(Sero)Prevalence of (Re)Emerging Major Arbovirus Infections in Africa: A Systematic Review and Meta-Analysis Protocol

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Abstract

Background

Arbovirus infection outbreaks are becoming more common in Africa. However, it is still difficult and crucial to better understand arbovirus transmission patterns, disease trends, and burdens. The epidemiology of these infections—dengue virus (DENV), Zika virus (ZIKV), chikungunya virus (CHIKV), West Nile virus (WNV), Rift Valley fever virus (RVFV), and yellow fever virus (YFV)—is unfortunately not well understood. This review provides an epidemiological inventory of DENV, ZIKV, CHIKV, WNV, RVFV, and YFV infections in Africa, with helpful results for risk mapping and upcoming prevention and control initiatives.

Methods

This systematic review protocol implements the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and an expert-evaluated design and laboratory assay and reporting evaluation (DARE) concept. Two independent reviewers conducted preliminary literature searches in PubMed in May 2023 to improve the search keywords, strategy, and inclusion criteria while considering the context and scientific significance. The final search will be conducted using PubMed, ScienceDirect (SCOPUS), the Web of Science Core Collection, African Journal Online and Google Scholar. Two reviewers will simultaneously and independently conduct searches, screen studies, and extract data. Quality assessment will be performed by two independent epidemiology experts, and discrepancies will be handled by consensus or by consulting a third reviewer. Meta-analysis will be performed to determine the pooled estimates of arbovirus circulation and transmission patterns in Africa.

Discussion

In this review, we present an epidemiological inventory with information that will be relevant for risk assessment, future arbovirus infection outbreak prevention, and arbovirus infection outbreak control in Africa. This will include estimating the patterns, trends, and burdens of arboviral infection across Africa, as well as identifying the regions with the highest risk of transmission. This approach will be crucial for developing well-informed policies for epidemic prevention.

Systematic review registration

The review is registered and accessible at Prospero with the registration ID CRD42023434939.

Background

Over the past two decades, there has been renewed interest in studying infections caused by arboviruses. This is because of the increasing disease outbreaks resulting from dengue virus (DENV), zika virus (ZIKV), chikungunya virus (CHIKV), West Nile virus (WNV), Rift Valley fever virus (RVFV) and yellow fever virus (YFV) [1–6]. These incidents provide timely warnings of the potential for stable

zoonoses to appear and spread with grave public health consequences. Thus, there has been continued collaboration between Africans and international agencies to build capacities for arbovirus surveillance and discovery [1]. However, the current burden of these arboviral diseases has not been fully elucidated, and understanding the epidemiology of these diseases is an ongoing challenge for multiple reasons.

First, surveillance of arboviral etiologic pathogens related to common acute febrile illness is challenging, given that most attention has been given to the malaria response [7–9]. Second, there is limited availability of routine diagnostic procedures for Arbovirus screening and detection [10]. Third, all 47 countries in the African region have shortfalls in their capacity to cope with arbovirus outbreak preparedness, surveillance and control [11]. Fourth, there is inadequate political commitment, limited financial support, insufficient well-qualified human resources, limited technical and logistical resources and a lack of community awareness of arboviral diseases [11]. Generally, existing epidemiological data on Arboviruses reflect only areas with sufficient capacity to detect and report infections when they occur. This essentially constrains national and international priority actions toward pandemic prevention, preparedness, and response.

The transmission of Arbovirus infections results in either inapparent infection or symptomatic infections ranging from mild undifferentiated illness to arthralgia, mild to severe encephalitis, hemorrhagic fever, or death [12–15]. Zika, dengue, yellow fever and chikungunya infections have caused the most morbidity and mortality in recent decades [11, 15, 16]. Especially in Africa, there are increasing numbers of reports on arboviruses [1–6], where countries are usually caught off guard due to inadequate and inconclusive data for planning outbreak preparedness, surveillance, and control strategies. Most of the existing data are based on serological assays for reporting cases of infections, which reveal several reporting irregularities [1, 8]. Thus, there are generally widespread limitations in our capacity to cope with arbovirus outbreak preparedness, surveillance, and control [17]. Thus, it is important to harmonize existing data through comprehensive reviews to understand the transmission rates of DENV, ZIKV, CHIKV, WNV, RVFV and YFV infections in Africa.

