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The Impacts of Climate Change on the Emergence and Reemergence of Mosquito-Borne Diseases in Temperate Zones: An Umbrella Review Protocol

As Alterações Climáticas e a (Re)Emergência de Doenças Transmitidas por Mosquitos nas Regiões Temperadas: Protocolo de uma Umbrella Review

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ABSTRACT

Introduction: Mosquito-borne diseases represent a global public health concern and are responsible for over 700 000 deaths globally every year. Additionally, many mosquito species have undergone a dramatic global expansion due to various factors, including climate change, and forecasts indicate that mosquito populations will persist in dispersing beyond their present geographic range, namely in temperate climates. The research literature on this topic has grown in recent years, including some systematic evidence synthesis. However, to provide a comprehensive overview of this growing literature needed for policy action, a summary of this evidence, including existing systematic reviews, is required. This study aims to undertake an umbrella review that explores the impacts of climate change on the emergence and reemergence of diseases transmitted by mosquitoes in temperate zones and the publication of the protocol is a fundamental step to ensure the credibility, transparency and reproducibility of this research.

Methods and Analysis: Studies published in scientific journals indexed by PubMed, EMBASE, Cochrane Library, Epistemonikos, and Web of Science Core Collection to be included in this umbrella review will meet the following criteria: the topic of study (climate change and mosquito-borne diseases), regions (temperate zones), study designs (systematic reviews and meta-analysis), language (any) and date (since inception until December 31st, 2023). Titles and abstracts from selected articles will be evaluated by two authors independently and any discrepancy will be resolved through consensus or, if not possible, through a third author. The data will be extracted, and the risk of bias will be evaluated. The quality of the methodology of the included reviews will be assessed using AMSTAR 2. A narrative synthesis will examine the included systematic reviews. The quality of evidence for all outcomes will be judged using the Grading of Recommendations Assessment, Development and Evaluation working group methodology.

Keywords: Climate Change; Meta-Analyses; Systematic Review; Vector Borne Diseases

RESUMO

Introdução: As doenças transmitidas por mosquitos representam um problema de saúde pública global, sendo responsáveis por mais de 700 000 mortes anualmente. Reconhece-se também que muitas espécies de mosquitos sofreram uma expansão global dramática por vários fatores, incluindo as alterações climáticas, e as previsões indicam que as populações de mosquitos persistirão na dispersão para além da sua atual distribuição geográfica, nomeadamente para regiões com climas temperados. A literatura científica sobre o tema tem crescido nos últimos anos, incluindo algumas revisões sistemáticas. No entanto, para fornecer uma visão abrangente desta literatura crescente necessária para a ação política, é necessário um resumo dessa evidência, incluindo das revisões sistemáticas existentes. O objetivo deste estudo é realizar uma revisão abrangente que explore os impactos das alterações climáticas na emergência e reemergência de doenças transmitidas por mosquitos nas regiões temperadas, e a publicação do seu protocolo constitui um passo fundamental para garantir a sua credibilidade, transparência e reprodutibilidade.

Métodos e Análise: Serão incluídos estudos publicados em revistas científicas indexadas pela PubMed, EMBASE, Cochrane Library, Epistemonikos e Web of Science Core Collection, que atendam aos seguintes critérios: tema de estudo (alterações climáticas e doenças transmitidas por mosquitos), regiões (regiões com clima temperado), desenhos de estudo (revisões sistemáticas e metanálises), idioma (qualquer um) e data (todos até 31 de dezembro de 2023). As revisões obtidas pela pesquisa serão analisadas de forma independente por dois autores e quaisquer discrepâncias serão resolvidas por consenso ou recorrendo a um terceiro autor. Os revisores extrairão os dados e avaliarão o risco de viés nos estudos selecionados. A AMSTAR 2 será utilizada como ferramenta de avaliação crítica da metodologia dos diferentes estudos. Uma síntese narrativa examinará as revisões sistemáticas incluídas. Posteriormente, a qualidade dos resultados será julgada usando a metodologia do grupo de trabalho de Avaliação, Desenvolvimento e Avaliação de Classificação de Recomendações.

