Spatial Analysis of Mosquito-Borne Diseases in Europe: A Scoping Review Protocol

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1. Introduction

Currently, due to climate change, deforestation, environmental degradation, urbanization, human mobility, globalization, and changes in public health practices, the incidence of vector-borne infectious diseases has been increasing [1]. This upsurge is due not only to these factors, but also to genetic alterations found in infectious agents and to greater resistance acquired by the vectors to insecticides [2]. Some of these factors explain the emergence of vectors and vector-borne diseases in new regions, namely in areas of the northern hemisphere, and a growing incidence in endemic areas [1].

Vector-borne diseases are human diseases caused by parasites, viruses, and bacteria that are transmitted by vectors. Mosquito vectors are living organisms, which can transmit pathogens of humans or animals to humans. These vectors are blood-sucking insects, which ingest disease-producing microorganisms during a blood meal from an infected host (human or animal) and then transmit them to a new host after the pathogen

has replicated. Often, when a vector becomes infectious, it is able to transmit the pathogen for the rest of their life with each subsequent sting/blood meal [3].
The diversity of mosquito-borne pathogens [4] and a decline in vector control efforts [5] have led to global increases in mosquito-borne disease transmission in recent decades [6]. Malaria, Dengue, Zika, Chikungunya and other vector-borne diseases infect more than one billion people and cause more than one million deaths each year worldwide [3]. Mosquitoes are dipterous insects from the Culicidae family [7], and are one of the most important vectors because, more than any other group of organisms, they are the biggest indirect cause of morbidity and mortality among humans [1]. Among the mosquito-borne diseases, given their importance in Europe and as emerging zoonoses, stand out Dengue, Chikungunya, Yellow Fever and Zika, caused by viruses, and Malaria, caused by protozoan parasites [1]. Since the 1970s, mosquito-borne pathogens have spread to previously infection-free areas and have caused an increase in the number of infections in endemic areas. Viruses transmitted by *Aedes aegypti* mosquitoes and also by *Aedes albopictus* are a major threat to a third of the world's population and a growing public health concern [8].

Invasive mosquitoes are recognized by their ability to colonise new territories. Since the 90’s has been noticed an increase in the spread of invasive mosquitoes in Europe highlighting the introduction of *Aedes aegipty* in Madeira, Portugal in the 20th century, the presence of *Aedes albopictus* in most part of southern Europe, the distribution of *Anopheles* mosquito from Portugal to south-eastern Sweden and the propagation of *Culex pipiens* mosquito distributed all over Europe.

Epidemiology is one of the core disciplines of health geography, as well as other disciplines with interest in the distribution and determinants of health [9]. Spatial analysis tools and Geographic Information Systems (GIS) are increasingly used in surveillance and epidemiological investigation. Spatial modeling of invasive species has been a particularly relevant research topic in recent years, as the prevalence of vector-borne diseases has expanded considerably, due to the intensification of human mobility and intercontinental trade [10]. Despite the recognition of the extreme importance of the geographical factors (for example, urban agglomerations, land use, fauna and flora, climatic conditions, etc.), spatial analysis has only been considered a fundamental tool for the study and investigation of invasive species since the second half of the last decade [11].

Spatial analysis allows different ways of approaching the problem, namely: mapping areas of susceptibility, vulnerability and risk; studying habitat adaptability or dispersion patterns; crossing multi-source information and integrating it in predictive models; identifying and visualizing spatio-temporal co-occurrence across multiple clusters [12-14]; and estimating the dynamics of vector-borne diseases [15] such as disease spread rate, cyclical pattern, direction, intensity and risk of spread to new regions [14]. Ultimately, spatio-temporal analysis can facilitate surveillance of vector-borne diseases by informing public health authorities where to make resources available to mitigate outbreaks [14].

With the growing number of public health research studies, new spatial analysis methods have been developed specifically to be applied in epidemiological studies [16]. Despite this being an emergent and promising research topic, reviews summarizing a body of research studies that have employed spatial analysis methods on mosquito-borne diseases research are scarce and focus mostly on specific mosquito-borne disease, more precisely on Dengue [16-19]. Therefore, the identification, systematization and description of the spatial analysis methods, software and ecological variables used in the applications of spatial statistics to mosquito-borne disease investigation will be useful to geographers, epidemiologists, biologists, among other researchers.

Under this background, the objective of the present scoping review is to identify and describe the methodological approaches used in investigations of the spatial variation of mosquito-borne diseases and its potential influencing ecological factors (e.g., environmental, socioeconomic, and healthcare-related) within the existing literature. This scoping review will focus on studies from Europe because it is a territory of completely different features than African, South American and Asian countries (where mosquito-borne disease are more burdensome and endemic) and has been strongly affected by urbanization, climate change and human mobility, which led to a recent (re)introduction of the mosquitoes and affected the transmission dynamics of a wide range of mosquito-borne diseases.