During the preliminary search, we identified several existing reviews that highlight the emerging challenges of arboviruses and the need for enhanced surveillance systems [2, 4, 8, 10, 18–22] in Africa. We also found thorough reviews that sought to estimate the disease burden of just a single arbovirus pathogen at a time [23–34]. As this topic is still a challenge and a top priority in the African continent, our study will go above and beyond by providing an inventory of arbovirus transmission patterns, illness trends, and burdens, as well as identifying the locations at greatest risk of transmission. The objective of this review is to estimate the transmission patterns, burdens, and distributions of major arbovirus infections in human populations in Africa.

Review Question

Our review covered an expert-evaluated design, laboratory assay and reporting evaluation (DARE) concept with the following aspects:

Design

We considered studies that tested samples obtained from febrile patients, suspected cases, close contacts, or the general African population to evaluate the (sero)prevalence of active or passive arbovirus infections. This includes screening or identifying cases in medical facilities or the general community in observational studies, outbreaks, and surveillance investigations.

Assay

We considered seroprevalence studies using well-validated in-house immunoassays or those using detection kits approved by the WHO-Listed Authority-recognized National Regulatory Authority [Food and Drug Administration (FDA) and/or National Medical Products Administration (NMPA)] with or without internal validation. For surveillance investigations, we considered studies using molecular diagnostics with internal and/or external controls during assay procedures (endogenous controls, cloned cDNA targets, purified DNA products and synthetic DNA from the amplicon sequence).

Reporting evaluation

We focused on studies whose report provides evidence of presumptive active, confirmed active or passive circulation or transmission of DENV, ZIKV, CHIKV, WNV, RVFV and YFV among inhabitants of Africa within the African setting. This approach is restricted to only laboratory-confirmed surveillance case definitions.

Thus, we want to answer the following questions with this review:

1. What is the distribution level and pattern of arbovirus infections in Africa estimated via immunoglobin (Ig) G?
2. What is the transmission level of active and presumptive active arbovirus infections in Africa estimated via IgM, viral isolation, or molecular tests?
3. What is the level of evidence and regional distribution pattern of arbovirus infections in Africa?
4. Which arbovirus etiological agent has significant potential for causing outbreaks in Africa?
5. What is the etiology of cases or trends in serotype replacement of major arboviruses in endemic regions in Africa?

Methods

The proposed systematic review and meta-analysis will be conducted following the updated preferred reporting items for systematic reviews and meta-analyses (PRISMA 2020) [35].

Eligibility criteria

Primary Summary Outcome

The burden of (re)emerging arbovirus infections (DENV, ZIKV, CHIKV, WNV, RVFV and YFV) in Africa reported via (sero)prevalence studies.

Primary endpoints

(sero)prevalence or (sero)incidence of laboratory-confirmed active, presumptive active and passive infection with DENV, ZIKV, CHIKV, WNV, RVFV and YFV detected via RNA, viral isolation, immunoglobulin (Ig) M, and IgG testing.

The study types included were as follows: observational studies (cross-sectional studies and retrospective and prospective cohort studies) and epidemiological and outbreak surveillance studies and reports.

The inclusion criterion was as follows

Human incidence or prevalence studies reported in any African country.

