






# Entry of dengue virus serotypes and their geographic distribution in Brazilian federative units: a systematic review

## *Entrada e distribuição geográfica dos sorotipos do vírus da dengue nas unidades federativas brasileiras: uma revisão sistemática*

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**ABSTRACT:** *Objective:* To describe the entry of Dengue virus (DENV) serotypes in Brazil and its federative units. *Methods:* A systematic review of studies published between 1980 and 2018 in databases and in the gray literature was performed using descriptors related to the years of entry of the DENV serotypes. Additionally, experts and official sources of information (Brazilian Ministry of Health) were consulted. *Results:* From 100 publications selected for the systematic review, 26 addressed the entry of DENV serotypes in the North region of the country, 33 in the Northeast, 24 in the Southeast, 14 in the Central-West, and five in the South. DENV-1 and DENV-4 were introduced in the North region in 1981. DENV-2 was introduced in the Southeast in 1990. DENV-3 was introduced in the North in 1999. *Conclusion:* The rapid expansion of dengue throughout the Brazilian territory was verified from the second half of the 1980s, with the gradual entry of the four serotypes, which resulted in the emergence of epidemics of arbovirus, which are currently verified in the country. Considering the epidemiology of the disease, more information should be disseminated and published in the wide-ranging scientific literature for a better understanding of the spread and circulation of DENV serotypes.

**Keywords:** Dengue. Dengue virus. Serogroup. Epidemiology. Systematic review.

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**RESUMO:** *Objetivo:* Descreveu-se a entrada de sorotipos do vírus da Dengue (DENV) no Brasil e em suas unidades federativas. *Métodos:* Realizou-se uma revisão sistemática de estudos publicados entre 1980 e 2018 em bancos de dados e na literatura cinzenta, utilizando-se descritores relacionados aos anos de entrada dos sorotipos do DENV. Além disso, consultou-se especialistas e fontes oficiais de informação (Ministério da Saúde do Brasil). *Resultados:* Das 100 publicações selecionadas para a revisão sistemática, 26 abordaram a entrada de sorotipos de DENV na região Norte do país, 33 no Nordeste, 24 no Sudeste, 14 no Centro-Oeste e cinco no Sul. O DENV-1 e o DENV-4 foram introduzidos na região Norte em 1981. O DENV-2 foi introduzido no Sudeste em 1990. O DENV-3 foi introduzido no Norte em 1999. *Conclusão:* A rápida expansão da dengue por todo o território brasileiro foi verificada a partir da segunda metade dos anos de 1980, com a entrada gradativa dos quatro sorotipos, o que resultou no surgimento de epidemias da arbovirose, que são atualmente verificadas no país. Considerando a epidemiologia da doença, mais informações devem ser divulgadas e publicadas na literatura científica de amplo alcance, para melhor entendimento da propagação e circulação dos sorotipos de DENV.

**Palavras-chave:** Dengue. Vírus da dengue. Sorogrupo. Epidemiologia. Revisão sistemática.

## INTRODUCTION

Dengue represents an important vector-borne disease worldwide due to its morbidity and impacts on public health<sup>1</sup>. In Brazil, the disease is currently the object of largest public health programs, which focus on *Aedes aegypti* control. This mosquito is adapted to reproduce in domestic and peridomestic environments, using different types of stagnant water containers<sup>2</sup>. The wide dispersion of this vector has also caused epidemics of other arboviruses, such as Zika fever<sup>3</sup> and Chikungunya fever<sup>4</sup>, which have been occurring since 2015 in different Brazilian federative units<sup>5-7</sup>.

The reasons underlying the spread of dengue in the tropics and subtropics of the globe are complex<sup>8,9</sup>. *Ae. aegypti* is found from Uruguay to the South of the United States of America, where dengue outbreaks have been reported in recent decades in countries such as Venezuela, Cuba, Paraguay, and Brazil. In addition, the countries of the Americas face the fact that social, economic and environmental conditions have simultaneously contributed to making dengue a health problem in their populations<sup>8,9</sup>.

