Review Article

Systematic Review of Dengue Detection and Diagnosis Methods from 2004 to 2023

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Abstract - Dengue is caused by the bite of an infected mosquito, leading to symptoms in humans such as fever, muscle aches, and headaches. In 2019, the World Health Organization reported 5.2 billion dengue incidents. Thanks to technology, there are methods for detecting and diagnosing dengue within a certain number of days after being bitten. The current study aims to analyze different dengue detection methods through a systematic review from 2004 to 2023. We adopted the hybrid PRISMA methodology, depicted in a flowchart, for data processing in the Scopus database. Boolean algorithms were used for searching documents related to dengue, followed by data processing using the R language and Biblioshiny libraries. This yielded 28,801 documents (articles, conference papers, and books), constituting 74.42%, 3.94%, and 0.12% of the total, respectively, discussing dengue and its detection methods. As a result, it becomes evident that countries like the USA publish a substantial number of documents, around 7,000, related to dengue, primarily due to substantial funding. However, the study does not reveal significant technological advancements for evaluating dengue detection, posing a challenge to healthcare centers regarding early diagnosis for the population affected by this infection.

Keywords - Dengue, Systematic review, Biblioshiny, Python, Scopus.

1. Introduction

On a global scale, dengue has had a significant impact on health. This arbovirus encompasses four serotype types, ranging from DEN-1 to DEN-4 [1], obtained from the dengue virus, and these are transmitted through the *Aedes Aegypti* and *Albopictus* vector types [2, 3]. In 2019, the World Health Organization reported 5.2 billion dengue incidences, divided into asymptomatic cases [4], mild symptomatic cases, and others due to misdiagnosis, all contributing to febrile illnesses [5]. Furthermore, this infection is termed endemic and occurs within the 100 countries encompassed by the World Health Organization (WHO) across Africa, the Americas, Southeast Asia, Eastern Mediterranean, and Western Pacific regions. By 2021, this viral disease will continue to impact countries such as Brazil, Colombia, the Philippines, Paraguay, Peru, and Vietnam. Presently, the global population is susceptible to acquiring this viral infection as it annually propagates between 100 and 400 million infections [5-8]. In Peru, the National Center of Epidemiology, Prevention, and Disease Control has mentioned the emergence of this virus since the 1990s, and its latent increase has been linked to stagnant water, rainfall, and climate change. From the year 2017 to 2021, the following statistical data has been reported: in 2017, there were 60,000 cases of dengue and 89 deaths; in 2018, the number significantly decreased to 4,698 cases and only 18 deaths;

while in 2019, it rose to 15,290 cases and 37 deaths. In 2020, there were 47,933 cases and 88 deaths; initially, in 2021, there were 48,296 cases and 45 deaths [9]. Based on this, the increase in dengue cases is evident each year, except for 2018.

On the other hand, a systematic review involves summarizing information in a structured manner to address a research question [10]. In other words, its main function is to address a research question using methodologies objectively. For this reason, it benefits the analysis and synthesis of scientific evidence [11, 12]. By employing systematic review, we provide information to timely detect dengue and enhance the response that can be offered by public health centers in the case of dengue. Therefore, the purpose of this research is to conduct a comprehensive mapping of dengue detection methods. The immediate spread of dengue often occurs during the summer seasons in a humid environment, which promotes the reproduction and life cycle of the Aedes mosquito. Dengue is transmitted to humans through a mosquito bite previously infected with the dengue virus [13]. The Pan American Health Organization mentions that one of the visible symptoms is fever, which can range from mild to severe, accompanied by headaches, muscle aches, and joint pains [14]. Until now, no cure has been found to treat this virus; however, global health

institutions state that immediate detection of this virus in the body reduces the mortality rate from severe dengue.

Furthermore, in [15] the rapid tests conducted in the early days of the dengue virus in humans, their objective is to determine the performance of the SD dengue DUO rapid test for the detection of NS1, IgM, and IgG in comparison to ELISA. Regarding the evaluated population, 286 serum tests were taken from dengue patients using both ELISA and the SD rapid test methods. The rapid test sensitivity yielded the following results: 68% for NS1 and IgM and 86% for IgG within the first three days. This indicates an improvement in its parameter from 75% to 87%, assuming no cross-reactions with other arboviruses were encountered. In conclusion, this research allows the SD rapid test to adequately detect NS1, IgM, and IgG, as indicated by the specificity and sensitivity values reported. It is recommended that this test be implemented in healthcare centers for immediate diagnosis. This study provides information on the efficient performance of one of the detection methods.

Additionally, in [16], another detection method is presented for the specific determination of dengue virus serotypes (RT-LAMP) to be viewed in real-time and in a single step. The purpose of this project is to establish the RT-LAMP test that is highly sensitive and specific for rapidly detecting and differentiating serotypes. They developed a primer mix for each of the serotypes present in the virus, allowing real-time monitoring of isothermal amplification at 63°C using a turbidimeter, yielding a result within 30 minutes. Its performance was evaluated in serum samples from infected patients, comparing it with other methods such as reverse PCR and virus isolation. The main outcome was that the RT-LAMP test demonstrated high sensitivity, detecting 100% positive cases and a specificity of 93% for dengue virus infection, surpassing the 87% and 81% of the respective mentioned detection methods. This method is concluded to be rapid, sensitive, and specific for detecting dengue serotypes. Thanks to this research, a valuable detection tool is added.

Similarly, a research team [17] discuss the rapid diagnosis of the dengue virus to improve clinical outcomes and initiate timely therapies designated to counteract this arbovirus in the human body. The main objective of this research is to evaluate the performance of ELISA and RDT tests for early virus detection. Their methodology included clinical tests in South America and isolation as a reference for evaluating sensitivity and specificity in the tests. The results yielded a sensitivity in RDT between 71.9% and 79.1%, whereas ELISA increased to a sensitivity of 85.6% to 95.9% on days 3-4 after acquiring the virus. In conclusion, ELISA demonstrates higher sensitivity for early virus diagnosis in the human body. This research contributes and benefits by allowing the observation and discrimination of the detection method with greater sensitivity, thereby improving virus diagnosis.

