number of cases	Expected cases	Annual cases/ 100000	Observed/ Expected	Relative risk (RR)
1	2022 – 2022	1056485	30123	729.25	2853.1	41.31	53.96
2	2022 – 2023	1006233	24804	1389.13	1233.3	17.86	21.98
3	2021 – 2023	439963	17819	911.07	1350.9	19.56	22.61
4	2023	324114	6591	223.72	2034.9	29.46	31.03

Table 2. Clusters of dengue incidence in Brazil by time frame, population, number of cases, expected cases, annual incidence per 100,000 inhabitants, observed/expected ratio, and relative risk (RR).

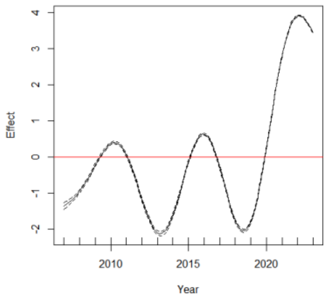
Figure S1. Goodness-of-fit graphics of possible Generalized Additive Models (GAM) with Poisson distribution in Rio Grande do Sul and mesoregions between 2007 and September 2023 using: (a) thin plate regression; (b) duchon splines; (c) cubic regression spline; (d) b-spline; and (e) p-splines smoothness terms

Rio Grande do Sul

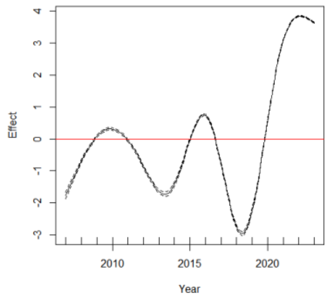
Thin plate regression splines



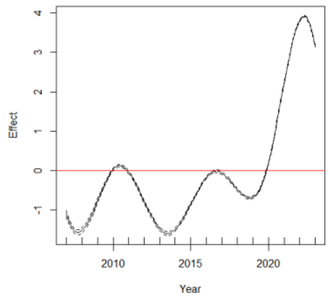
Duchon splines



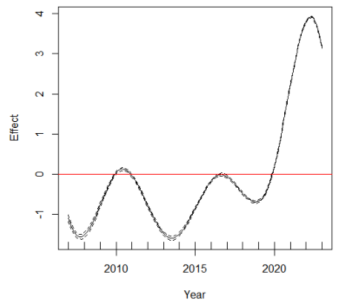
Cubic regression splines



B-splines

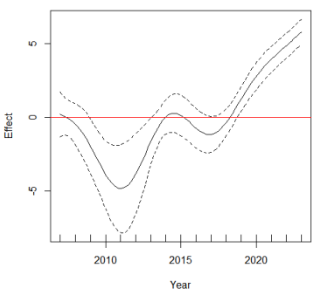


P-splines

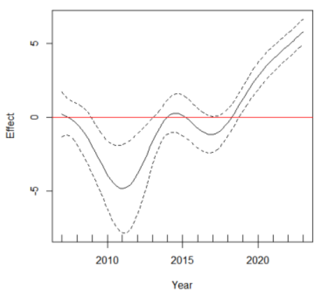


Rio Grande do Sul – Central-Western

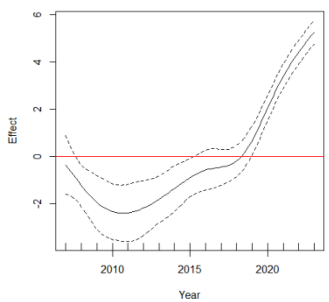
Thin plate regression splines



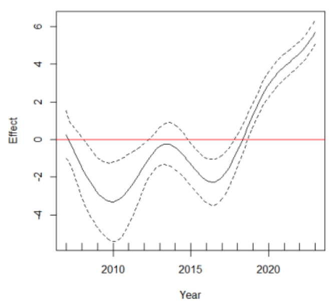
Duchon splines



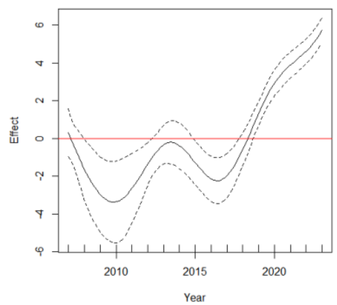
Cubic regression splines



B-splines

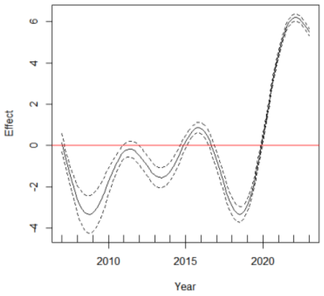


P-splines

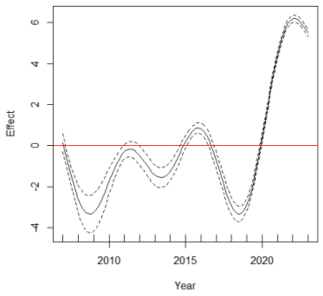


Rio Grande do Sul – Central-Eastern

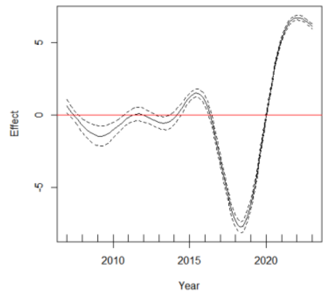
Thin plate regression splines



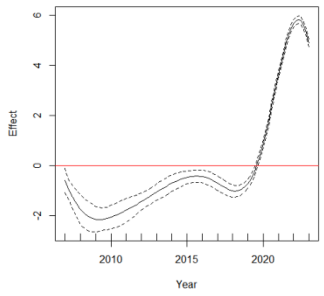
Duchon splines



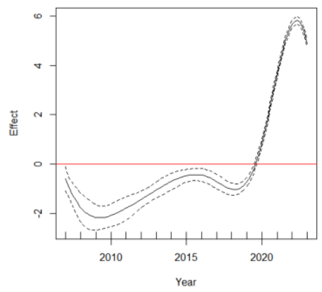
Cubic regression splines



B-splines

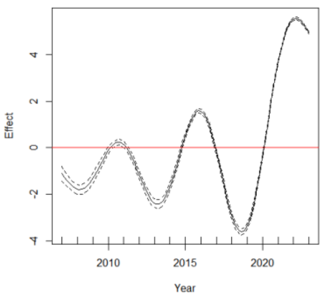


P-splines

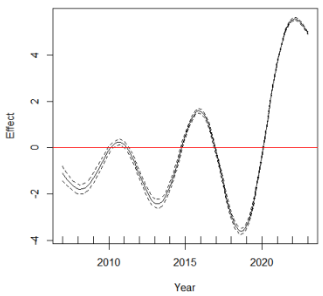


Rio Grande do Sul – Metropolitan

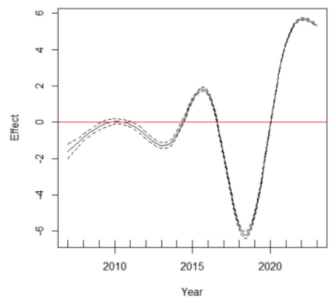
Thin plate regression splines



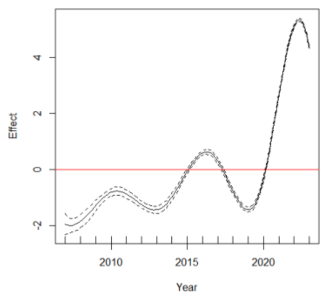
Duchon splines



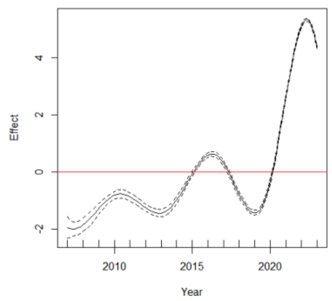
Cubic regression splines



B-splines

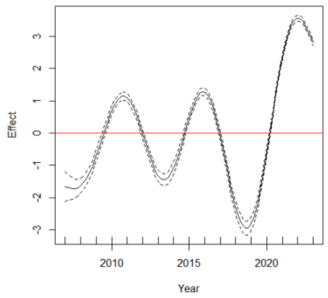


P-splines

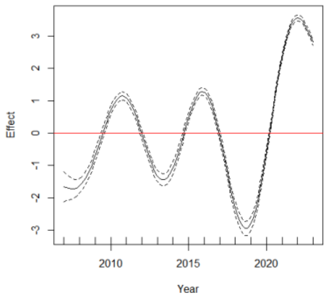


Rio Grande do Sul – Northeast

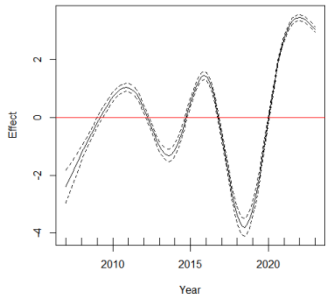
Thin plate regression splines



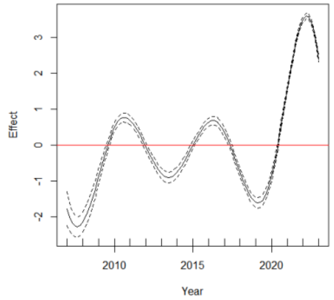
Duchon splines



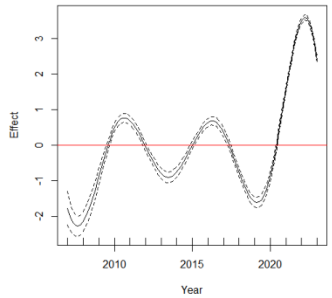
Cubic regression splines