Reports of dengue epidemics in Brazil have been described since 1846, in the states of São Paulo and Rio de Janeiro. However, the first citations of clinical cases of the disease in the scientific literature are from 1916 in the city of São Paulo<sup>10</sup>, and 1923 in Niterói<sup>11</sup>. In the years of 1953 and 1954, a serological survey carried out among individuals residing in the Brazilian Amazon identified antibodies of Dengue virus (DENV) serotypes DENV-1 and DENV-2, thus indicating that the virus may have formerly circulated in the region<sup>12</sup>.

The first dengue epidemic clinically and laboratory-confirmed in the country occurred in 1981 and 1982, in Boa Vista (state of Roraima) and was caused by serotypes DENV-1 and DENV-4<sup>13</sup>. DENV-2 was introduced in Rio de Janeiro in 1990. Nine years later, in 1999,

DENV-3 was introduced in the states of Amapá, Pará, Roraima, and Tocantins (data provided by the Brazilian Ministry of Health). In 2008, a new record of DENV-4 circulation was registered in the state of Amazonas<sup>14</sup>. Overall, in the last 20 years, the country experienced four major epidemics associated with different predominant viral serotypes: DENV-1 (1998), DENV-3 (2002), DENV-2 (2008), and DENV-4 (2010)<sup>15</sup>.

In 2019, 1,544,987 cases were notified, with an incidence of 735.2 cases/100,000 inhabitants<sup>15</sup>. Despite the low mortality rate, the disease contributes to the loss of healthy years of life in Brazil, as it affects a large number of people, from all age groups, and can cause some degree of disability during the infection and lead to death, especially among children<sup>16,17</sup>.

Considering the several studies that show the circulation of DENV and also the relevance and magnitude of dengue in Brazil, the elaboration of a systematic review has become relevant. In addition, Brazil has proximity to other dengue endemic countries, which makes surveillance important in terms of knowledge of circulating virus serotypes. The present study aims to present a systematic review of the scientific literature on the entry of DENV serotypes in Brazil and its federative units over the years.

## METHODS

### STUDY AREA

Brazil is politically and administratively divided into 27 federative units (26 states and the Federal District) and 5,570 municipalities<sup>18</sup>. The 27 federative units are grouped into five geographic regions: North (seven states), Northeast (nine states), Central-West (three states and the Federal District), Southeast (four states), and South (three states)<sup>19</sup>.

### STUDY DESIGN

This is a systematic review of the literature from different electronic databases, using descriptors associated with the year of entry of DENV serotypes and its circulation in Brazil and its 27 federative units. The search for and selection of the publications was performed in the second semester of 2019, with studies from 1980 to 2018.

The study was conducted following these steps: research in the electronic databases, research in the gray literature, consultation of experts from the Brazilian Ministry of Health, reading and analysis of the publications, and selection of publications for the final version of the systematic review.

The used electronic databases were:

- Scientific Electronic Library Online (SciELO);
- Virtual Health Library (VHL);
- U. S. National Library of Medicine (PubMed).

The gray literature was surveyed on Google Scholar for additional publications with the aim of avoiding an inadequate or non-comprehensive selection including full-text publications only, which would reduce the representativeness of the studies identified or included<sup>20</sup>. For the years for which data on the entry of DENV serotypes was missing, information was requested from specialists at the Brazilian Ministry of Health, who provided Microsoft Office Excel (Washington, USA) database spreadsheets with data recorded from 1999 to 2018.