The El Niño phenomenon is one of the main triggers for dengue. Various studies show a correlation between the mosquito population and the El Niño phenomenon. The Pacific Ocean's influence on the surrounding climate leads to abrupt temperature changes and promotes the proliferation of various diseases, including the dengue virus. In [18], It mentions that the El Niño phenomenon, which involves disruptions in ocean and atmospheric circulation patterns, is one of the factors contributing to the transmission of the dengue virus.

This leads to increased environmental temperature and the extended extrinsic incubation period of dengue, consequently promoting its proliferation. Furthermore, [19] mentions that this phenomenon rapidly increases mosquito proliferation and makes humans more susceptible to acquiring this virus. In Peru, 192,000 cases of infections have been reported in the year 2023 so far, with the main cause being the Coastal El Niño phenomenon and the lack of proper healthcare attention to address these cases.

This is why our main objective is to understand, through a systematic analysis, the various methods of dengue detection. This is how the concern to understand various diagnostic methods for the Dengue Virus remains constant. Governments in Amazonian areas and those close to climates conducive to dengue proliferation require scientific evaluation and validation to achieve regulatory approval and incorporate these new dengue detection methods. The infrastructure to adopt a new detection method necessitates economic and political commitment, which impacts the training of healthcare professionals and public awareness. Unfortunately, access to these new technologies often comes after a disaster has occurred.

The present research will proceed to outline the methodology for addressing all information related to dengue virus detection. Subsequently, the main results analyzed from a number of documents will be presented. These documents will be read to establish validation between systematically found information and that which is selected by chance. Finally, a discussion will be presented, comparing the gathered information against the aforementioned research. Ultimately, corresponding conclusions and recommendations for future investigations will be proposed, marking a starting point for generating new knowledge within the community.

2. Methodology
2.1. Flowchart
A flowchart explains the procedures to be carried out, similar to [20], which is considered an essential tool for problem-solving, analyzing issues, proposing solutions, and resolving them. This tool serves as a guide to the development of our systematic review, complementing the methodology employed, as shown in Figure 1.
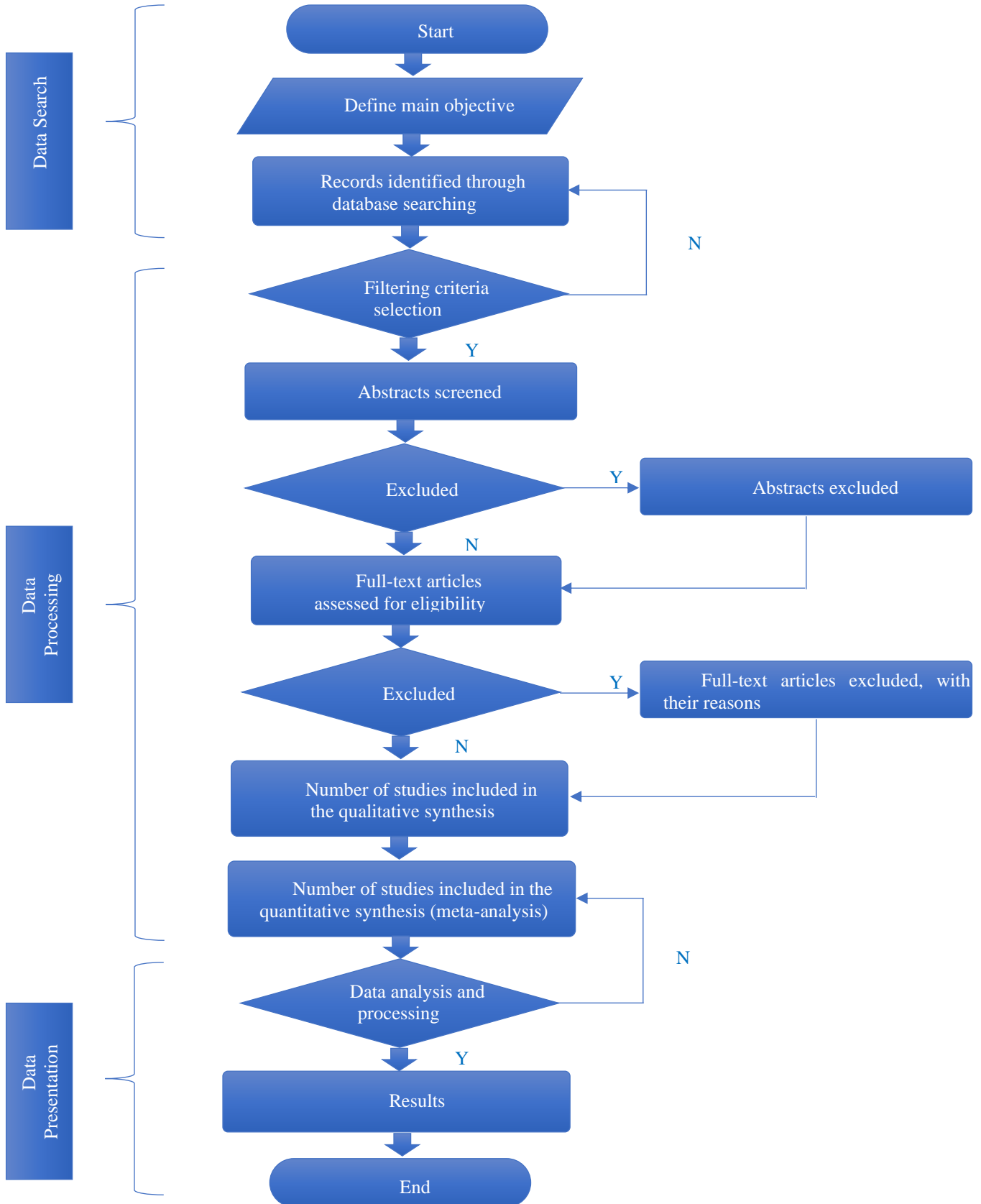
Fig. 1 Methodology flowchart

Table 1. Open access classification

Type	Documents
All Open Access	19875
Green	15287
Gold	11101
Bronze	5275
Hybrid Gold	1310

Data retrieval is the initial phase to initiate the process, where the main objective is defined, and records are identified through a comprehensive search using a database [21].

The second phase involves data processing, where the validation of selection filters is carried out. If this occurs, data screening is performed [22]. After the screening, a validation of data exclusion is performed to move on to the eligibility stage, where data exclusions and their reasons are also carried out. Finally, articles on qualitative and quantitative synthesis are included [23].