2. Materials and Methods

The scoping review will follow the five-stage methodological framework proposed by Arksey and O'Malley [20] that included (1) identifying the research question and (2) the relevant studies; (3) selecting the studies according to inclusion criteria; (4) charting and interpreting data; and (5) summarizing and reporting of results. Results will be reported according to PRISMA-ScR (PRISMA extension for Scoping Reviews) [21].

(1) Identifying the research question

To guide the present review, we will foccus on the following main research question: 'which spatial analysis methods are used to investigate the spatiotemporal variation of mosquito-borne diseases in Europe and their biotic and abiotic factors that may relate to its presence?'

(2) Identifying the relevant studies

Searches will be conducted using the PubMed (http://www.ncbi.nim.nih.gov/pubmed), Scopus (https://www.scopus.com/) and Web of Science (https://www.webofknowledge.com/) from inception until September 2021.

We used the following set of keywords related with the methodological approach - "Spatial analysis", "mapping", "space-time", "geographic information system", "spatial cluster*", "spatio-temporal", "spatiotemporal", "geographic distribution" - a second set of keywords related with the disease, infection and/or vector - "encephalitis", "malaria", "dengue", "yellow fever", "West Nile", "Chikungunya", "Zika", "filariasis", "Sindbis", "Pogosta disease", "Karelian fever", "Ockelbo disease", "tularemia", "Mosquito" - and a last set of keywords to restrict the search to European studies (ECDC (European Centre for Disease Prevention and Control) definition) - "Europe", "Austria", "Belgium", "Bulgaria", "Croatia", "Cyprus", "Czechia", "Denmark", "Estonia", "Finland", "France", "Germany", "Greece", "Hungary", "Iceland", "Ireland", "Italy", "Latvia", "Liechtenstein", "Lithuania", "Luxembourg", "Malta", "Netherlands", "Norway", "Poland", "Portugal", "Romania", "Slovakia", "Slovenia", "Spain", "Sweden", "UK", "United Kingdom".

Then, all references will be imported into a reference management software (EndNote 20, Clarivate Analytics (Philadelphia, PA, USA)) and duplicates will be eliminated (The EndNote Team, 2013).

(3) Selecting the studies according to inclusion criteria

We will select studies that focused on mosquito-borne diseases and used spatial analysis methods. Studies will be excluded hierarchically on the basis of the following exclusion criteria: 1) study type (reviews, reports, abstracts, editorials, comments); 2) not written in Portuguese, Spanish, Italian, French, German or English; 3) not about mosquito-borne diseases/infections or their vectors; and 4) no spatial analysis was conducted. No temporal restrictions will be imposed.

Two reviewers (SM and AIR) will screen the titles and abstracts to identify studies that did not meet the inclusion criteria or without full-text available. Afterwards, full texts of potentially eligible studies will be read and those that did not meet the inclusion criteria will be eliminated. In case of divergent opinions between the two reviewers, consensus will be reached by a third reviewer (JR). New potentially relevant studies will be sought by forward and backward citation tracking of the articles included in the review.

The study selection process will be represented in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart [22].

(4) Charting and interpreting data

The results will be structured by general characteristics (e.g., country/region, year of publication); by themes according with the diseases and/or mosquitoes studied; by the scale of analysis (size of the spatial units) and geographic extent (global, continental, regional or local); type of outcome data used (notification or survey); methodology used for spatial analysis; and studied ecological determinants. Regarding the type of outcome data used, notifications correspond to data on diseases/infections that, by statutory requirements, must be reported to the public health authority whenever a case is detected, while surveys are typically sample-based and designed for research purposes or to assess the prevalence of infection/disease within a certain territory [23]. The methodology for spatial analysis will be divided in three main groups as proposed by Elliot & Wartenberg - disease mapping; geographic correlation studies; and disease clusters, and clustering [24]. Disease mapping studies commonly measure morbidity or mortality for small geographic areas through the use of smoothed or unsmoothed maps (e.g., graduated color maps, graduated symbol maps, heatmaps, etc.). Geographic correlation studies aim to examine geographic variations across population groups in exposure to ecological factors in relation to health outcomes measured on a certain geographic scale. Disease clusters and clustering studies consist of the investigation of excess of events above some background rate bounded in time and space.

Regarding the determinants, these will be grouped into two categories: biotic and abiotic. Biotic factors are related to, or caused by living organisms, and abiotic factors are relating to, or caused by the non-living part of an ecosystem that shapes its environment. To name a few, as biotic factors we have the vector abundance, host abundance, population density and as abiotic factors we have climatic and socioeconomic factors.

(5) Collating, Summarizing, and Reporting Results

We will synthesize the data according to the previously mentioned research question and scope of inquiry. Tables and figures will be created to systematize and summarize the information. Counts and proportions will be used to summarize study findings and characteristics.

3. Discussion

The Scoping Review of the Spatial Analysis of Mosquito-borne Diseases will generate an evidence map of the literature and provide a detailed summary of the methodologies applied in the study of the spatial variation of mosquito-borne diseases and the potential influence on ecological factors.