## SEARCH STRATEGY

The searches were conducted using descriptors cataloged in the Health Sciences Descriptor (DeCS) and in the Medical Subject Headings (MeSH), in Portuguese, English, Spanish, and French. Studies that contained these terms in the title or in the summary were selected. The Boolean operators “AND” and “OR” were used as well as quotation marks to facilitate the search of the manuscripts. In each of the databases (SciELO, VHL, and PubMed), combinations of terms, together or separately, were used in the four aforementioned languages: Dengue (similar terms: “Dengue fever,” “Dengue virus infection,” “Dengue hemorrhagic fever,” “Dengue shock syndrome”), Dengue Virus (similar terms: “DENV,” “Serotype,” “Serotyping,” “Serology Typing,” “DENV-1,” “DENV-2,” “DENV-3,” “DENV-4,” “Serotype 1,” “Serotype 2,” “Serotype 3,” “Serotype 4,” “Dengue virus detection,” “Dengue virus isolation,” “Dengue virus introduction”), Circulation (similar terms: “co-circulation,” “viral circulation,” “seroepidemiological study of dengue,” “identification of serotypes of dengue,” “first registration of Dengue virus,” “first registration of Dengue virus serotype”).

The systematic search was independently reproduced by two researchers under the guidance of a librarian from Universidade Federal de Minas Gerais. The systematic review was recorded in the International Prospective Register of Systematic Reviews, registration number CRD42018095017<sup>21</sup>. The research followed PRISMA guidelines for systematic review<sup>22</sup>.

## SELECTION AND ANALYSIS OF PUBLICATIONS

Studies were selected based on a designed form including information regarding: federative unit where the study took place, author and year of publication, journal of publication, study type, and main results. The inclusion criteria were studies in the format of original articles, review articles, brief communications, short communications, case reports, research notes, editorials, abstracts, updates, official data (bulletins, epidemiological reports, and manuals from the Brazilian Ministry of Health), technical notes, dissertations, and theses, published between 1980 and 2018, in international or national journals or in electronic pages available for access, in English, Portuguese, Spanish, or French, and indexed in one

of the aforementioned bases. Only publications containing, in any part of the text, data regarding the year of entry and/or circulation of DENV in Brazil and its 27 federative units were selected for the systematic review. It should be emphasized that the information was used both if the authors were responsible for the first publication on the DENV introduction and if they only cited it (for example, if the information was in the “Introduction” or “Discussion” sections). All the studies that did not meet the inclusion criteria were excluded from the study. Each methodological step of the systematic review was independently performed by two researchers, and the results were compared. Cases of disagreement were resolved by a third researcher, who was called to help reach a consensus on the inclusion or exclusion of studies.

The results are described in tables, graphs, and maps prepared using the Microsoft Office Excel and Microsoft Office Word software version 2010 (USA), GraphPad Prism version 5.0 (La Jolla, California, USA), and QGIS version 2.18 (Las Palmas, Spain), respectively.

## RESULTS

Of the total of 2,048 studies resulting from the initial search, 37 studies were excluded because they were duplicated; and 1,860, for being unrelated to the topic of the review. Subsequently, 16 studies were excluded after reading the abstract and 35 after reading the full text because they did not present the information sought. Thus, 68 papers were selected for the present review based on the search strategy adopted. Additionally, 32 studies were selected from the gray literature. Therefore, the present systematic review was organized based on a total of 100 studies, considering those selected from the search strategy and those resulting from the gray literature. The results obtained from each step of the selection of all the evaluated studies are presented in the study flowchart (Figure 1).

From the 100 selected publications, 26 addressed the entry of DENV serotypes in federative units of the North region of Brazil (two in Acre, none in Amapá, ten in Amazonas, four in Pará, six in Roraima, three in Rondônia, and one in Tocantins). Thirty-three addressed the Northeast region (two in Alagoas, seven in Bahia, eight in Ceará, four in Maranhão, three in Pernambuco, three in Piauí, five in Rio Grande do Norte, and one in Sergipe). The Southeast region was the subject of 24 studies (two in Espírito Santo, five in Minas Gerais, 13 in Rio de Janeiro, and four in São Paulo). Fourteen publications addressed the Central-West region (two in the Federal District, two in Goiás, six in Mato Grosso, and four in Mato Grosso do Sul). Lastly, the entry of DENV serotypes in the South region was explored by five studies (two in Paraná, none in Santa Catarina, and three in Rio Grande do Sul). One of the selected articles included information about three states (Pará, Roraima, and Bahia) and is, therefore, cited three times. Nevertheless, it was considered as a single publication in the total number of 100 (Supplementary Table 1).