Palavras-chave: Alterações Climáticas; Doenças Transmitidas por Vectores; Meta-Análises; Revisão Sistemática

INTRODUCTION

Vector-borne diseases (VBD) are infections that affect both humans and animals. They occur when a vector (such as mosquitoes, aquatic snails, blackflies, fleas, lice, sandflies, ticks, triatome bugs and tsetse flies) transmits an infectious agent (like parasites, viruses and bacteria) to a human or animal.[1]

More than 80% of the global population is at risk of vector-borne disease, with mosquito-borne diseases (MBD) being the largest contributor to human vector-borne disease burden, transmitting diseases such as malaria, dengue, Zika, West Nile virus infection, and Chikungunya.[2-4] Together they cause over 700 000 human deaths globally every year, which

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represents more than 17% of deaths from infectious diseases.[5,6]

Therefore, it is well recognized that MBD represents a global public health concern, spanning the whole continuum from low-income to high-income countries.[7] Nevertheless, socioeconomic factors are known to play a significant role, with a negative association between disease and the national gross domestic product per person.[4]

These diseases not only have major health impacts and an increased risk of mortality but cause substantial morbidity, disability and productivity losses. However, many diseases spread by mosquitoes can be avoided through preventive measures and community mobilization (Table 1).[5,8,9]

The Earth's climate is changing with increasing global temperatures projected. The magnitude will depend on the amount of heat-trapping greenhouse gases emitted, which directly influences the average global temperature.[10,11]

Climate change affects more than simply the environment; it poses a serious threat to human health. Growing global concerns about climate change highlight the need of developing mitigation and adaptation strategies.[12] In the field of infectious diseases, a key adaptation strategy is to improve surveillance of VBD. However, there is also a need for better surveillance, monitoring, and research to determine whether and how different vector-borne diseases are affected by meteorological patterns and climate change.[12]

The literature describes that many mosquito species have undergone a dramatic global expansion due to factors such as anthropogenic environmental changes, ecological plasticity, competitive aptitude, increased international trade and travel, rapid and unplanned urbanization, lack of surveillance and lack of control.[4,5] Specifically, the rise in global temperatures and precipitation patterns seems to be affecting the physiology of mosquitos, poikilotherm species (the environmental temperature influences their body temperature), by altering their ability to survive, reproduce, and transmit disease.[12,15-18] Furthermore, extreme climate events, such as floods and droughts, are expected to be more frequent and both contribute to areas of still water, which is a key factor for mosquito reproduction and can cause migration and displacement that increases human density.[19,20-22]

The latest forecasts indicate that mosquito populations that used to be seen exclusively in tropical and some subtropical climates will further disperse beyond their present geographic range, namely in temperate climates.[6,12-14,23,24]

While human life expectancy continues to increase and life years lost to infectious diseases decline, future threats of infectious diseases will probably emerge from diseases that have newly appeared in a population (emerging infections) or that have existed previously but are rapidly increasing in incidence or geographic range (reemerging infections).[25] Over the last two decades, nearly a third of all events linked to emerging infectious diseases were vector-borne, in particular, infections spread by mosquitoes.[12]

An integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems, recognizing the interdependence between each other's health as defined in the World Health Organization's 'One Health' concept, is required to address challenges such as the (re)emergence of infectious diseases and to find strategies to tackle them at all levels with holistic solutions.[26]

The research literature on this topic has grown in recent years, including some systematic synthesis of evidence. Nonetheless, to provide the comprehensive overview

Table 1 – Prevention and control from mosquitoes

Level	Action to reduce the risk	
Individual	Mosquito-avoidance	Avoid outdoor activities when mosquitoes are most active and high virus activity levels have been detected.
	Use of personal repellents	Use adequate insect repellents all day. Wear long-sleeved clothing. Sleep under an impregnated mosquito net.
	Removal of residential mosquito sources (breeding sites)	Empty, cover or throw out items that hold water weekly. Close windows and doors or use screens. Indoor residual spraying.
	Every traveler returning from a MBD endemic country to a country where vectors of MBD exist, should be extra careful during the first three weeks.	
Community	Community education and awareness	About prevention, symptoms, promote online resources, create partnerships with media and the community.
	Research and innovation	To discover new control methods and improve the existing ones.
	Vector control programs	Implement integrated vector management strategies.
	Environmental management	Reduce mosquito breeding habitats.
	Health systems strengthening	Improve access, surveillance, diagnosis, and treatment.

needed for policy action, a summary of this evidence, including existing systematic reviews, is required.[12]

This umbrella review will have a main objective: to define the impact of climate change on the emergence and reemergence of MBD in countries with a temperate climate. Our secondary interrelated objectives will be: (1) to characterize the extent, range, and nature of evidence synthesis on climate change and MBD in the temperate region; (2) to analyze the connections between climate change in the temperate regions and MBD; (3) to explore, if any, the strategies to mitigate the (re)emergence of MBD; (4) to evaluate the health burden; and (5) to characterize the economic impact.[27]

The publication of this study protocol aims to promote collaboration within the research community and is a fundamental step in ensuring the credibility, transparency, and reproducibility of this research.