Due to the growing interest and methodological development for spatial Analysis of mosquito-borne diseases, a large number of studies must meet the search criteria. This process was undertaken to refine the research strategy as far as possible, given the high level and broad nature of this scoping review.

Although the search strategy has been clearly defined, some limitations in this scoping review are anticipated. Studies can be omitted if they are not indexed in the searched databases or if they are not available in English.

Overall, the scoping analysis will be used to generate an evidence map to identify, prioritize and select efficiently thematic areas for further analysis and evaluation concerning Europe. Subsequent reports and assessments that will be derived from this scoping review can be used t support policies and development programs for communication and outreach materials about the spatiotemporal distribution of Mosquito-Borne Diseases and the factors associated with these diseases.

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References

1. INSA, Doenças associadas a artrópodes vetores e roedores, M.S. Núncio and M.J. Alves, Editors. 2019, Instituto Nacional de Saúde Doutor Ricardo Jorge, IP - Departamento de Doenças Infeciosas - Centro de Estudos de Vetores e Doenças Infeciosas Doutor Francisco Cambournac: Lisboa.
2. INSA. Rede de Vigilância de Vetores - REVIVE. 2020; Available from: http://www.insa.min-saude.pt/category/areas-de-atuacao/doencas-infeciosas/revive-rede-de-vigilancia-de-vetores/.
3. WHO. Vector-borne diseases. 2020; Available from: https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases.
4. Beckham, J.D. and K.L. Tyler, Arbovirus Infections. Continuum (Minneap Minn), 2015. 21(6 Neuroinfectious Disease): p. 1599-611.
5. Floore, T.G., Mosquito Larval Control Practices: Past and Present. Journal of the American Mosquito Control Association. 22(3): p. 527-533.
6. WHO, A global brief on vector-borne diseases. 2014. p. 56.
7. Almeida, A.P.G.d., Os mosquitos em Portugal século XX. Acta Med Port, 2011. 24(6): p. 961-974.

8. Rossi, G., et al., The spread of mosquito-borne viruses in modern times: A spatio-temporal analysis of dengue and chikungunya. Spatial and Spatio-temporal Epidemiology, 2018. 26: p. 113-125.
9. Aikins, E. and A.I. Ribeiro, Elements of Health and Medical Geography. 2020.
10. Balcan, D., et al., Multiscale mobility networks and the spatial spreading of infectious diseases. Proceedings of the National Academy of Sciences of the United States of America, 2009. 106(51): p. 21484-21489.
11. Malone, J.B., et al., Use of geospatial surveillance and response systems for vector-borne diseases in the elimination phase. Tropical Medicine and Infectious Disease, 2019. 4(15).
12. Freitas, M.I.C. and L. Cunha, Cartografia da vulnerabilidade socioambiental: convergências e divergências a partir de algumas experiências em Portugal e no Brasil. URBE - Revista Brasileira de Gestão Urbana, 2013. 5(449): p. 15.
13. Beard, R., E. Wentz, and M. Scotch, A systematic review of spatial decision support systems in public health informatics supporting the identification of high risk areas for zoonotic disease outbreaks. International Journal of Health Geographics, 2018. 17(1).
14. Desjardins, M.R., et al., Space-time clusters and co-occurrence of chikungunya and dengue fever in Colombia from 2015 to 2016. Acta Trop, 2018. 185: p. 77-85.
15. Eisen, L. and S. Lozano-Fuentes, Use of Mapping and Spatial and Space-Time Modeling Approaches in Operational Control of Aedes aegypti and Dengue. PLoS Neglected Tropical Diseases, 2009. 3(4): p. e411.
16. Oliveira, M.A.D., H. Ribeiro, and C. Castillo-Salgado, Geospatial analysis applied to epidemiological studies of dengue: a systematic review. Revista Brasileira de Epidemiologia, 2013. 16(4): p. 907-917.
17. Aswi, A., et al., Bayesian spatial and spatio-temporal approaches to modelling dengue fever: a systematic review. Epide-miology and Infection, 2019. 147.
18. Louis, V.R., et al., Modeling tools for dengue risk mapping - a systematic review. Int J Health Geogr, 2014. 13: p. 50.
19. Odhiambo, J.N., et al., Spatial and spatio-temporal methods for mapping malaria risk: a systematic review. BMJ Glob Health, 2020. 5(10).
20. Arksey, H. and L. O'Malley, Scoping studies: towards a methodological framework. International Journal of Social Re-search Methodology, 2005. 8(1): p. 19-32.
21. Tricco, A.C., et al., PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Annals of Internal Medicine, 2018. 169(7): p. 467-473.
22. Moher, D., et al., Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Medicine, 2009. 6(7): p. e1000097.

23. Porta, M., A Dictionary of Epidemiology. Fifth edition ed. 2008, New York: Oxford University Press (OUP).
24. Elliott, P. and D. Wartenberg, Spatial epidemiology: current approaches and future challenges. Environ Health Perspect, 2004. 112(9): p. 998-1006.