In the data presentation phase, the last stage of the flowchart, treatments and analyses from the second phase are validated. If performed, it displays the final results, thus concluding the process [24].

2.2. PRISMA
The methodology to be used is PRISMA, which enhances the identification and synthesis of dengue detection methods, provides a framework for conducting a systematic review, and ensures transparency in the search [25], [26]. This method provides a flowchart in four phases: identification, screening, eligibility, and inclusion [27], [28].

The previously mentioned phases are explained as follows: Phase 1 involves querying the database using logical operators AND and OR and removing duplicates [29]. In Phase 2, study relationships are evaluated for inclusion, and exclusion criteria are established [21], [26], [30]. Phase 3 involves a further review and resolution of discrepancies. In the final phase, it discusses analysis, sensitivity, and specificity [23].

2.3. Data Search
Thanks to the Scopus database, we can navigate and search for bibliographic references according to the filters we choose [31]. Therefore, this research is limited to searching for information on bibliometric reviews about the dengue virus and its detection methods.

In the extensive searches on Scopus, we used logical operators like OR and AND to refine the information search [32]. In [33], it explains the importance of using AND in their search, as when navigating in Scopus, the combined words with that operator must absolutely be present, making them mandatory words in the search results. Meanwhile, for [10], OR extends the information search further, and the words are not obligated to appear in the search results.

2.4. Data Processing
The selected information, limited to carefully chosen documents, will contribute to the quality of the analyzed and processed information [34, 35]. This is why, out of the vast amount of information provided by the Scopus database, only review articles, conference papers, and books will be processed [34].

The search algorithm will be based on a boolean search algorithm that, through its logical operators, will expand and narrow down the search into a specialized and targeted one [36]. This stage will also require manual intervention to add some important documents, such as letters or unclassified communications that provide relevant information for our main objective.

The information is processed using the R language through specialized libraries for bibliometric data analysis [37]. Following this, graphs will be generated to represent the information more comprehensibly and engagingly visually. Therefore, the platforms to be used will be RStudio with the Biblioshiny libraries, and for graphs, the Google Colab platform using numpy and matplotlib libraries[38, 39].

Biblioshiny: A library of the RStudio platform, created under the R programming language, aimed at analyzing bibliometric data from various databases [40]. Through its API, it can utilize the computer's resources to process data such as sources, authors, and documents and apply clustering methods or display K-structures. Biblioshiny is part of the Bibliometrix libraries, which offer an analysis package under validated instruments created by Massimo Aria and Corrado Cuccurullo, known as the K-synth team [37].

Matplotlib: A library created in 2002 with the goal of drawing and displaying graphs. This library uses Python scripts and is widely used by people working with mathematical calculations through Numpy [36, 41]. The components that these libraries work with include demonstrating color bars, labels, bar stacking, rotation, and capstyle for graphing categorical variables with specific functionalities [42–44].

Finally, through the Scopus platform, it is possible to quantify documents according to an Open Access classification, including Gold, Green, all open access, Gold, and Hybrid Gold.

2.5. Data Presentation
With the data already processed in Biblioshiny, the preparation for generating thematic maps was carried out, showing the number of journals discussing dengue detection methods [45, 46], as well as the citation count and the countries that have previously published on the aforementioned topic [47, 48]. Bar charts were created to illustrate the most widely used detection methods globally.

Additionally, a geographical map displaying the cases of dengue infection in Peru was generated. Finally, trend analysis graphs were created to depict the dengue case trends along with the dengue mortality rate.

3. Results

Conducting a systematic review of dengue detection methods using the hybrid PRISMA methodology is crucial. This approach aims to evaluate both existing diagnostic methods and recent technological advancements, highlighting their advantages and innovations by comparing their diagnostic effectiveness based on sensitivity and specificity. This will scientifically justify further studies or clinical applications in a substantiated manner.

3.1. Data Search

For the data search, gathering information based on the main objective, which is focused on a systematic analysis of dengue detection methods, was necessary. Additionally, selection criteria must be established, considering the diagnostic methods for dengue and the technological means that could be employed, such as machine learning, neural networks, big data, and artificial intelligence[49–51].

The following search algorithm is presented for the Scopus database based on the selection criteria:
(TITLE-ABS-KEY (dengue) AND TITLE-ABS-KEY (diagnosis) OR TITLE-ABS-KEY (transmission) OR TITLE-ABS-KEY (methods) OR TITLE-ABS-KEY (serology) OR TITLE-ABS-KEY (sensitivity) OR TITLE-ABS-KEY (specificity) OR TITLE-ABS-KEY (elisa) OR TITLE-ABS-KEY (pcr) OR TITLE-ABS-KEY (rt-pcr) OR TITLE-ABS-KEY (molecular AND techniques) OR TITLE-ABS-KEY (nat) OR TITLE-ABS-KEY (pcr-nested) OR TITLE-ABS-KEY (sample) OR TITLE-ABS-KEY (biological) OR TITLE-ABS-KEY (fever) OR TITLE-ABS-KEY (ns1 AND antigen) OR TITLE-ABS-KEY (epidemiology) OR TITLE-ABS-KEY (mortality) OR TITLE-ABS-KEY (children) OR TITLE-ABS-KEY (adults) OR TITLE-ABS-KEY (pregnant) OR TITLE-ABS-KEY (rural) OR TITLE-ABS-KEY (urban) OR TITLE-ABS-KEY (machine AND learning) OR TITLE-ABS-KEY (deep) OR TITLE-ABS-KEY (neural AND networks) OR TITLE-ABS-KEY (clustering) OR TITLE-ABS-KEY (big AND data) OR TITLE-ABS-KEY (automata) OR TITLE-ABS-KEY (convolution) OR TITLE-ABS-KEY (robot) OR TITLE-ABS-KEY (expert AND system) OR TITLE-ABS-KEY (forest) OR TITLE-ABS-KEY (artificial AND intelligence))

The following Boolean algorithm, TITLE-ABS-KEY (dengue) AND TITLE-ABS-KEY (diagnosis) serves as the primary function to remain obligatory in the search for information. As for the rest of the structures, which are mainly contained with the Boolean connector OR, they may or may not be present in the search results.