The consultation of experts allowed to fill in the gaps of missing information regarding the years of entry of specific serotypes: all serotypes in Amapá, DENV-3 in Pará, DENV-2 and

DENV-3 in Roraima, DENV-4 in Rondônia, and DENV-1 and DENV-4 in Tocantins (North region); DENV-3 in Alagoas, all serotypes in Paraíba and Sergipe, and DENV-1 in Piauí and Rio Grande do Norte (Northeast region); DENV-4 in the Federal District and Goiás, DENV-1 in Mato Grosso, and DENV-3 in Mato Grosso do Sul (Central-West region); DENV-1 and DENV-3 in Paraná and all serotypes in Santa Catarina (South region) (Supplementary Table 1).

Serotypes DENV-1 and DENV-4 were introduced in the country in 1981; DENV-2, in 1990; and DENV-3, in 2001. Table 1 presents the year of entry of the four dengue serotypes in the country by region and federative unit.

When grouping the authors' observations on the entry of DENV serotypes into periods of four and five years (Figure 2), it was observed that 14 years after the entry of the serotypes DENV-1 and DENV-4 in the state of Roraima (1981), in the period between 1995 and 1999, serotypes DENV-1 and DENV-2 were concurrently introduced in the states of Amazonas, Espírito Santo, Minas Gerais, and Piauí; serotypes DENV-2 and DENV-3 were introduced in Roraima; and DENV-1, DENV-2, and DENV-3 were identified for the first time in the state of Pará. In the period from 2000 to 2004, DENV-2 and DENV-3 were introduced in the states of Maranhão and Santa Catarina, whereas Acre, Paraíba, and Sergipe stood out with the concomitant introduction of serotypes DENV-1, DENV-2, and DENV-3. Between 2010 and 2013, three serotypes were again introduced in Rio Grande do Sul: DENV-1, DENV-2, and DENV-4 (Figure 2 and Table 1).