B-splines

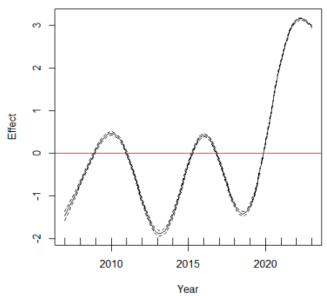


P-splines

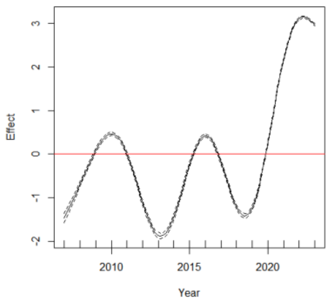


Rio Grande do Sul – Northwest

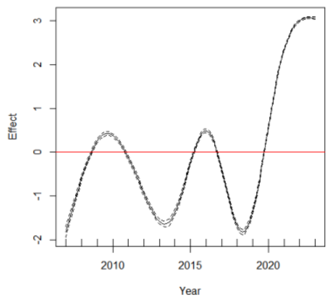
Thin plate regression splines



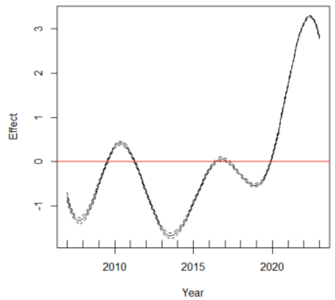
Duchon splines



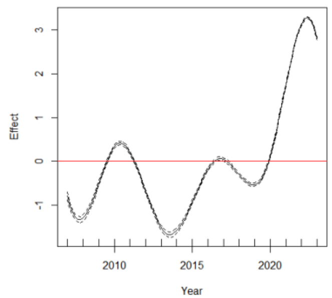
Cubic regression splines



B-splines



P-splines



Rio Grande do Sul – Southeast

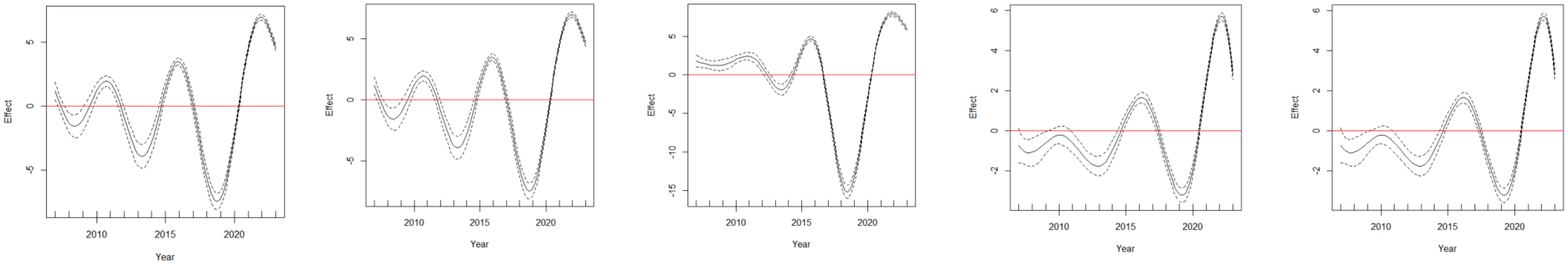
Thin plate regression splines

Duchon splines

Cubic regression splines

B-splines

P-splines



Rio Grande do Sul – Southwest

Thin plate regression splines

Duchon splines

Cubic regression splines

B-splines

P-splines

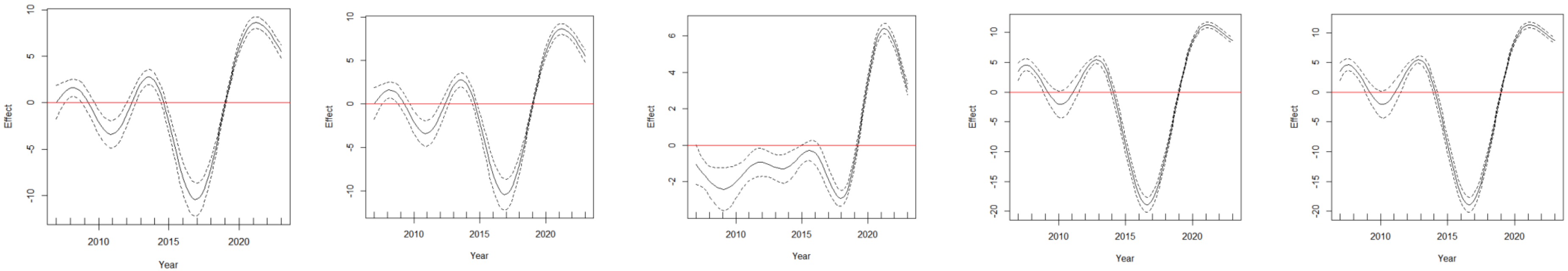


Figure S2. Moran Global Index of dengue incidence in Rio Grande do Sul municipalities, Brazil, from 2012 to sep/2023.

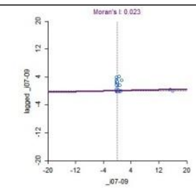
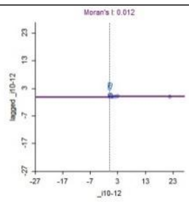
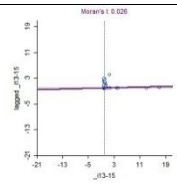
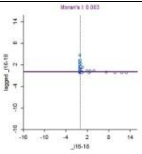
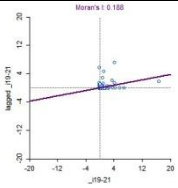
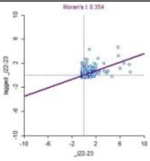
2007-2009	2010-2012	2013-2015
		
2016-2018	2019-2021	2022-2023
		

Table S1. Goodness-of-fit summary of Generalized Additive Models using different smoothness terms in order to identify dengue trends in Rio Grande do Sul and mesorregions, Brasil, 2007 to september 2023

Área	**Smooth classes**	**Thin plate regression splines**	**Duchon splines**	**Cubic regression splines**	**B-splines**	**P-splines**
Rio Grande do Sul	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000
	Deviance explained	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148
Meso 1	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000
	Deviance explained	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148
Meso 2	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000

	Deviance explained	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148
Meso 3	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000
	Deviance explained	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148
Meso 4	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000
	Deviance explained	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148
Meso 5	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000
	Deviance	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%

	explained					
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148
Meso 6	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000