Table 2. Types of documents

Document Type	Items	Percentage
Article	26,403	74.42%
Review	4,193	11.82%
Conference Paper	1,397	394%
Letter	1,281	3.61%
Book Chapter	660	1.86%
Note	607	1.71%
Editorial	586	1.65%
Short Survey	312	0.88%
Conference Review	109	0.31%
Erratum	102	0.29%
Book	41	0.12%
Data Paper	15	0.04%
Retracted	5	0.01%

The Scopus database has allowed us to perform the search for information and incorporate our search algorithm thanks to its interactive platform. Scopus offers interactive search capabilities, and for applying the search algorithm, we have chosen to focus on Boolean connectors in Titles, Abstracts, and Keywords due to their versatility and high word match with our main objective. The primary search yielded 35,480 documents.

An important contribution of accessing Scopus information is that it provided us with a categorized quantification of the direct or indirect typification of reading. Table 1 shows the documents according to their Open Access classification, where certain article classifications fall into more than one category due to being Open Access but depending on registration for reading, causing Scopus to also classify it as Bronze or Green.

3.2. Data Processing

Information processing is characterized by filtering our information and having a classification bias to align more closely with the objective supporting dengue and its diagnoses. While the Scopus database provides valuable scientific information and documents, it includes correction or adaptation documents within its content, which would not contribute significantly compared to articles with important data presented in books. Among the over 35,000 scientific documents obtained by our Boolean algorithm, different types of documents are found, as shown in Table 2.

In order to systematically analyze the documents, only scientific documents of types such as articles, reviews, conference papers, and books were considered valid. On the other hand, with this new filter, the information processing remains robust, which is why an information cut will be carried out. The implementation of cutoffs is based on a historical analysis of information data compared with the historical bibliographic match given by the Boolean algorithm.
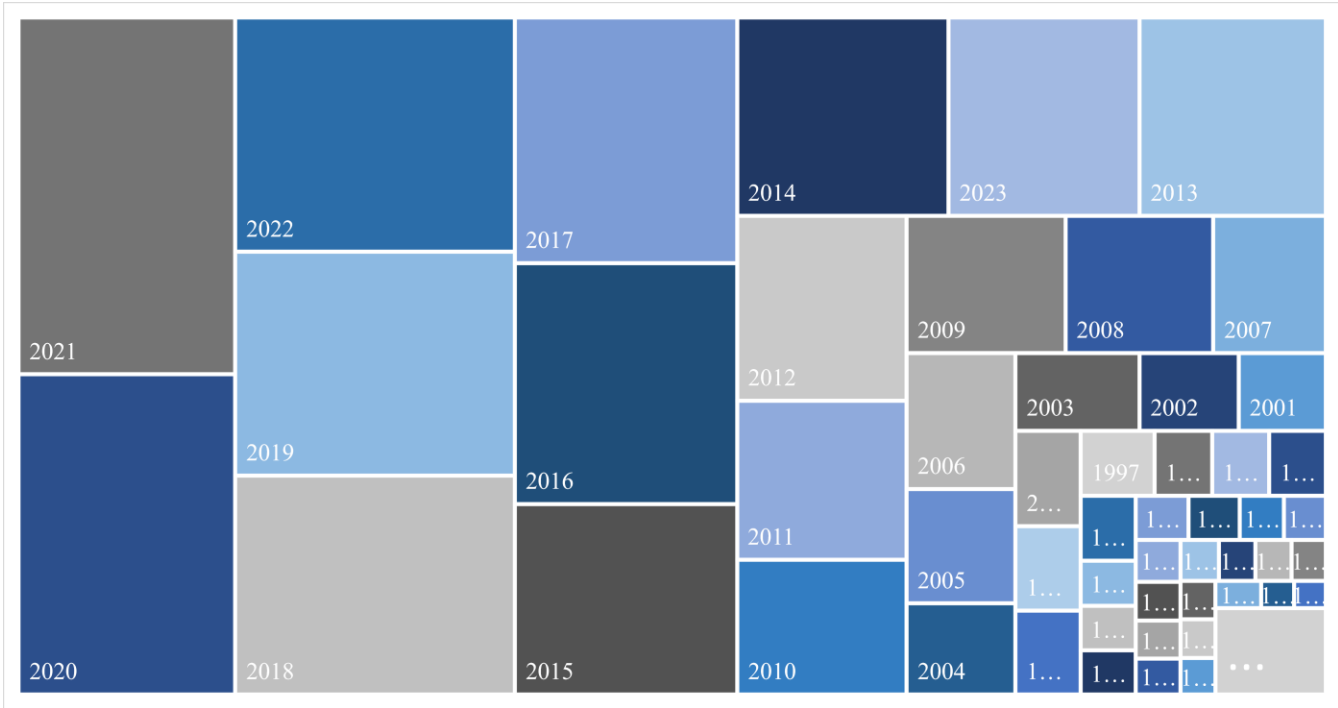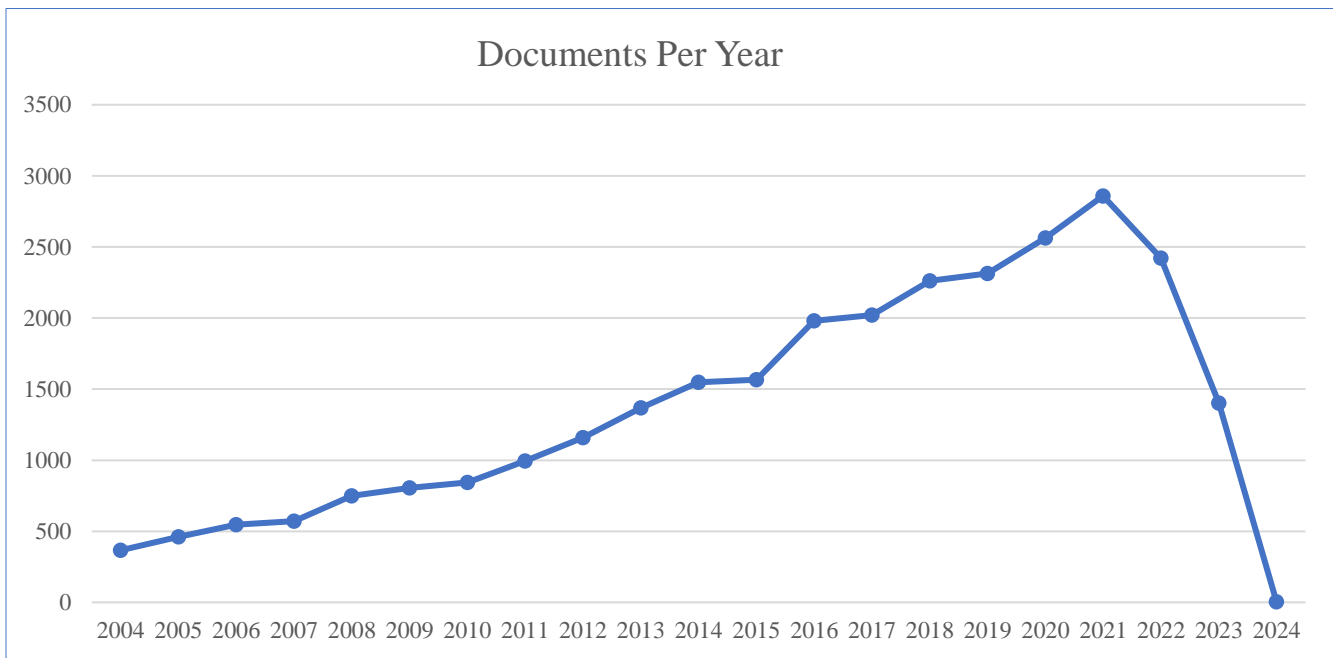
Fig. 2 Documents per year by source