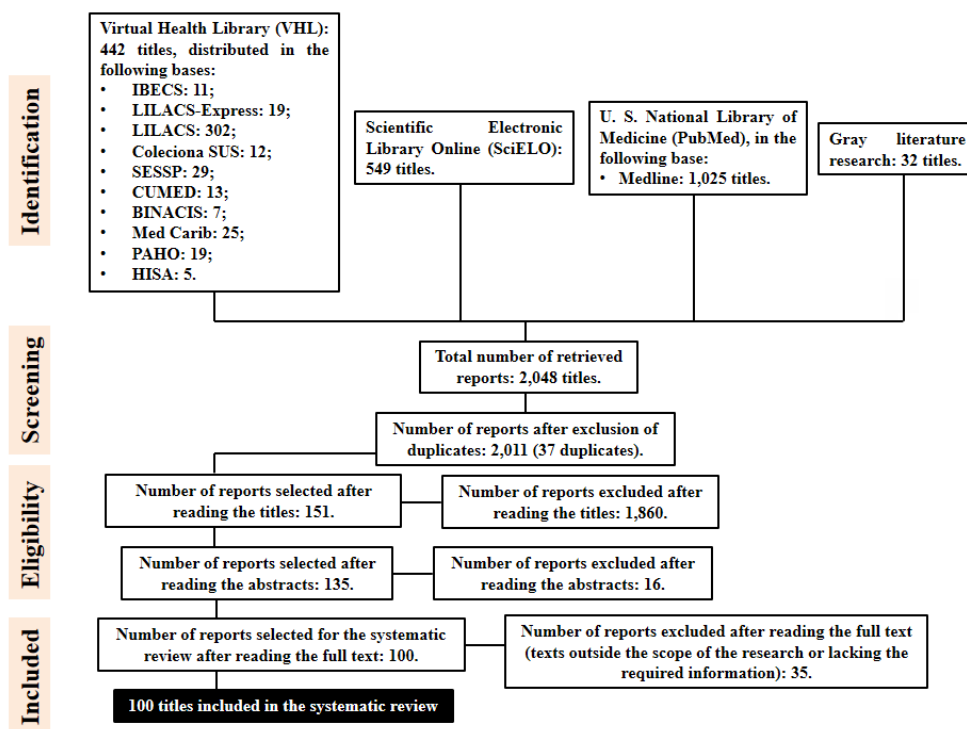


Figure 1. Flowchart of the systematic review of studies on the introduction of Dengue virus (DENV) serotypes in Brazil and its federative units published between 1980 and 2018.

Table 1. Years of entry of Dengue virus serotypes in Brazil by federative unit, according to the publications from 1980 to 2018 selected for this systematic review.

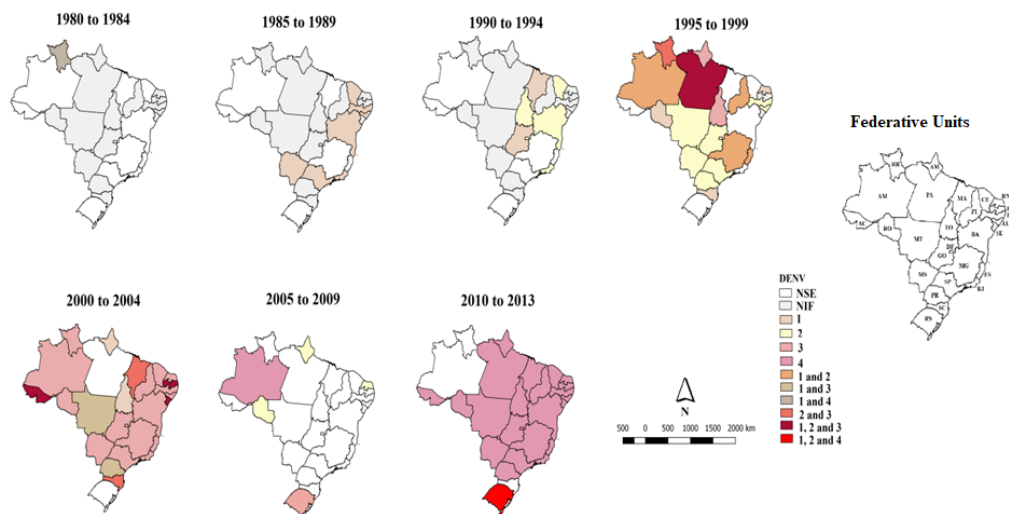
Regions and federative units	Year of entry of each serotype			
	DENV-1	DENV-2	DENV-3	DENV-4
<b>North</b>				
Acre	2000	2000	2004	2012
Amapá	2001 <sup>a</sup>	2006 <sup>a</sup>	1999 <sup>a</sup>	2012 <sup>b</sup>
Amazonas	1998	1998	2002	2008
Pará	1995	1997	1999 <sup>a</sup>	2010
Roraima	1981	1999 <sup>a</sup>	1999 <sup>a</sup>	1981
Rondônia	1999	2006	2004	2013 <sup>b</sup>
Tocantins	2000 <sup>a</sup>	1991	1999 <sup>a</sup>	2011 <sup>b</sup>
<b>Northeast</b>				
Alagoas	1986	1995	2000 <sup>a</sup>	2012 <sup>b</sup>
Bahia	1987	1994	2002	2011
Ceará	1986	1994	2002	2011
Maranhão	1994	2001	2002	2011
Paraíba	2001 <sup>a</sup>	2001 <sup>a</sup>	2002 <sup>a</sup>	2012 <sup>b</sup>
Pernambuco	1987	1998	2002	2011 <sup>b</sup>
Piauí	1999 <sup>a</sup>	1995	2002	2011 <sup>b</sup>
Rio Grande do Norte	1999 <sup>a</sup>	2008	2002	2011
Sergipe	2000 <sup>a</sup>	2001 <sup>a</sup>	2002 <sup>a</sup>	2012 <sup>b</sup>
<b>Southeast</b>				
Espírito Santo	1996	1995	2003	2013
Minas Gerais	1996	1998	2002	2011
Rio de Janeiro	1986	1990	2001	2011
São Paulo	1987	1996	2002	2011
<b>Central-West</b>				
Federal District	1998	1991	2003	2012 <sup>b</sup>
Goiás	1994	1999	2002	2011 <sup>b</sup>
Mato Grosso	2000 <sup>a</sup>	1995	2001	2011
Mato Grosso do Sul	1987	1996	2000 <sup>a</sup>	2012
<b>South</b>				
Paraná	2001 <sup>a</sup>	1995	2000 <sup>a</sup>	2013
Rio Grande do Sul	2010	2010	2007	2011
Santa Catarina	1999 <sup>a</sup>	2003 <sup>a</sup>	2002 <sup>a</sup>	NSI <sup>b</sup>