	Deviance explained	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148
Meso 7	Family	Gaussian	Gaussian	Gaussian	Gaussian	Gaussian
	Link function	Identity	Identity	Identity	Identity	Identity
	Intercept	16.759***	5.580e-67	16.759***	16.759***	16.759***
	Planted área and deflorestation	1.000	1.159e-09	4.698**	1.000	1.000
	Deviance explained	6.4e-05%	-7.7%	2.17%	6.4e-05%	6.4e-05%
	GCV[1]	3668.3	3929.7	3624.3	3668.3	3668.3
	AIC[2]	8319.148	8370.99	8310.033	8319.148	8319.148

Table S2. Municipalities in risk cluster (Relative Risk – RR>1) based on Spatio-temporal scan analysis of dengue in Rio Grande do Sul, Brasil, 2007–september 2023

Risk cluster (RR>1)	**Municipality**
Cluster 1	Sapiranga, Campo Bom, Ararica, Dois irmãos, Nova Hartz, Novo Hamburgo, Estância Velha, Parobé, Santa Maria do Herval, São Leopoldo, Lindolfo Color, Presidente Lucena, Igrejinha, Taquara, Portão, Picada Café, Três Coroas, Sapucaia do Sul
Cluster 2	Nova Ramada, Ajuricaba, Santo Augusto, Condor, Chiapeta, Panambi, Bozano, Inhacora, Catuipe, Coronel Bicaco, São Valério do Sul, Pejuçara, Ijuí, Palmeira das Missões, Alegria, Campo Novo, Redentora, São Martinho, Dois Irmãos das Missões, Braga, Coronel de Barros, Sede Nova, Independência, Santa Barbara do Sul, São Pedro das Missões, São José do Inhacorá, Augusto Pestana, Boa Vista das Missões, Novo Barreiro, Bom Progresso, Boa Vista do Buricá, Erval Seco, Boa Vista do Cadeado, Santo Ângelo, Chapada, Humaita, Três de Maio, Jaboticaba, Miraguai, Girua, Cruz Alta, São José das Missões, Entre-Ijuis, Nova Candelária, Lajeado do Bugre, Eugênio de Castro, Barra Funda, Sagrada Família, Saldanha Marinho, Nova Boa Vista, Seberi, Três Passos, Novo Xingu, Cerro Grande, Crissiumal, Novo Tiradentes, Sete de Setembro, Sarandi, Tenente Portela, Joia, Pinhal, Horizontina, Almirante Tamandaré, Taquaruçu do Sul, Constantina, Liberato Salzano, Palmitinho, Vista Alegre, Santa Rosa, Cristal do Sul, Rondinha, Senador Salgado Filho, Rodeio Bonito, Tiradentes do Sul, Frederico Westphalen, Esperança do Sul, Vitória das Missões, Guarani das Missões, Tuparendi, Colorado, Ibiruba, Vista Gaúcha, Tucunduva, Engenho Velho, Boa Vista do Incra, Coqueiros do Sul, Derrubadas, Doutor Maurício Cardoso, Caiçara, Carazinho, Ametista do Sul, Mato Queimado, Fortaleza dos Valos, Ronda Alta, Barra do Guarita, Caibate, Selbach, Não-me-Toque, Quinze de Novembro, Pinheirinho do Vale, Novo Machado.