Fig. 3 Documents by year

For this purpose, using Scopus's graphing tool, it was possible to analyze that in the year 2004, the first significant valley appeared in the information of the Boolean algorithm, which will be our starting point for processing bibliometric information.

On the other hand, Scopus offers bibliometric information compatible with systematic analysis platforms through BIBTEX file extensions. With the new data processing, 28,801 documents were obtained.

The newly obtained data was graphed using the graphical functions of matplotlib through its graphic and classifying components by converting the Bibtex file to CSV. Relationships were then analyzed among the number of documents and applications, authors, countries, subject areas, and years of publication.

3.3. Data Presentation

As a final result, it was possible to work with 32,694 documents. Thanks to Biblioshiny, which accepts .bib files, and Matplotlib through Python scripts, graphical results were obtained.

In Figure 3, a historical record of documents per year related to our search algorithm, which aims to understand dengue diagnoses, can be observed. It can be noted that scientific production followed a linear progression. Additionally, there is a growth following events like the El Niño phenomenon, with increases approaching around 20% more than the previous year. In 2022, there is a decrease in

article production, which can be interpreted as indicating no significant climatic events in 2021. On the other hand, in 2023, the full extent of articles cannot be seen since the analysis only includes data up until July.

Furthermore, in Figure 4, a donut chart displays a total of 28,801 documents, of which 22,934 are scientific articles, representing 79.6%. Following this, there are 3,883 reviews, accounting for 13.5%. Subsequently, we have book chapters with a total of 655, constituting 2.3%. Lastly, 38 books, representing 0.1%, are included within the search algorithm outlined by our objectives.
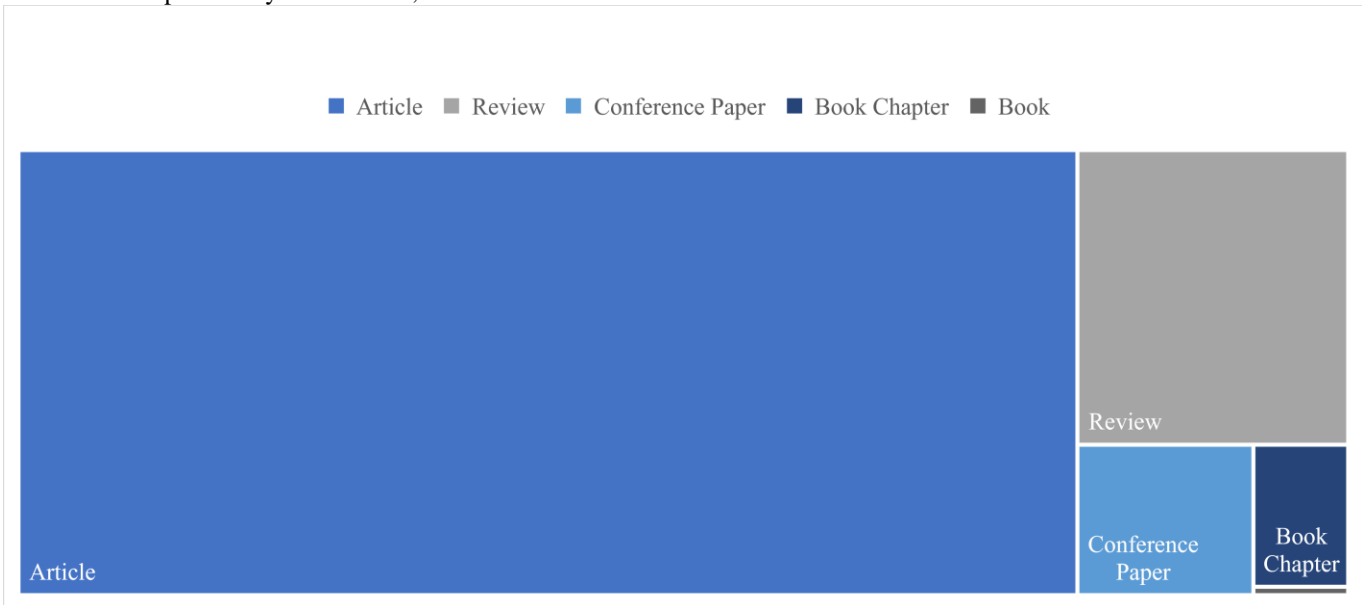
Fig. 4 Documents by type
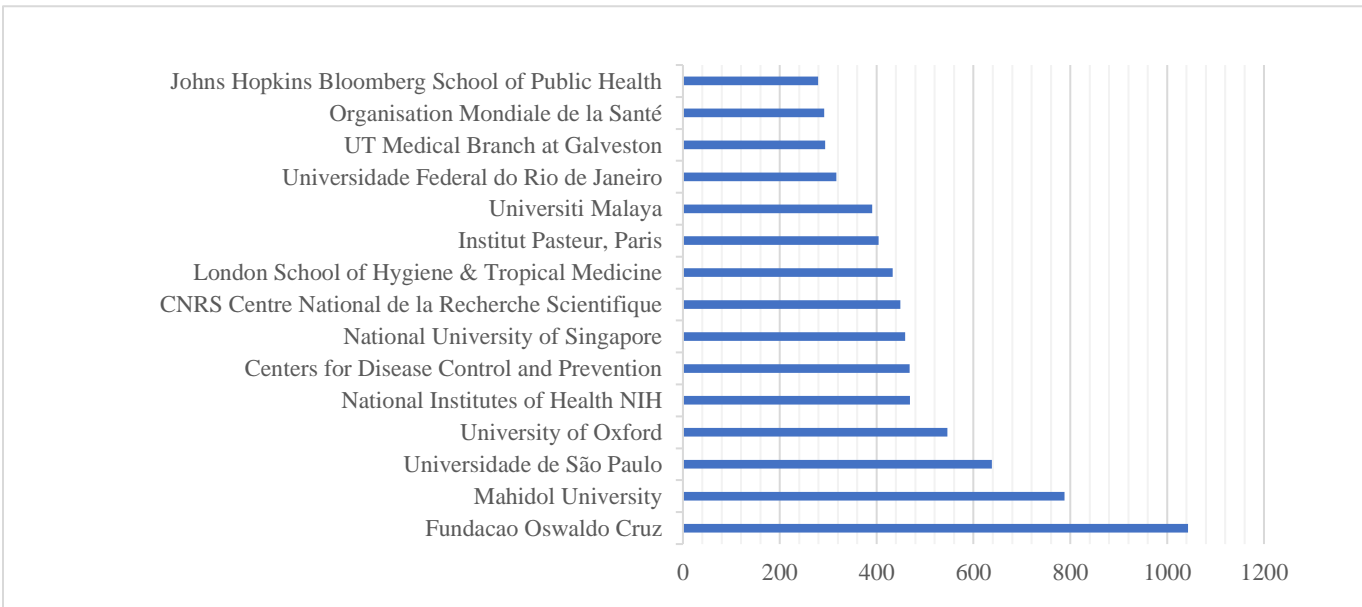
Fig. 5 Documents by affiliation