DENV: Dengue virus; NSI: no serotype introduction; <sup>a</sup>in the consultation of the experts, data on the years of entry were provided from 1999 onward; therefore, 1999 was considered the year of entry of the serotypes DENV-1, DENV-2, and DENV-3; <sup>b</sup>for serotype DENV-4, the information about the year of entry provided by the experts is correct, and this serotype started circulating in the country again in 2008 and spread to all states except Santa Catarina.

## DISCUSSION

Our systematic review provides an overview of the entry of the four DENV serotypes in Brazil and its federative units, from 1980 to 2018. The 100 publications evaluated refer to 25 of the 27 federative units distributed in the five Brazilian regions. Further information on the years of entry for the four DENV serotypes was obtained by consulting experts. Since the first laboratory-confirmed epidemic caused by serotypes DENV-1 and DENV-4 in 1981, there was a delay of nine years until the entry of serotype DENV-2 in 1990, and another nine years until the entry of serotype DENV-3 in 1999. Then, 27 years later, the serotype DENV-4 started circulating again in the country in 2008. As the literature refers to studies on dengue epidemics in Brazil in 1846<sup>10,11</sup> and in 1953 and 1954<sup>12</sup>, the authors believe that some of these serotypes may have been introduced in the country before the years presented in this study. However, according to the search criteria established in this systematic review, only published studies that provided proven scientific evidence of the years of entry were pooled.

Regarding the temporal distribution of dengue in Brazil, two distinct periods were observed. The number of cases reported did not exceed 100,000 from 1980 to 1990. After this period, the numbers gradually increased and reached more than one million



NSE: no serotype entry; NIF: no information found; 1: DENV-1; 2: DENV-2; 3: DENV-3; 4: DENV-4; 1 and 2: DENV-1 and DENV-2; 1 and 3: DENV-1 and DENV-3; 1 and 4: DENV-1 and DENV-4; 2 and 3: DENV-2 and DENV-3; 1, 2 and 3: DENV-1, DENV-2, and DENV-3; 1, 2 and 4: DENV-1, DENV-2, and DENV-4.

Figure 2. Entry of Dengue virus serotypes in Brazil by federative unit and considering periods of four (2010 to 2013) and five years (1980 to 1984, 1985 to 1989, 1990 to 1994, 1995 to 1999, 2000 to 2004, and 2005 to 2009), according to the publications between 1980 and 2018 selected for this systematic review.



in the last years<sup>7,122,123</sup>. This initial phase was characterized by localized and sporadic epidemic waves in urban centers, with the introduction of serotypes DENV-1, DENV-2, and DENV-4<sup>13,88</sup>. The Brazilian territory is characterized by the occurrence of dengue epidemics every two or three years. Since 1991, dengue fever has shown a seasonal pattern with peaks of notable epidemics in 1998 (507,715 cases), 2002 (696,472 cases), 2010 (1,011,548 cases), 2013 (1,452,489 cases), 2015 (1,688,688 cases), and 2016 (1,500,535 cases)<sup>124</sup>. This is due to the introduction of DENV-3, the resurgence of DENV-4, and the concomitant circulation of the four serotypes<sup>7,89,125</sup>.