METHODS AND ANALYSIS

This umbrella review (systematic review of systematic reviews) will follow the methodological guidelines published in a measurement tool to assess systematic reviews, AMSTAR 2. The AMSTAR 2 is a 16-item checklist designed to assist in the identification of high-quality systematic reviews of studies of healthcare interventions through a rating process that classifies the overall confidence of the results (high, moderate, low and critically low).[28]

This project was registered in the International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42023482368).

Eligibility criteria

We will identify systematic reviews and meta-analyses that correlate climate change with MBD in the countries of the temperate region.

Studies to be included in this umbrella review will meet the following criteria: topic of study (climate change and mosquito-borne diseases), regions (temperate regions), study designs (systematic reviews and meta-analysis), language (any) and date (since inception until December 31st, 2023). Articles that were not systematic reviews or meta-analyses and duplicated articles will be excluded. The eligibility criteria are shown in Table 2.

The Köppen-Geiger climate classification system will be used to define the regions with a temperate climate.[29] For countries with more than one classification, we will select the climate present in the regions with the highest proportion of the population. Countries will be organized according to their continent, income, healthcare system, and literacy rate.

Information sources

All articles published in scientific journals indexed by PubMed, EMBASE, Cochrane Library, Epistemonikos, and Web of Science Core Collection until December 31st, 2023, in any language, will be considered.

Search strategy

Comprehensive search strategies will be carried out in the aforementioned databases, under the guidance of a medical librarian skilled in conducting systematic review searches. A literature search strategy will contain controlled vocabulary [e.g., Medical Subject Headings-(MeSH)] and text word searches adapted to each one of the databases regarding its own special requirements. The search strategy to be used in PubMed is illustrated in Table 3. Furthermore, the reference list of included publications will be scrutinized to identify any additional pertinent studies.

Data management

Once the literature search is complete, the results from different electronic databases will be exported to EndNote to exclude duplication.

Selection process

Firstly, selected article titles and abstracts will be evaluated by two authors independently and will be screened considering the inclusion and exclusion criteria. At this stage, records meeting all inclusion criteria with the answer “yes” or “unclear” will proceed. Any discrepancy will be resolved through consensus or, if not possible, through a third author.

Then, a list of publications to be read in full-text will be created and evaluated, once again, by two independent authors, and will be screened using the inclusion and exclusion criteria again (at this point, “unclear” will not be an option). The justifications for exclusion will be documented.

The PRISMA flow diagram (Fig. 1) will be used to

Table 2 – Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Only systematic reviews or meta-analysis	Not a systematic reviews or meta-analysis
Studies that target diseases in humans	Duplicated articles
Studies that include countries from the temperate region	Non-human studies
Studies that explicitly connects climate factors and mosquito borne diseases	Primary research
Since inception until December 31st, 2023	Studies published in 2024
Any language	