Affiliations are a crucial aspect in the detection of dengue diagnoses, as they allow us to visualize the entities that are most actively researching a specific topic. Therefore, in Figure 5, the 15 entities that conduct the most research on dengue and its detection are displayed. Standing out among them is the Oswaldo Cruz Foundation, located in Brazil and dedicated to medical research, with 1043 documents. Following that is the University of Mahidol in Thailand, with 788 documents. The University of São Paulo comes next with 638 documents. It is worth noting that these affiliations belong to countries with a history of dengue. This prevalence will also be reflected in authors and countries most engaged in related research.

In Figure 6, the territories that investigate dengue diagnosis the most are shown, with the United States standing out with 7,128 documents found between 2004 and 2023, followed by India with 3,936 documents and Brazil with 3,327. As mentioned before, the countries that have a higher incidence of dengue are the ones found in this research. However, the United States is not part of this group, as it is not a critical region for dengue, but it does have highly specialized laboratories. On the other hand, the United States has a larger economic budget compared to other countries, and there was a prevalence of authors publishing scientific documents from dengue-affected countries but with affiliation to the United States.
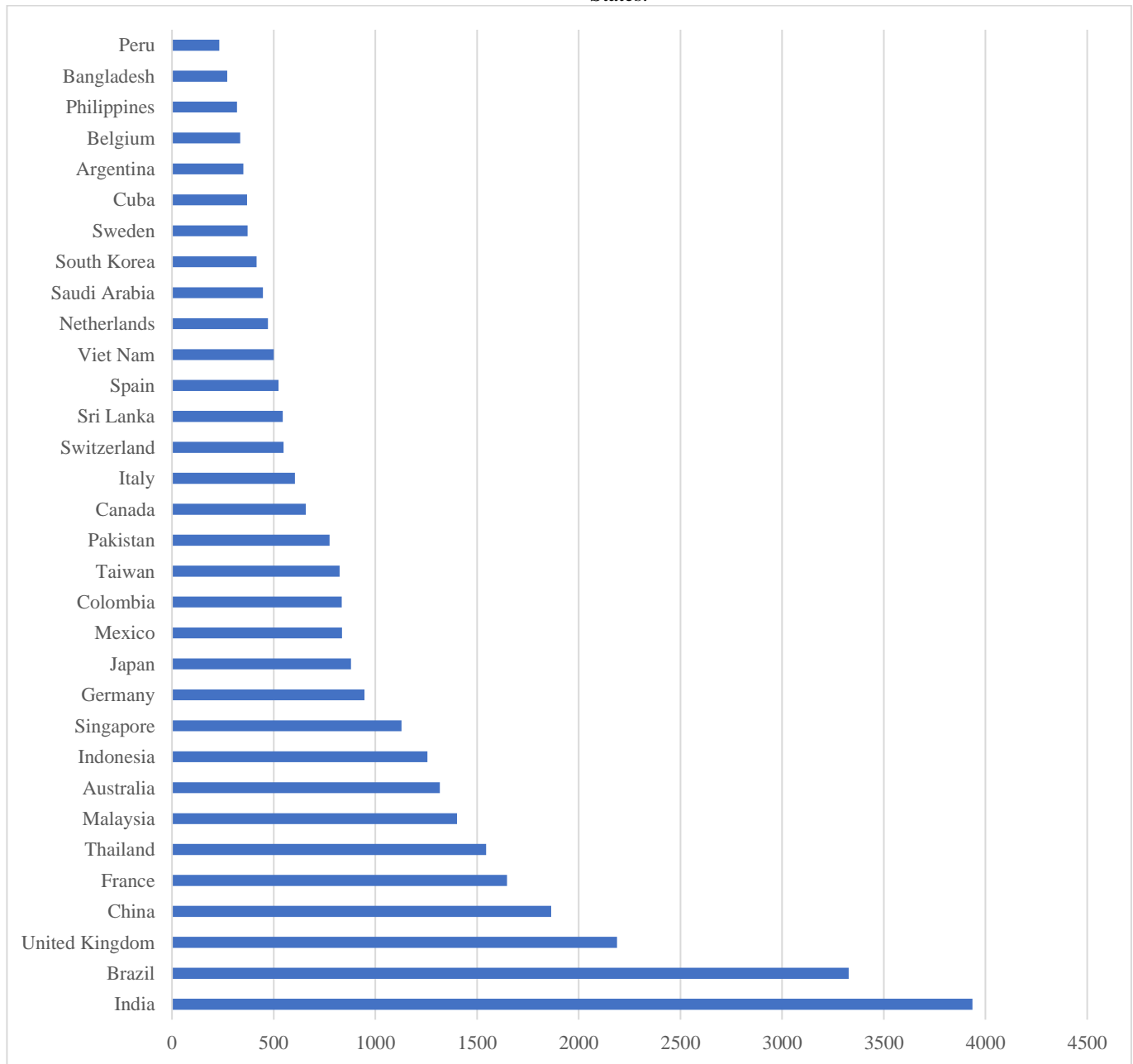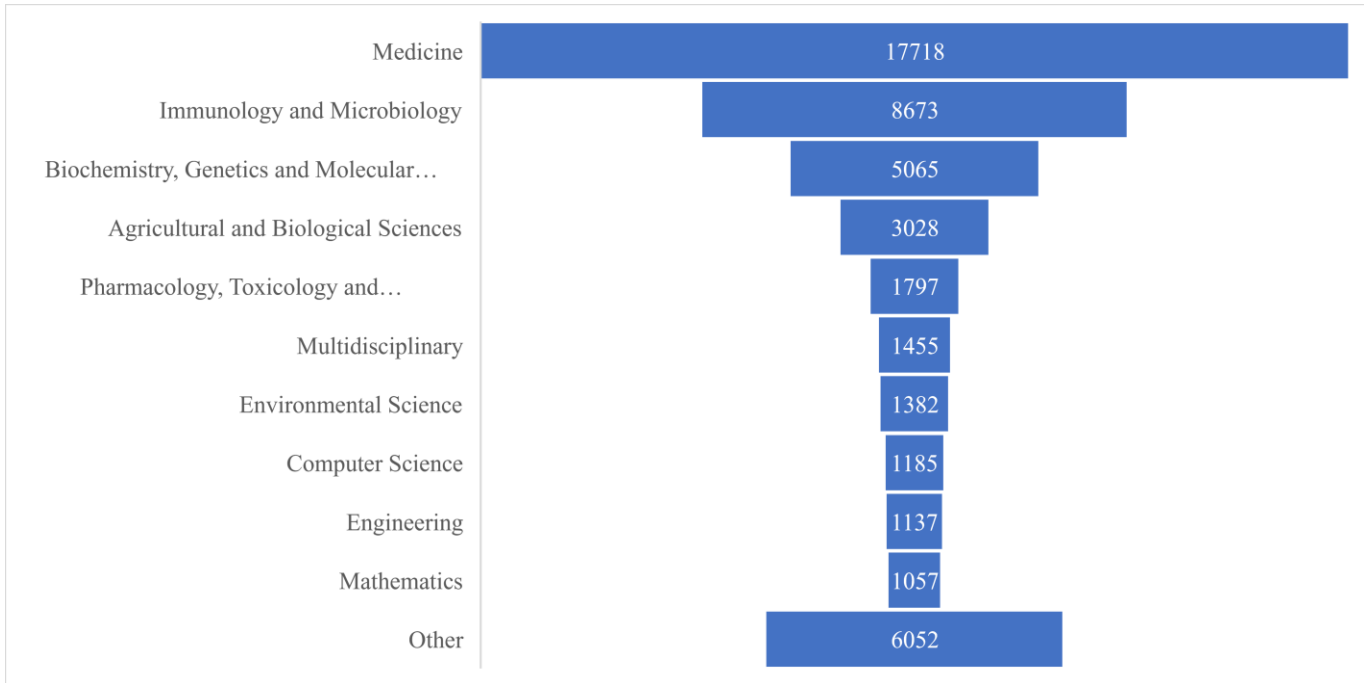

Fig. 6 Documents by country

Fig. 7 Documents by subject area

Regarding the areas with the most scientific documents related to our objective, we have medicine with 17,718 documents, accounting for 36.5%. Followed by immunology and microbiology with 8,673 documents, corresponding to 17.9%. Biochemistry, genetics, and molecular biology contribute 5,065 documents, making up 10.4%.