Considering these peaks of epidemics, over the years, some Brazilian states have shown the introduction of two or more DENV serotypes in short periods of time. In the interval between 1995 and 1999, states of different regions of the country showed the introduction of serotypes DENV-1 and DENV-2 (Amazonas — North region; Piauí — Northeast region; and Espírito Santo and Minas Gerais — Southeast region), serotypes DENV-2 and DENV-3 (Roraima — North region), and serotypes DENV-1, DENV-2, and DENV-3 (Pará — North region). A similar occurrence was observed between 2000 and 2004, when serotypes DENV-2 and DENV-3 emerged in Maranhão (Northeast region) and Santa Catarina (South region), serotypes DENV-1 and DENV-3 were introduced in Mato Grosso (Central-West region) and Paraná (South region), and serotypes DENV-1, DENV-2, and DENV-3 were found circulating in Acre (North region), Paraíba, and Sergipe (Northeast region). The state of Rio Grande do Sul (South region) also showed the introduction of serotypes DENV-1, DENV-2, and DENV-4 in an interval of four years (between 2010 and 2013). The entry and transmission of DENV serotypes in different regions of the country can be explained by the number of municipalities infested with *Ae. aegypti* mosquitoes, the population mobility, and the rapid and unplanned urbanization that began in the 1990s<sup>125-129</sup>.

In addition, dengue epidemics have occurred more frequently in the Northeast region of the country, with a large number of serious cases and reported deaths. DENV-1 and DENV-2 showed different temporal patterns of introduction in nine states of the Northeast. DENV-1 was identified in 1986 and 1987 in the states of Alagoas<sup>47</sup>, Bahia<sup>49-52</sup>, Ceará<sup>55-61</sup>, and Pernambuco<sup>68</sup>, whereas DENV-2 was introduced in 1994 and 1995 in Alagoas<sup>47</sup>, Bahia<sup>49-52</sup>, Ceará<sup>55,57-61</sup>, and Piauí<sup>70</sup>. On the other hand, DENV-3 and DENV-4 were introduced around the same years in all federative units of this region, with concomitant occurrences in all states.

In the Southeast region, the state of Rio de Janeiro emerged with the highest number of dengue reports in 1986, when DENV-1 (33,568 cases) was introduced in this federative unit<sup>122,123</sup>. Since then, the state has always presented annual records of the disease<sup>124</sup>. It should be noted that the first case of DENV-2 identified in 1990 also occurred in this state<sup>89</sup>.

Moreover, among all the regions of the country, the Southeast presented the most complete information in the literature databases regarding the circulation of the four

DENV serotypes. It was noted that the years of introduction of DENV-1 were very similar in Rio de Janeiro (1986)<sup>86,87</sup> and São Paulo (1987)<sup>99</sup>. Similarly, DENV-2 was introduced in São Paulo in 1996<sup>99</sup> and in Minas Gerais in 1998<sup>81</sup>. The introduction of DENV-3 occurred in sequential years, beginning in 2001 in Rio de Janeiro<sup>92</sup>, in 2002 in São Paulo<sup>101</sup> and Minas Gerais<sup>81</sup>, and in 2003 in Espírito Santo<sup>79</sup>. In 2011, DENV-4 reached the states of Rio de Janeiro<sup>95</sup>, Minas Gerais<sup>84</sup>, and São Paulo<sup>100</sup>, finally reaching Espírito Santo in 2013<sup>80</sup>.