Cluster 3	Sério, Canudos do Vale, Progresso, Forquetinha, Marques de Souza, Boqueirão do Leão, Santa Clara do Sul, Mato Leitão, Travesseiro, Pouso Novo, Venancio Aires, Coqueiros de Baixo, Capitão, Nova Brescia, Sinimbu, Lajeado, Cruzeiro do Sul, Arroio do Meio, Estrela, Gramado Xavier, Relvado, Herveiras, São José do Herval, Colinas, Bom Retiro do Sul, Santa Cruz do Sul, Passo do Sobrado, Roca Sales, Encantado, Doutor Ricardo.
Cluster 4	Dilermando de Aguiar, São Pedro do Sul, Toropi, Mata, Santa Maria, São Martinho da Serra, Quevedos, Itaara, São Vicente do Sul, Jari, Jaguari

3.2 Artigo 2

Influence of socio-environonmental factors on the dengue fever epidemic in Rio Grande do Sul, Brazil, from 2013 to 2023

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Influence of socio-environonmental factors on the dengue fever epidemic in Rio Grande do Sul, Brazil, from 2013 to 2023

Authors

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Dengue epidemic in RS: socio-environmental factors

Key-words: arboviroses; dengue; epidemic; epidemiological monitoring; public health; Rio Grande do Sul.

Influence of socio-environonmental factors on the dengue epidemic in Rio Grande do Sul, Brazil, from 2013 to 2023

Authors

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Abstract

Dengue has expanded into areas previously considered protected in Brazil, such as the Southern region, and is expanding throughout Rio Grande do Sul. This expansion may be related to several factors. Thus, the objective of this article is to evaluate the influence of urbanization rates, rural density, and environmental quality on the average dengue incidence rate in Rio Grande do Sul from 2013 to 2023. Secondary data from information systems were used, and the degree of influence in the state's different mesoregions was assessed using geographically weighted regression (GWR) analysis using R software. The variables analyzed showed heterogeneous influence on disease incidence in the state, with an expanding influence of urbanization rates and rural density in 2022. Therefore, we hope that the results presented in this study can guide the implementation of public policies targeted at-risk populations.

Introduction

Dengue is an arbovirus of great relevance in tropical and subtropical countries and has established itself, over the decades, as one of the main public health challenges in Brazil (*1,2*). Although historically the highest incidence rates were observed in the North, Northeast, Southeast and Central-West regions, the disease has advanced to geographic areas previously considered less prone and protected, such as Southern Brazil (*3*,*4*). This advance demonstrates important transformations in socio-environmental and climatic patterns, which favor the proliferation of *Aedes aegypti*, the main vector of dengue, and thus the spread of the virus among the population, including in climatic zones previously unfavorable to the presence of the vector (*5*,*6*,*7*).

The state of Rio Grande do Sul, traditionally characterized by a subtropical temperate climate and low vector infestation rates, has begun to record alarming numbers of dengue cases in recent years. *Aedes aegypti* was first identified in the state in the municipality of Caxias do Sul in 1995, and the first autochthonus case was recorded 12 years later, in 2007, in the municipality of Giruá (*8*,*9*). Since then, a rapid expansion of the disease has been observed throughout the state, totaling 91.15% (453/497) municipalities affected in 2022, with more than 35,000 cases reported in 2023 alone (*10*,*11*,*12*).

This epidemiological shift may be associated with multiple determining factors, as average temperatures increase, the intensification of extreme events related to climate change, disorderly urbanization, and failures in environmental management and urban infrastructure—including basic sanitation and solid waste control (*2*,*4*,*13*). Additionally, socioeconomic factors—such as inequalities in access to health care and information—contribute to the vulnerability of certain populations to the disease (*14*).

Given the above, it is crucial to understand the spatiotemporal dynamics of dengue transmission and the determinants associated with the disease in Rio Grande do Sul. This analysis allows us to understand the local factors driving the spread of the disease and informs the formulation of more effective public surveillance, prevention, and control policies. Therefore, this article aims to identify and discuss environmental and socioeconomic factors associated with dengue incidence in the state of Rio Grande do Sul, Brazil, from 2007 to 2023.

Materials and Methods

Epidemiological data

Rio Grande do Sul is the sixt most populous state in Brazil, located at latitude 27˚03042@ and 33˚45009@ South and longitude 49˚42041@ and 57˚40057@ West and is the southernmost state in Brazil (Figure 1), bordering Argentina and Uruguay. The state covers an area of 281,707.151 km, and is divided into 497 municipalities. In 2021, the population was 11,466,630, representing 5.65% (11,466,630/203,062,512) of Brazilian population (*15*). The climate of Rio Grande do Sul is subtropical temperate, classified as humid mesothermal (Köppen classification). Because of its geographical position, it presents significant differences from the rest of Brazil. Temperatures show great seasonal variation, with average temperatures range between 15°C and 18°C, with minimum temperatures dropping to -10°C and maximum temperatures reaching 40°C (*16*).