Table 3 – Search strategy

PubMed/MEDLINE	
MeSH	"Vector Borne Diseases"[Mesh] AND ("Climate Change"[Mesh] OR "Environment"[Mesh] OR "Climate"[Mesh] OR "Weather"[Mesh] OR "Humidity"[Mesh] OR "Altitude"[Mesh]) Filters applied: Meta-Analysis, Review, Systematic Review OR
MBD and Vectors (All fields)	((('encephalitis' AND 'mosquito*') OR ('dengue' OR 'chikungunya' OR 'zika' OR 'west nile' OR 'west' AND 'nile' OR 'malaria' OR 'yellow fever' OR 'rift valley fever' OR 'leishmaniasis' OR 'arboviruses' OR 'mosquito-borne' OR 'mosquito' OR 'Aedes' OR 'albopictus' OR 'aegypti' OR 'atropalpus' OR 'japonicus' OR 'koreicus' OR 'Anopheles' OR 'Coquillettidia' OR 'Culex' OR 'Culiseta' OR Mansonia' OR 'Ochlerotatus' OR 'Phlebotomus' OR 'Stegomyia') OR 'mosquito-borne' OR 'mosquito')) AND
Temperate countries (All fields)	('temperate' OR 'temperate countries' OR 'temperate region' OR 'temperate zone' OR 'Albania' OR 'Argentina' OR 'Australia' OR 'Austria' OR 'Bangladesh' OR 'Belgium' OR 'Bhutan' OR 'Bosnia' OR 'Herzegovina' OR 'Bosnia and Herzegovina' OR 'Brazil' OR 'Bulgaria' OR 'Chile' OR 'China' OR 'Croatia' OR 'Denmark' OR 'Faroe Islands' OR 'France' OR 'Georgia' OR 'Germany' OR 'Greece' OR 'Hungary' OR 'Ireland' OR 'Israel' OR 'Italy' OR 'Japan' OR 'Kosovo' OR 'Laos' OR 'Lebanon' OR 'Lesotho' OR 'Liechtenstein' OR 'Luxembourg' OR 'Malawi' OR 'Malta' OR 'Monaco' OR 'Montenegro' OR 'Myanmar' OR 'Nepal' OR 'Netherlands' OR 'New Zealand' OR 'North Macedonia' OR 'Paraguay' OR 'Portugal' OR 'Romania' OR 'San Marino' OR 'Serbia' OR 'Slovakia' OR 'Slovenia' OR 'South Africa' OR 'South Korea' OR 'Spain' OR 'Switzerland' OR 'Taiwan' OR 'Turkey' OR 'United Kingdom' OR United States of America' OR 'Uruguay' OR 'Vatican City' OR 'Vietnam' OR 'Zambia') AND
Climate change (All fields)	('climate change' OR climate OR environment OR temperature OR warm OR droughts OR floods OR heatwaves OR rainfall OR precipitation OR 'land use' OR humidity OR rainfall OR altitude OR 'geographic information system') AND
Study design (All fields)	('systematic reviews' OR 'meta-analyses' OR 'reviews')

summarize the study selection processes.

Data collection process and items

One author will extract the data through the proposed form (Table 4) and perform a narrative analysis, and a second reviewer will check the extracted data.[27] Once again, disagreements will be resolved by discussion or by a third author. The overall process will be checked by a third and fourth author. References will be managed through EndNote.

This study will include mosquito-related infections with dengue virus, chikungunya virus, zika virus, west Nile virus, yellow fever virus, Rift Valley fever virus, arboviruses, encephalitis, leishmaniasis, and malaria. Therefore, these mosquitoes will include *Aedes* species, *Anopheles* species, *Coquillettidia* species, *Culex* species, *Culiseta* species, *Mansonia* species, *Ochletotatus* species, *Phlebotomus* genus and *Stegomyia* species.

Outcomes and prioritization

The primary outcome of this review is to identify the mosquito borne diseases that are emerging and reemerging due to climate changes in temperate zones. The secondary outcomes are: (1) to characterize the extent, range, and nature of evidence synthesis on climate change and MBD in the temperate zone; (2) to analyze the connections between climate change in the temperate regions and MBD; (3) to explore, if any, the strategies to mitigate the (re) emergence of MBD; (4) to evaluate the health burden; and (5) to characterize the economic impact.[27]

Risk of bias in individual studies

Two reviewers will independently assess the methodological quality of the included reviews using 'A MeaSurement Tool to Assess Systematic Reviews 2' (AMSTAR 2), a critical appraisal tool for systematic reviews.[28] In cases of disagreement, consensus will be reached through discussion and, if not possible, through a third reviewer.

Data synthesis

A narrative synthesis will examine the included systematic reviews. The data will be reported and organized in tables in a narrative form. Important data, such as study characteristics, findings, and key conclusions will be compiled into tables. Furthermore, a narrative synthesis will be carried out to provide a thorough description of the outcomes.