In the Central-West region, the entry of DENV-1 was verified in 1987 in the state of Mato Grosso do Sul<sup>114</sup>, and four years later the introduction of serotype DENV-2 was reported in the Federal District<sup>103</sup>. After a period of nine years, DENV-3 was registered in the region, particularly in the state of Mato Grosso<sup>108</sup>. Following the dynamics reported in other regions, DENV-4 was introduced in the states of Goiás (according to experts' consultation) and Mato Grosso<sup>112</sup> in 2011.

In the South, the entry of dengue followed a different pattern, with none of the serotypes being introduced in similar years in the three states. Although dengue has been reported in the Brazilian territory since the early 1980s, dengue fever was reported in the South region years later. DENV-2 was the first serotype to circulate in the region, introduced in the state of Paraná in 1995. DENV-1 was introduced in Santa Catarina in 1999, whereas DENV-3 was introduced in Paraná in 2000 (according to experts' consultation) and DENV-4 reached Rio Grande do Sul in 2011<sup>121</sup>. Until the conclusion of this research, no DENV-4 reports had been observed in Santa Catarina, thus indicating that this serotype did not reach the state yet (according to experts' consultation).

The wide climatic variability of Brazil is explained by the size of the territory, the extent of the coastline, altitude variation, and mainly by the presence of different air masses that modify the temperature and humidity conditions of the five regions<sup>130</sup>. These conditions favor the proliferation and maintenance of the country's primary dengue vector, *Ae. aegypti*<sup>47,131</sup>.

The states of the North are located in the area of the Legal Amazon and are mostly covered by tropical forest. Environmental factors, such as high temperatures and high humidity throughout the year and an extended rainy season, along with social elements, provide the ideal conditions for the proliferation of vectors and the consequent spread of diseases such as dengue<sup>26,63</sup>.

The Northeast is the poorest region of the country, and most of its states are situated in a semi-arid area, with sparse rains and poor sociodemographic conditions. In addition, these states suffer from limitations on water supply, high temperatures during most of the year, and present other environmental and ecological conditions that make them vulnerable to the introduction, reintroduction, or maintenance of the circulation of DENV serotypes<sup>64,127</sup>.

In the Southeast and Central-West regions, besides the meteorological conditions that may favor the vector, other factors, such as transport, tourism, sanitary conditions, and aspects related to population immunity, can favor the spread of the virus<sup>104,105,107</sup>.

The Southeast is the most developed and populous region of the country, whereas the Central-West is an area of agricultural-based economy on the southern border of the Amazon<sup>108,112,115,116</sup>.

The South is characterized by a moderate climate, which is colder than the rest of the country. Therefore, for many years, except for the state of Paraná, the region was spared of dengue epidemics<sup>120,121</sup>. Moreover, the incidence of autochthonous dengue cases is mainly seasonal: it increases between December and April, when conditions are favorable to the development of the vector<sup>120,131</sup>.

Overall, the present systematic review included important data. Although some epidemiological information on the introduction of DENV serotypes in a few federative units of Brazil was lacking, the performed literature research was as embraceable as possible and the selection of sources aimed at identifying all the relevant data. Nevertheless, this analysis has its limitations. Considering that the authors were only able to review the published data found by their search techniques, it is worth mentioning that isolated reports from some federative units may have escaped the author's attention and that other findings, mainly from the gray literature, are still lacking a more prominent place in the literature of the electronic databases.

Moreover, some publications of certain federative units reported the occurrence of dengue cases but failed to mention the viral serotype responsible for that outbreak or epidemic. Some authors report that laboratory support consisting of both serological analysis and viral isolation is considered the cornerstone of active dengue surveillance, particularly due to the need for precocious diagnostic confirmation of the first suspected cases in a non-endemic area.

In conclusion, dengue epidemics in Brazil have been attributed to the dissemination of different DENV serotypes, the permanent migratory flow of viral travelers, and the increase of vector infestation throughout the territory. In addition, urbanization probably had the greatest impact on increasing the occurrence of dengue within the country. Furthermore, continuous epidemiological surveillance is essential for the detection of new DENV lineages and for better understanding the regional patterns of dissemination of these viruses.

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