Rio Grande do Sul is divided into three major economic regions: (1) the southern region, with a large concentration of land, large livestock farms, and mechanized planting of rice, soybeans, and wheat, with a greater income inequality; (2) the northeastern region, which includes the state capital, has more industries and smaller properties, and (3) the northern region, which European immigrants mostly colonize, has forest cover, valleys, and plains with small agricultural lands (Figure 1) (*17*). In addition, the state can be separeted in seven mesoregions: Metropolitan Porto Alegre, Central-Western Rio-grandense, Central-Eastern Rio-grandense, Northeast Rio-grandense, Northwest Rio-grandense, Southeast Rio-grandense and Southwest Rio-grandenset (Figure 1).

Data on the number of confirmed cases and municipalities with dengue occurrences in Rio Grande do Sul between Januray 2013 and December 2023 were obtained from SINAN, provided by the Brazilian Ministry of Health (*18*,*19*). Cases included in this study were confirmed based on clinical-epidemiological or laboratory criteria, as outlined in the Ministry of Health's Epidemiological Surveillance Guide (*20*).

Urbanization rate

The urbanization rate—a demographic indicator that measures the proportion of the population living in urban areas relative to the total population of the municipality—was obtained from data from the 2010 and 2022 censuses via SIDRA—the Statistical Tables Database of the Brazilian Institute of Geography and Statistics (IBGE) (*21*). To calculate the rate, the total urban population of each municipality was divided by the total population (urban population + rural population) and multiplied by 100 (*22*).

Rural density

Rural density was defined as the concentration of people living in rural areas and is expressed as the number of inhabitants per km². The rural population of each municipality was obtained from the 2010 and 2022 censuses via SIDRA – Statistical Tables Database of the Brazilian Institute of Geography and Statistics (IBGE) (*21*). The rural area of each municipality was obtained through the total area of the municipality reduced by its urbanized area, according to IBGE data (*23*).

Enviromental quality – Environmental Performance Index (EPI)

Environmental quality was assessed using the Socio-Environmental Performance Index (EPI). This index assesses sixteen variables related to six types of policies: Environmental Health, Air Quality, Water Resources, Productive Natural Resources, Biodiversity and Habitat, and Energy (*24*). This index focuses on two broad protection objectives: (1) reducing environmental stresses on human health, and (2) promoting ecosystem vitality and consistent management of natural resources (*24*).

The Socio-Environmental Performance Index was obtained using the Social Progress Index (IPS Brazil 2025) (*25*).

Modelling approach

To understand how the analyzed variables influenced dengue in each municipalities in 2010 and 2022, the average incidence rate was calculated to express the frequency with which new dengue cases occurred in the population, on average, over the period. The annual population estimate for each municipality, obtained through the Brazilian Institute of Statistics and Geography (IBGE) via the SUS Information and Information Technology Department (DataSUS) (*18*).

To examine spatial variation in the relationships between these variables, Geographically Weighted Regression (GWR) was applied directly. Given the study's focus on capturing local heterogeneity across municipalities, GWR was deemed appropriate without first fitting a global Ordinary Least Squares (OLS) model. This approach allows regression coefficients to vary spatially, highlighting localized patterns that may be obscured in a global model. Multicollinearity among predictors and spatial autocorrelation of residuals were evaluated to ensure model robustness (*26*). An adaptive kernel with bandwidth selected via cross-validation was used for calibration. Local coefficients, R^2 values, and residuals were mapped to identify spatial heterogeneity in the relationships. Analyses were conducted in R (version 4.4.2) using the packages sf, sp, GWmodel, dplyr, readxl, ggplot2, and patchwork.

Results

A total of 127,945 dengue cases were reported in Rio Grande do Sul from January 2013 to December 2023, with an incidence rate of 103.72 cases per 100,000 inhabitants. Of these, 105,867 cases (82.74%) were reported between 2022 and 2023 alone, with an average incidence rate of 471.73 cases per 100,000 inhabitants for the two-year period, with expansion throughout the territory. Regarding the variables analyzed – urbanization rate, rural density, and environmental quality – a heterogeneous influence on dengue incidence was observed in the different mesoregions of the state.

Urbanization Rate

In 2010, it was observed that the urbanization rate had a positive effect in the Metropolitan and Northeast mesoregions of the state, where a one-point increase percentage in urbanization implied a proportional increase in the average rate of dengue incidence. In contrast, in the Southwest region, the influence of the urbanization rate on the average dengue incidence rate was weak over the same period (Figure 1A).

In 2022, the effect of urbanization expanded to other mesoregions, with more areas becoming affected by this factor. This expansion is evident in the Southwest mesoregion, with the influence increasing from -0.009–0.014 in 2010 to 0.018–0.03 in 2022. It is noteworthy, however, that in parts of the Northwest and Central-Eastern Rio Grande do Sul mesoregions, the urbanization rate had a negative effect on the average dengue incidence rate (Figure 1B).

Rural Density

Regarding rural density, a distinct spatial and temporal pattern was observed. In 2010, the most significant positive influences were observed in the Southwest and Northeast mesoregions, indicating that higher concentrations of rural populations in these areas were associated with higher average dengue incidence rates. Conversely, a significant negative effect was identified in parts of the Northwest and Central-West mesoregions, which may indicate a protective factor (Figure 2A).

In 2022, the negative influence of rural density became less intense and began to be concentrated in the Northwest mesoregion. The positive effect, although not as intense, demonstrated territorial expansion toward the Southwest and consolidated in the Northeast and Metropolitan mesoregions (Figure 2B).

Environmental Quality – Socio-Environmental Performance Index

Environmental quality, measured using the Socioenvironmental Performance Index, demonstrated contrasting effects across the state's different mesoregions. A significant negative influence was identified in the Central-Western mesoregions, as well as portions of the Northeast and Northwest mesoregions, where better environmental conditions were shown to be associated with a lower average dengue incidence rate (Figure 3).

At the same time, a positive influence of environmental quality on the average incidence rate of dengue was observed in the Northeast, Metropolitan, Southeast and Central-Eastern mesoregions (Figure 3).