Exclusion Criteria

1) Nonhuman prevalence or incidence, 2) Human incidence or prevalence studies reported in Africans living outside Africa, 3) case reports, case series, editorials, letters to editors, reviews, commentaries, qualitative studies, basic science research studies, 4) nonempirical research/modelled data, Randomized control trials

Case definitions

The reporting outcomes of the included studies were evaluated based on the following definitions:

1. *Confirmed or active infection*: a positive real-time polymerase chain reaction (RT–PCR) or molecular detection result.
2. *Presumptive acute infection*: positive anti-IgM antibody detection via an immunodiagnostic assay
3. *Prior exposure*: positive anti-IgG detection via an immunodiagnostic assay

For a better understanding of the distribution and transmission patterns of DENV, ZIKV, CHIKV, WNV, RVFV and YFV, we considered the following definitions relative to the time of sampling reported in each study:

1. Epidemiologic period of sampling: We used **epidemic** data to refer to studies that were sampled either during an outbreak or between outbreak periods. Studies in which samples were taken before and after an epidemic or outbreak, respectively, were classified as **preepidemic** or **postepidemic** periods. If we are unable to determine this from the study, we will look at the country's report for that infection to determine the period.
2. Distribution pattern in the population: We will use **sporadic** to refer to the irregular or random occurrence or reporting of the infection in the countries/regions where studies were conducted. In

cases where the occurrence of the infection is reportedly constant or seasonal, we classified it as **endemic**. If the level of infection is unknown or no reports exist concerning its circulation in the population, we will refer to it as **unknown**.

Literature search strategy

The literature search will be constructed to locate arbovirus-related articles in key databases, such as PubMed, ScienceDirect (SCOPUS), the Web of Science Core Collection, African Journal Online and Google Scholar. We utilize a three-step strategy for the search. First, two authors performed an individual search on PubMed to identify articles relevant to the topic. We then compared and analysed the terms used in the titles and abstracts of relevant articles and the index terms. We used the PubMed MeSH tool to identify synonyms of the text and keywords. A full search strategy for the key databases was subsequently developed and reviewed (Table 1). Second, the search strategy, which included all identified keywords and index terms, was used to query the selected databases by two independent reviewers. The search terms for Africa were expanded to include all countries, as shown in Table 1. Studies published from January 2000 to August 2023 and written in either English or French were included. The third strategy will include a manual search that consists of scanning reference lists of eligible studies and relevant systematic review articles.

Methods of study selection

All identified citations will be uploaded to the EndNote website (https://endnote.com/weblogin/), and duplicates will be removed. We will follow the best practice guidelines for title and abstract screening of large-evidence systematic reviews and meta-analyses published by two independent reviewers adapted from Polanin *et al.*, [36] for screening the titles and abstracts (Table 2). Potentially relevant studies will be retrieved in full, and their citation details will be imported into the JBI system for unified management, assessment and review of information (JBI SUMARI) [37].