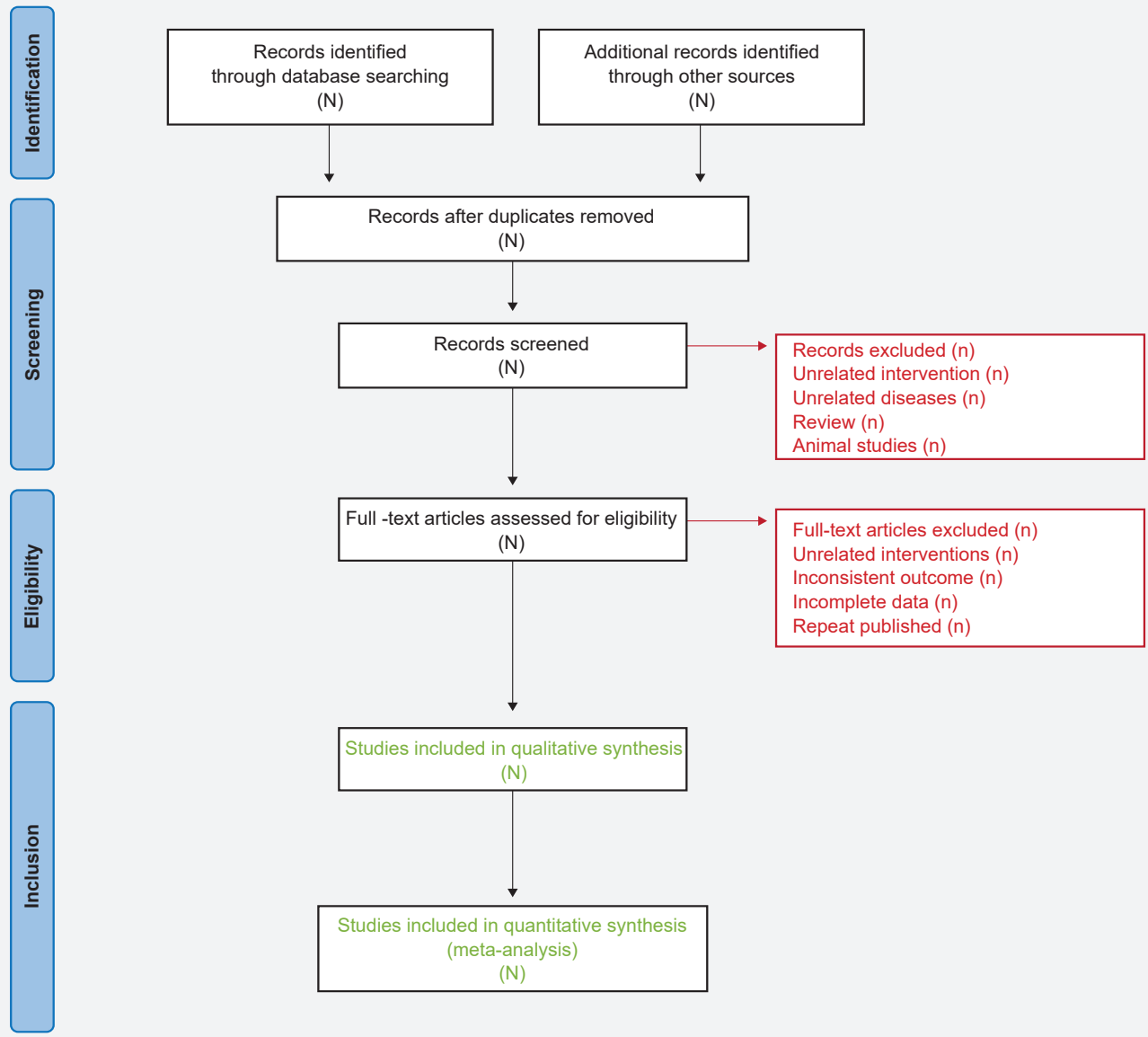

Figure 1 – PRISMA flow diagram

Meta-bias(es)

To determine whether reporting bias is present, we will determine whether the protocol of the reviews was published before the study was started. We will evaluate whether selective reporting of outcomes is present (outcome reporting bias).

Confidence in cumulative evidence

The quality of evidence for all outcomes will be judged using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group methodology. The quality of evidence will be assessed across the domains of risk of bias, consistency, directness, precision and publication bias. Additional domains may be considered where appropriate. Quality will be adjudicated as high (further research is very unlikely to change our confidence in the estimate of effect), moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low (very uncertain about the estimate of effect).