Discussion

Although Southern Brazil was previously considered a relatively protected region from dengue transmission because seasonal temperatures are too low for efficient virus transmission (*3*), our study demonstrates the expansion of the disease in Rio Grande do Sul in recent years, especially between 2022 and 2023.

This expansion of the disease along the southern border suggests greater climatic suitability for *Aedes* mosquitoes and a risk of co-circulation of vector-borne diseases between Argentina, Paraguay, and Brazil (*1*). An integrated analysis of rural density, urbanization rate, and environmental quality reveals a complex network of factors that directly influence dengue incidence in the state. Although dengue has historically been associated with densely populated urban areas (*27*), the results demonstrate that, in Rio Grande do Sul, the disease has surpassed these limits, reaching rural and rural-urban transition areas, reflecting the capacity adaptive behavior of the *Aedes aegypti* and changes in socio-environmental patterns and territorial dynamics, demonstrated by the influence of rural density on the average incidence rate of the disease in the state's mesoregions.

The relationship between population density in rural areas and the increase in the number of dengue cases, as observed in our study, has already been demonstrated in the literature. Although dengue is associated with the urban environment, its spread to smaller municipalities and rural areas has been observed, driven by factors such as poor sanitation, inadequate water storage—creating suitable habitats for the vector's development—and increased population density in these regions (*2*,*3*,*5*). Areas with higher population density, even in rural areas, present favorable conditions for the spread of dengue, especially if there is low coverage of basic services. Corroborating this observation, Almeida et al. (*28*) identified the presence of larvae of mosquitoes of the genus *Aedes* in rural areas of Mato do Grosso do Sul and highlighted that although the Brazilian Ministry of Health has a technical protocol for the control of arboviruses, these measures do not cover rural areas.

Along the same lines, Valadares (*29*) highlights that the administrative rule of urban perimeter defines rural areas as spaces of exclusion, since they are located outside the areas for which the public administration creates development strategies. Thus, our results demonstrate that rural density is no longer considered a barrier to the disease but rather an important factor associated with its transmission, especially when associated with socio-environmental vulnerability. They also demonstrate the need to expand attention and adopt dengue control measures in these rural areas.

It is also worth noting that currently observed climate change is accompanied by altered precipitation patterns, flooding, and a greater likelihood of extreme weather events. These phenomena are potentially linked to the expansion of the geographic range of vectors and, therefore, a potential increase in the spread of arboviral diseases (*30,31*). Extreme hydrometeorological events, such as droughts and heavy rainfall, interact with local living conditions, affecting mosquito infestation and their rate of contact with humans. These effects on dengue transmission depend on local social and ecological conditions, which determine the types of larval habitats available and household water storage (*32*).

In 2023 and 2024, the state of Rio Grande do Sul experienced heavy rainfall and flooding. Not only can increased rainfall create new habitat for larvae and vectors and increase the survival of adult mosquitoes, but more rural areas experience an immediate increase in dengue risk during extremely humid conditions, which can persist for up to three months (*32*,*33*), consequently worsening the epidemiological situation in the state. In addition to the direct impact of intense hydrometeorological conditions, rural flooding can result in significant population migration to urban areas, potentially increasing population density in already overcrowded environments, potentially increasing the risk of dengue transmission (*30*).

Rapid and often disorderly urbanization has been identified as one of the main factors associated with the increase in the incidence of dengue fever (*4*). According to Rio Grande do Sul (*34*), there was a 2.40% increase in the state's urbanization rate during the period from 2010 to 2022, totaling 87.50% of urbanized area in 2022, concentrated mainly in the Southwest, Metropolitan and Southeast mesoregions. In our study, an intensification of the influence of the urbanization rate on the dengue incidence rate in the state was observed between the period 2010 e 2022, especially in the Southwest and Southeast mesoregions that concentrate some of the highest urbanization rates in the state.

Urban growth, especially in peripheral areas with poor infrastructure, favors the proliferation of the *Aedes aegypti* mosquito due to the high concentration of artificial breeding sites, such as water storage containers, debris, and accumulated garbage (*5*). This high population density, combined with deficiencies in basic sanitation and solid waste collection, ultimately creates a favorable environment for the maintenance of the vector and the spread of the virus (*13*). This accelerated urbanization, without proper environmental and urban planning, has contributed to the spread of dengue in recent decades (*2*).

Thus, the urbanization rate alone is not the only determining factor, but its association with social and environmental inequalities ultimately transforms urban centers into zones of high epidemiological vulnerability. This may explain the lack of uniformity in the effect of the urbanization rate on dengue incidence in Rio Grande do Sul, where it was observed that in some regions the variable favors an increase in cases, while in others it is associated with a decrease, which may be linked to differences in urban structure or vector control.

Furthermore, the influence of residential areas on mosquito incidence also becomes evident under certain environmental circumstances, such as lower rainfall. Roads have drainage systems that collect stormwater runoff and release it into areas to prevent flooding. However, concrete structures that encroach on canals or accumulate trash can often impair adequate drainage in residential areas, preventing full water flow and resulting in pools of water (*33*).

Environmental quality is a determining factor in mosquito proliferation and, consequently, in the incidence of dengue (*4*). In our study, we observed no homogeneity in this variable, which in some mesoregions proved to be a protective factor against the disease and in others correlated with higher incidence, possibly reflecting urban realities in which areas with environmental infrastructure coexist with high population density and greater exposure to the virus.

Poor environmental quality—characterized by precarious basic sanitation conditions, such as inadequate water supply and garbage collection services—is one of the main risk factors for the spread of dengue (*32*). Degraded environments, with accumulated garbage, lack of regular waste collection, and the presence of stagnant water, provide ideal conditions for the reproduction of the vector (*3*). Thus, areas with low basic sanitation coverage, poor water resource management, and inadequate solid waste disposal are more vulnerable to the spread of dengue (*2*).

According to the World Health Organization (*6*), interventions that improve urban infrastructure and reduce environmental pollution are essential for controlling arboviruses, as they limit breeding sites and hinder the vector's life cycle. On the other hand, environmental fragmentation and uncontrolled urban growth contribute to ecosystem alterations, favoring the mosquito's adaptation to different habitats (*13*). Furthermore, this fragmentation of the natural environment, combined with uncontrolled urban growth, alters local ecosystems and allows the vector to adapt to new habitats, including in rural and transitional areas (*13*).