Table 1
Development of Search Strategies

Keywords:	**“Arbovirus infections” (D001102), Seroepidemiologic Studies (D016036), prevalence (D015995), incidence (D015994), Africa (D000349).**
Potential synonyms	**“Arbovirus infections”** **“Seroepidemiologic studies”-seroprevalence, seroepidemiology, sero-incidence,** **Prevalence** **Incidence** **Africa: Africa, central; Africa, Southern; Africa, Western; Africa, sub of Sahara; Africa, Northern.**
Search String combinations	• “Arbovirus infections” AND “Seroepidemiologic Studies” AND Africa • “Arbovirus infections” AND prevalence AND Africa • “Arbovirus infections” AND incidence AND Africa • “Arbovirus infections” [expanded] AND seroprevalence OR prevalence OR incidence AND Africa[expanded]
Expanded search for Africa	"Nigeria"[Title/Abstract] OR "Ethiopia"[Title/Abstract] OR "Egypt"[Title/Abstract] OR "Congo"[Title/Abstract] OR "Tanzania"[Title/Abstract] OR "South Africa" [Title/Abstract] OR "Kenya"[Title/Abstract] OR "Uganda"[Title/Abstract] OR "Algeria" [Title/Abstract] OR "Sudan"[Title/Abstract] OR "Morocco"[Title/Abstract] OR "Angola"[Title/Abstract] OR "Mozambique"[Title/Abstract] OR "Ghana" [Title/Abstract] OR "Madagascar"[Title/Abstract] OR "Cameroon"[Title/Abstract] OR "Cote d Ivoire"[Title/Abstract] OR "Niger"[Title/Abstract] OR "Burkina Faso" [Title/Abstract] OR "Mali"[Title/Abstract] OR "Malawi"[Title/Abstract] OR "Zambia" [Title/Abstract] OR "Senegal"[Title/Abstract] OR "Chad"[Title/Abstract] OR "Somalia" [Title/Abstract] OR "Zimbabwe"[Title/Abstract] OR "Guinea"[Title/Abstract] OR "Rwanda"[Title/Abstract] OR "Benin"[Title/Abstract] OR "Burundi"[Title/Abstract] OR "Tunisia"[Title/Abstract] OR "Togo"[Title/Abstract] OR "Sierra Leone"[All Fields] OR "Libya"[Title/Abstract] OR "Congo"[Title/Abstract] OR "Liberia"[Title/Abstract] OR "Central African Republic"[Title/Abstract] OR "Mauritania"[Title/Abstract] OR "Eritrea"[Title/Abstract] OR "Namibia"[Title/Abstract] OR "Gambia"[Title/Abstract] OR "Botswana"[Title/Abstract] OR "Gabon"[Title/Abstract] OR "Lesotho" [Title/Abstract] OR "Guinea-Bissau"[Title/Abstract] OR "Equatorial Guinea" [Title/Abstract] OR "Mauritius"[Title/Abstract] OR "Eswatini"[Title/Abstract] OR "Djibouti"[Title/Abstract] OR "Comoros"[Title/Abstract] OR "Cape Verde" [Title/Abstract]
Expanded search for Arboviruses	Dengue virus or zika virus or chikungunya virus or West Nile Virus or Rift Valley Fever virus or yellow fever virus

Keywords are provided with their unique indexed identities in PubMed. The prevalence and incidence of Arbovirus infections were indexed as preferred terms for searching. Thus, we did not use synonyms. For Arbovirus infections, we expanded the search to include individual searches for dengue virus (DENV), zika virus (ZIKV), chikungunya virus (CHIKV), West Nile virus (WNV) and Rift Valley Fever virus (RVFV).

Table 2
Citation, title, and abstract screening tools

S/N	Question	Response	Example guidelines
1	Does the citation indicate publication on or after 2000?	Yes/No	If not, stop screening
2	Does the title or abstract use English or French?		If not, stop screening
3	Does the title or abstract NOT indicate arbovirus (sero)prevalence systematic review		If not, stop screening
4	Does the title or abstract indicate that this is NOT a correction, erratum, or conference proceedings?		If not, stop screening
5	Does the abstract indicate that a **hospital or population-based sampling approach** was used and included **inhabitants** of an African country?		If not, stop screening and exclude. **Example of excluded studies.** • The study sampled Africans residing on other continents. • The study sampled a mixture of native Africans and nonnative Africans. • The study only sampled animals.
6	Does the abstract indicate that the study was observational, surveillance or outbreak investigation?		**Keywords**: cross-sectional, cohort, longitudinal, prospective, sentinel, population-based, case-based or aggregated surveillance. If neither keyword appeared, stop screening
7	Does the abstract indicate that Arboviruses were studied?		**Keywords**: nonmalaria febrile illness, Arbovirus infections, dengue virus, zika virus, chikungunya virus, West Nile Virus, Rift Valley Fever virus If no, stop screening and exclude.
8	Does the abstract indicate that the study used a quantitative design?		**Keywords**: (sero)prevalence, incidence If not, stop screening
9	Should this article be included?		**Yes**: All 8 screening questions answered Yes or unclear **No**: at least one answers “No”

Full-text screening of selected articles was conducted against the eligibility criteria according to population, setting, measurement, outcome, and study design characteristics within eligible studies as

described below:

Setting

All studies included participants residing as inhabitants of an African country. Studies that included population groups not specified as inhabitants in an African country were excluded.