Table 4 – Proposed data extraction template, indicating domains for which reviewers will extract data

Research objective	Data extraction domains
To characterize the extent, range, and nature of evidence synthesis on climate change and MBD in the temperate region	• Name of record • Year of publication • Countries covered characterized by (i) name, (ii) continent, (iii) income, (iv) health system type and coverage, (v) literacy rate, (vi) % urban population, (vii) international arrivals, (viii) crop production • MBD • Mosquito species • Review methodology (systematic, meta-analysis) • Number of database searched • Date range of database searched • Date range of included primary studies • Type of primary studies included in the review (quantitative, qualitative, mixed-methods, other) • Number of primary research records reviewed • Aim of the study
To analyze the connections between climate change in the temperate regions and MBD	• Relationships examined between concepts (e.g., climate change broadly AND (re-)emergence of MBD in countries of the temperate region; increase temperature AND emergence of dengue in Portugal) and rationale for this examination • Proximal impact(s), if applicable • Intermediate impact(s), if applicable • Distal impact(s), if applicable • Specific climate change (e.g., rainfall, humidity, temperature, extreme events) • Scale of impact (e.g., sporadic vector findings, vector introduction, outbreaks, endemic) • Key findings about the relationships studied • Any further relevant data
To explore, if any, the strategies to mitigate the (re-)emergence of MBD	• Recommend strategies to address impacts, when possible, categorized as: (i) community-level or population-level; (ii) Regional-level or global-level; (iii) policy responses; (iv) future research
To explore, if any, the health burden	• Incidence and prevalence • Mortality rates • DALYs • QALYs
To explore, if any, the economic impact	• Direct medical costs • Indirect medical costs • Intangible costs • Economic impact on healthcare systems • Macroeconomic impact

DISCUSSION

This protocol is an important starting point for performing an umbrella review to identify the impact of climate change on the emergence and reemergence of diseases transmitted by mosquitoes in temperate zones. The publication of this protocol before carrying out the umbrella review enables a peer-review evaluation to improve the quality to the planned review.

The epidemiology of MBD is traditionally associated with environmental conditions, complicated by anthropological factors, which makes their control challenging.[19] To effectively address public health concerns, lower the burden of disease, and enhance the health and well-being of populations worldwide, stakeholders must have a thorough understanding of emergent and reemergent mosquito-borne diseases.[12]

This work is timely, given the growing body of literature on the relationship between health and climate change and the urgent need for synthesized data to guide international policies. Awareness of (re)emergent mosquito-borne diseases allows stakeholders to take immediate preventive actions. A thorough understanding of newly emerging diseases helps to set up a reliable surveillance system for early detection and to allocate resources effectively.[12]

There are some limitations, namely the fact that only systematic reviews and meta-analysis are going to be considered, and the quality of this umbrella review will ultimately reflect the quality of the underlying systematic reviews included.[30] However, the umbrella review presented in this protocol will provide one of the highest levels of evidence and a comprehensive summary regarding the impacts of climate change on the emergence and reemergence of diseases transmitted by mosquitoes in temperate zones in a transparent and structured format, allowing the detection of possible research gaps which will inform policymakers of the countries in the temperate zones on how to timely adapt to the diseases that are endemic in countries from the tropical and subtropical region areas. Furthermore, this research study will bring updated information about this topic to the scientific community, highlight methodological flaws in the previous studies, and highlight areas that require more investigation.

CONCLUSION

Mosquito-borne diseases represent a global public health concern, mainly because of the diversity of diseases that can be transmitted. Since many mosquito species have undergone a dramatic global expansion and are expected to persist in dispersing beyond their present geographic range, a transparent and systematic summary of the existing evidence is needed to assist the relevant stakeholders from the countries in the temperate zones.

The relevance of investigating this subject arises from the need to have a comprehensive overview of the growing literature required for policy action to tackle this emerging problem. It will represent an innovative study in the sense that it is the first umbrella review on this topic and the first review to include all temperate zones.[31]

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AUTHOR CONTRIBUTIONS

All authors contributed equally to this manuscript and approved the final version to be published.

COMPETING INTERESTS

SD has received consulting fees from Transmissible Public Health Consultancy (Q3/4 2022) for the development of Early Warning System prototype (unrelated to manuscript).

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All other authors have declared that no competing interests exist.

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