The observed results demonstrate that environmental preservation and efficient management of urban and peri-urban spaces are essential to reducing the incidence of the disease. Recognizing associated factors enables understanding the areas and periods at greatest risk, enabling alerts for epidemiological and environmental surveillance, both for vector control and for organizing the necessary assistance to treat cases, since communities living on the edge of previous barriers are considered particularly susceptible to future outbreaks due to their lack of immunity (*2*,*3*).

The limitations of this study are related to the use of secondary data sources. Although an increase in the number of dengue cases has been observed in Rio Grande do Sul in recent years, the true magnitude of the situation may be underestimated due to limitations in secondary surveillance systems, a high rate of asymptomatic infections, self-management of symptoms, and underreported or incorrect diagnoses (*35*,*36*).

It is also noteworthy that in Brazil, few publications have identified that relate dengue to sociodemographic variables, and that access to health services in Brazil is strongly influenced by social status and location, with people living far from health facilities tending to seek medical help only in more serious situations (*2*, *37*). Since a relationship between dengue incidence and rural population density was observed, this may be a factor in underreporting of dengue cases in the state and in the development of more severe conditions that reach the health system.

Our results also demonstrate the increasing incidence of dengue fever in the state and that the effects of the analyzed variables are territorially heterogeneous, with no single relationship between these variables and dengue fever, indicating dependence on the local context. Thus, considering that local data on population health indicators are important for health monitoring and guiding resource allocation, we hope that the results presented can guide and contribute to decisions on health policies, monitoring the impact of health interventions directed at actions to prevent dengue fever and control its vectors on a regional basis, targeting populations considered to be at greater epidemiological risk and considering the socio-environmental specificities of each mesoregion.

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Figures

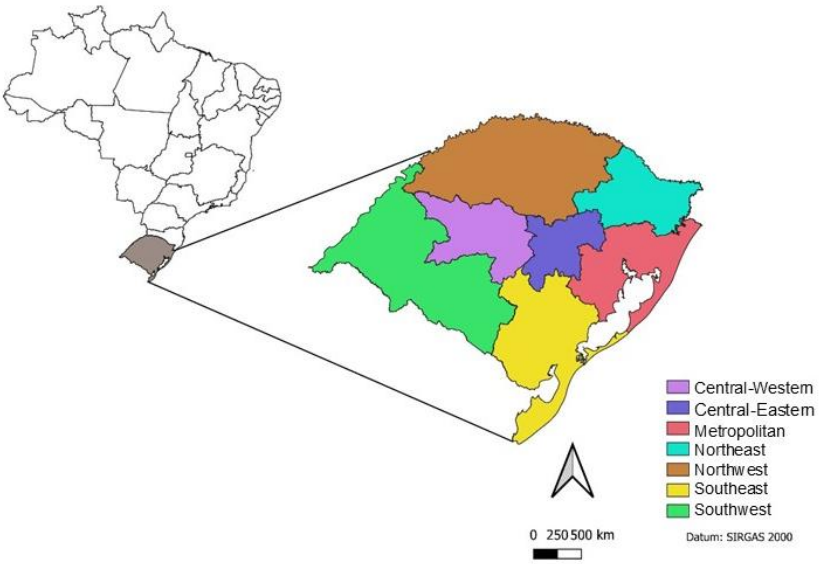

Figure 1. Division of the macro-regions of Rio Grande do Sul, Brazil, according to SIRGAS 2000, highlighting the regions Centro Ocidental, Centro Oriental, Metropolitan Porto Alegre, Northeast, Northwest, Southeast, and Southwest Rio-grandense.

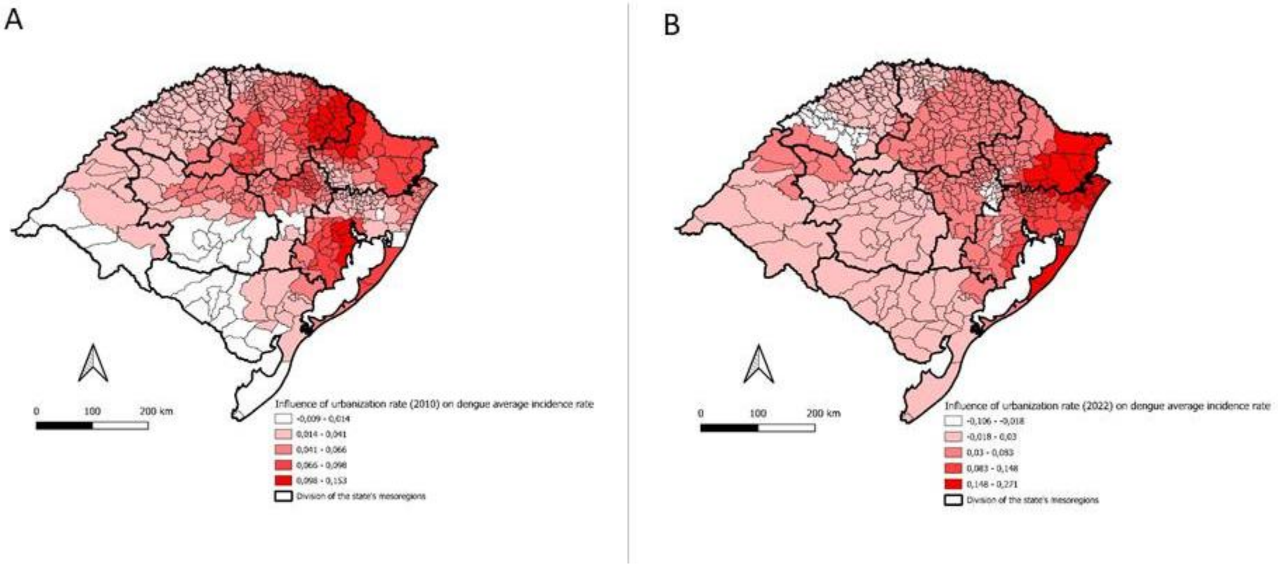

Figure 2. The level of influence of the urbanization rate on the average incidence rate of dengue in the different mesoregions of the state of Rio Grande do Sul, in the years 2010 (A) and 2022 (B).