The graphed information indicates that the areas corresponding to natural sciences have the highest number of publications. Finally, in line with our objective, engineering contributes 1,137 scientific documents, representing 2.3%. Similarly, computer science contributes 1,185 documents, encompassing 2.4%.
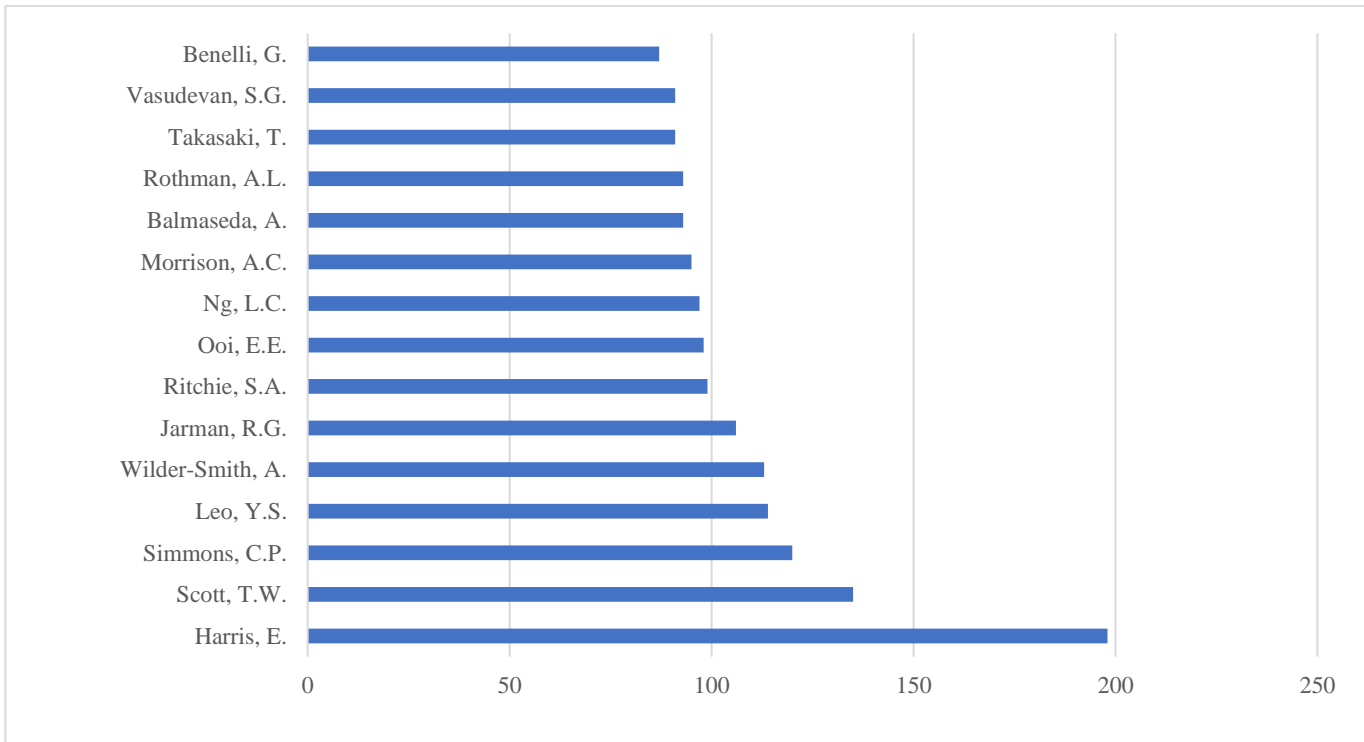

Fig. 8 Documents by author

Based on their specialities, authors exhibit a high publication rate, with Harris E. standing out with 198 documents related to dengue and its diagnostics. Following closely is Scott T.W. with 135 documents and Simmons C.P. with 120. Authors often align with affiliations and countries. In this particular case, the top three authors are from the United States. As observed in the previous figures, these authors contribute significantly to the number of publications.

4. Discussion

The found and published documents suggest that dengue remains an important topic in society. For this reason, various types of scientific documents, such as reviews, conference papers, and books with their respective chapters, were included to address this issue's manifestations comprehensively.

A total of 28,801 scientific documents were evaluated and compared to [8], who found comparative evidence with 286 serum tests. According to their strategic quantification methods, they discovered that ELISA stands out among the main tests. However, our approach found more relevant data regarding the global diagnosis of dengue from 2004 to 2023.

On the other hand, in [9], a method for determining serotypes is presented using RT-LAMP tests with their innovative way of detecting dengue and high specificity. These results contribute to the objective of this research, where much of the information found is related to obtaining a detection method with high sensitivity and specificity.

Finally, in [10], it is found that the sensitization of RTD and ELISA has become the norm for dengue detection in Latin American countries. However, through our search, we encountered other methods with higher sensitivity. It would only be necessary to find a method for mass production to commercialize these tests and for political representatives to adopt this new technology in their healthcare systems for more accurate dengue detection.

Examining the historical production of publications provided a clearer picture of where to direct the information processing. While the countries with the most research are the United States and India, it is also worth mentioning that Peru, as one of the countries with a high dengue death rate, has only 233 documents between 2004 and 2023. This highlights a significant need for research and publications in those areas. However, this investigation lacks an analysis of dengue reports and their main diagnoses referring to state entities that do not index their information as scientific documents in the Scopus database and only present information through national platforms.

The annual publication count gives us an extensive view of how scientific research has evolved over the years. The evolution of publications is emphasized in the context of severe climatic cases and high dengue outbreaks in tropical regions worldwide.

Furthermore, collaborations are evident, such as in the case of Brazil [44], where national universities and institutes address information retrieval through issues faced in different regions of the country, or interinstitutional alliances, as seen in the affiliations of the Oswaldo Cruz Foundation and the United States [13].

Regarding the authors who conduct the most research, a direct relationship is observed between the countries that conduct the most research, such as India and the United States, and the quantity of publications per author. However, there is no straightforward relationship between the countries most affected by dengue and those conducting the most dengue research. Economic factors and technological limitations explain these disparities.

Lastly, this research lacked an analysis of respective CiteScores and Source-Normalized Impact per Paper (SNIP) to bias journal publishing with high impact indexes and relative impact quantification or appropriate percentiles for selection. Although Scopus offers document selection based on Open Access categories such as Green, Bronze, Gold, and Hybrid Gold [31], these are insufficient to determine whether certain publications have a high impact. Nevertheless, the analysis of the most cited documents according to our Boolean search algorithm and the Scopus platform was accomplished.

5. Conclusion

The present research achieved its objective of understanding the global reality of dengue and its diagnostic methods through systematic analysis. A total of 28,801 scientific documents were processed, including articles, reviews, conference papers, and books. The data obtained from Scopus in Bibtex format and processed using the R language and Biblioshiny libraries yielded analyzed data from a historical perspective, narrowing the research scope to the last 20 years, starting from 2004 and ending on July 31, 2023. Additionally, it was found that the highest number of scientific documents related to dengue detection methods was in 2021.

Moreover, it was discovered that the United States is the country conducting the most dengue research, a relationship closely tied to its economic capacity. On the other hand, a relationship between affiliations and tropical countries, such as Brazil and its substantial volume of published documents, was observed.

Finally, the studied papers revealed a lack of consistent trend towards developing a dengue detection device and limited use of artificial intelligence or various forms of machine learning. However, it is worth noting that there is a year-on-year increase in scientific documents related to

dengue. Furthermore, various entities are making efforts to support vulnerable populations in tropical regions, as seen in Brazil.

As a future direction, it is proposed to enhance this research by cross-referencing information from the Web of Science. Additionally, the intention is to initiate a starting point for dengue research in Peru, encouraging the creation of scientific production in this area and fostering innovation in the development of a device that employs novel techniques for dengue detection. The aim is to mass-produce this device, supporting vulnerable individuals affected by this disease.

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