Population

The population was defined as febrile patients, suspected cases, close contacts and the general population. The general population is defined as sampled from communities and households from the whole country or a defined subnational population area. Suspected patients were defined as patients enrolled with the case definition under surveillance. Studies considering any of these populations were considered for inclusion.

Measurement

Studies reporting active or presumptive cases were included if they were based on nucleic acid testing targeting virus-specific antigenic/conserved regions or immunoassays targeting IgM. Additionally, for prior infection investigations (seroprevalence), reporting of cases must be based on immunoassays targeting IgG.

Outcomes

Dengue virus, Zika virus, chikungunya virus, West Nile virus, and Rift Valley fever virus (sero) prevalence were reported as the primary or secondary outcomes of all the studies. The definition of seroprevalence should be reported via IgG or IgM measurement in serum/plasma or whole blood with immunoassays. Active case definition should be reported via nucleic acid detection of viral antigenic or conserved sequences.

Study Design

Observational studies (cross-sectional, cohort, longitudinal), sentinel, population-based, case-based or aggregated surveillance reported in the English or French language will be included. Studies in other languages will be eligible if a translation is available. Experimental trials that reported findings on arbovirus prevalence were excluded. Case reports, abstracts, case series, editorials, and articles without available full texts were excluded. Moreover, only studies published after December 31, 1999, were eligible for inclusion.

Two independent reviewers performed the full-text review, and any disagreements were resolved through discussion or by consulting a third reviewer. The results of the search will be reported according to the PRISMA 2020 flow diagram [35].

Table 3
Full-text screening tool.

Question	Yes	No	Unsure
Was the study conducted in an African country and includes inhabitants of the Country?			
Did the study include febrile patients, suspected cases, close contacts and general participants sampled from communities or households?			
Was the case definition of arbovirus infection based on nucleic acid testing or immunoassays targeting IgM and/or IgG?			
Was DENV, ZIKV, CHIKV, WNV, RVFV and YFV tested and reported as a primary or secondary outcome in samples obtained from the participant?			
Was the study used an observational, surveillance or outbreak investigation design?			
Should the study be included in data extraction?			

Data Extraction

The data extraction will be performed by two independent reviewers using the data extraction summary provided in Table 4. The following variables were extracted from the eligible studies after full-text review: name of first author, year of publication, sampling period, study population, sampling setting, age range of participants, method of sampling, epidemiologic timeline, level of disease in the sampling region before investigation, etiological agent(s) investigated, total number of participants screened, total samples tested, laboratory method for diagnosis of infection, and predefined outcomes (the number of laboratory-confirmed participants). In the case of multinational studies, data will be separated to present the estimate for each country when possible. The process will be piloted and reviewed by a third author. When possible, the authors of the included articles were contacted for missing information or additional data.

Table 4
Data extraction form

Category	Type of data
Demographic information	Authors
	Publication year
	Sampling time
	Study population
	Sapling setting
	Age range
	Country
	Sub-Region
Methods of outcome evaluation	Study design
	Method of sampling
	Epidemiological timelines
	Level of disease in the sampling Region
	Etiological agent investigated
	Total number recruited
	Total sample tested
	Method of testing
Reporting Evaluation	Number of positive cases
	Variant type
	Reported prevalence
	Additional Note

Scoring and quality assessment of the studies

We developed a modified scoring system to appropriately weigh both serological and epidemiological evidence for arbovirus infections in Africa based on standard guidelines. [38, 39]. In our scoring system, study design, laboratory assay and reporting outcome were the three main considerations. The details of the tool adopted for quality assessment are described below.

Designs

Study population: Studies in which individuals are sampled from a population that is a close representation of the national population receive a higher score. In this category, studies that involve community/household sampling or sentinel surveillance will receive more weight. For studies reporting (sero)prevalence from suspected cases, febrile patients, close contacts and other undefined populations, points will be assigned based on acceptable case definitions and the closeness of the sampling frame to the target population. The undefined population includes targeted patient groups such as HIV patients and pregnant women, among others.