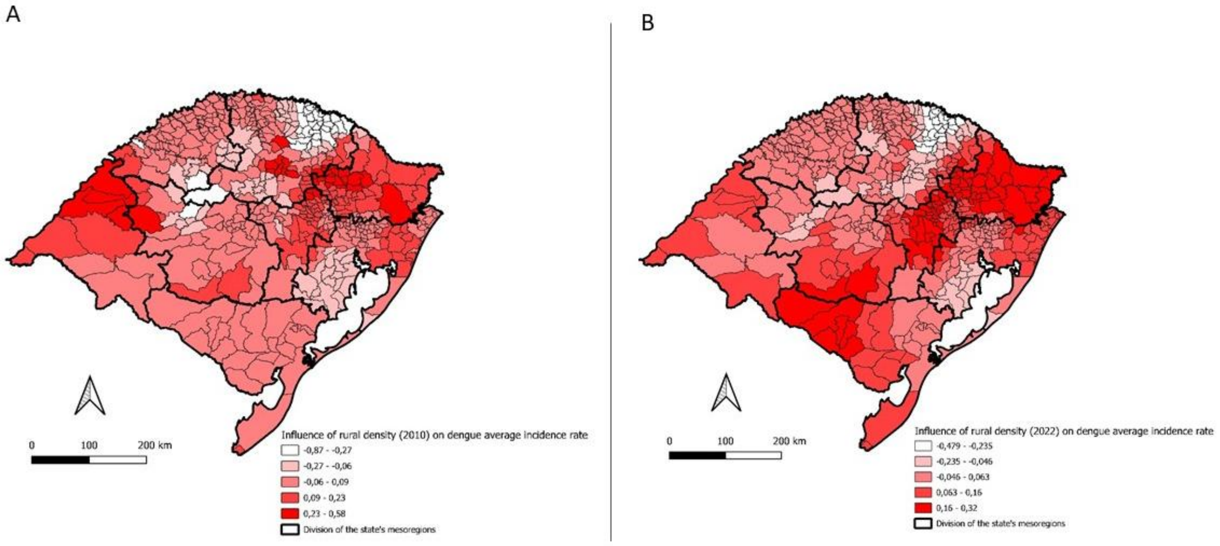

Figure 3. The level of influence of the rural density on the average incidence rate of dengue in the different mesoregions of the state of Rio Grande do Sul, in the years 2010 (A) and 2022 (B).

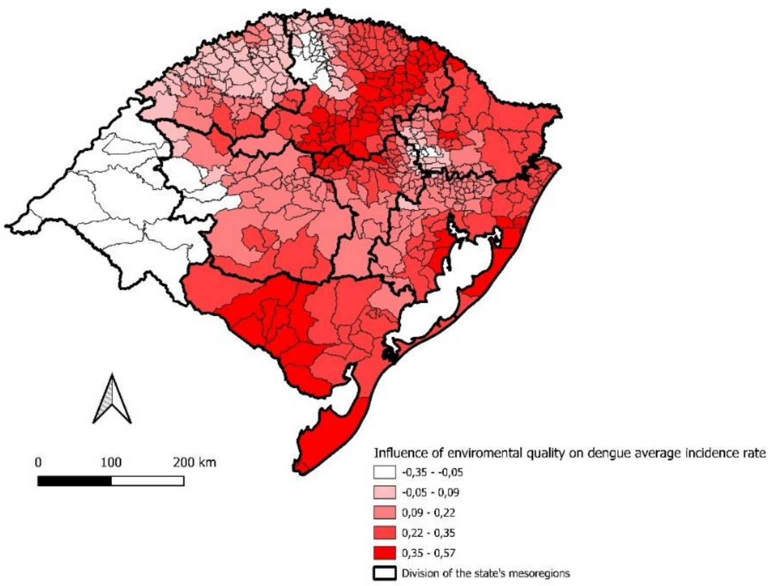

Figure 3. The level of environmental quality – socio-environmental performance on the average incidence rate of dengue in the different mesoregions of the state of Rio Grande do Sul, Brazil.

4 Considerações Finais

A dengue é considerada uma das dez principais ameaças à saúde pública mundial, com estimativas apontando que mais de quatro bilhões de pessoas se encontram expostas ao risco de infecção. O Brasil, desde 1986, se encontra em situação de hiperendemicidade com sucessivos períodos de epidemias e impactos social e econômico crescentes.

A presente tese evidenciou o complexo cenário epidemiológico da dengue no Rio Grande do Sul, um estado que historicamente era considerado fora do eixo principal de transmissão da doença no Brasil. Os resultados obtidos ao longo deste estudo revelam uma expansão significativa e crescente de casos autóctones nas diversas mesorregiões do estado.

Fatores como a taxa de urbanização, densidade rural e qualidade ambiental demonstraram influenciar de forma heterogênea a incidência da doença no estado ao longo do período analisado. Essa atuação heterogênea demonstra que a epidemiologia da dengue está relacionada a uma complexa rede de fatores, que interagem entre si e que acabam por receber influência também da realidade da população local. A combinação desses elementos evidencia a necessidade de revisão e adequação de estratégias de vigilância epidemiológica, com foco em ações intersetoriais, educação em saúde e fortalecimento da atenção básica.

Conclui-se, assim, que a dengue no Rio Grande do Sul deixou de ser um fenômeno sazonal e passou a ser uma realidade epidemiológica que exige vigilância constante, políticas públicas e engajamento da população. O enfrentamento efetivo da doença passa pelo reconhecimento de suas múltiplas dimensões e pela articulação de soluções que envolvam também os setores de saneamento básico, meio ambiente, educação sanitária e planejamento urbano.

Dessa forma, espera-se que os resultados demonstrados na presente tese possam contribuir para o reconhecimento da situação epidemiológica no estado, oferecendo subsídios para a formulação de políticas públicas mais eficazes no controle da dengue no contexto socioambiental do estado.

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