Methods of sampling

Studies reporting the method used to recruit participants or sampling methods (convenient sample or randomly selected samples) received higher scores. In particular, the highest score was given for studies that provided a detailed sampling framework or used stratified/multistage sampling, followed by simplified random or convenience sampling. If a study does not report how they recruited their study participants, the study will receive zero points.

Laboratory Assay

We will consider studies using well-validated in-house assays or those using detection kits approved by GPC/WHO-recognized national regulatory authority [Food and Drug Administration (FDA) and/or National Medical Products Administration (NMPA)] with internal or external validations for a higher point. Viral neutralization assays or immunofluorescence assays will be considered the gold standard and will be the most common choice. For studies using molecular diagnostics with internal and/or external controls (endogenous controls, cloned cDNA targets, purified DNA products and synthetic DNA of the amplicon sequence), we will assign the same weight as neutralization assays.

Reporting Outcomes

For outcome analysis, accounting for population strata (regional demographic factors) or test performance is highly important for interpreting serological results. A higher point will be assigned for studies accounting for these adjustments, with the appropriate numerators and denominators used.

Quality Assessment

Two independent reviewers performed the quality assessment of the included articles, and a third reviewer resolved any disagreements. Based on the overall score obtained, the study quality was classified into four grades, A, B, C and D, according to their quartiles. The adapted guidelines for quality assessment and scoring are shown in **text box 1** and Table 5 below.

Text box 1: Guidelines for the quality assessment of the included articles.

Quality assessment tool: Methodology and reporting outcome assessment guide.

Study population

1. **Was the study target population a close representation of the national population in relation to age and sex?** Check if the sample proportionally reflects the age and sex structure of the larger group. Here, focus mainly on eligibility criteria and an actual sample collected. "***The target population"*** refers to the group of people or entities to which the results of the study will be generalized. The general, regional or community or patients groups are the targeted population
2. **Was data collected directly from the subjects (as opposed to a proxy)?** Check if samples for arboviruses screening were collected directly from included participants.

Representativeness of Sample

1. **Was the sampling frame a true or close representation of the target population?** Check if the selected population for sampling includes all genders and age groups that otherwise represent what can be found in the general target population. For example, check if the study underrepresents or overrepresents male or female gender, children, adults, or a special group of interests.
2. **Was some form of random selection used to select the sample, or was a census undertaken**? Here look for the method of recruitment, and whether it appropriately defines random sampling (simple random sampling, stratified random sampling, cluster sampling, systematic sampling).
3. **Was the likelihood of nonresponse bias minimal?** For general observational studies check for the participation bias relative to the number of people who consent to partake in the study and final sample available for results presentation. If it exceeds 30%, indicate "significant reporting bias". Additionally, check if the response rate for the study was ≥70% or if an analysis was performed that showed no important difference in relevant risk factors for arbovirus infection between those that were included in the analysis versus those that were not (responders and nonresponders).

Laboratory Assay and Reporting Outcome

1. **Was the study instrument that measured the parameter of interest shown to have validity and reliability?** Check for the diagnostic performance of the assay, internal and external validation characteristics, and regulatory authority's approval.
2. **Was the same mode of data collection and sample analysis used for all subjects and all samples?** Check all subjects were equally sampled using the same methods or different methods for certain subjects. Additionally, check if the same instrument was used to measure all samples under the same or similar conditions.
3. **Were the numerator(s) and denominator(s) for the parameter of interest appropriate?** Check to see if there were no errors in the reporting of the numerator AND denominator(s) for the prevalence estimation. The paper presented appropriate numerator(s) AND denominator(s) for the parameter of interest.

Table 5
Quality assessment tool: Definition of the scoring sheet

Indicators	Parameters	Max. Score	Given score
Study Population	Was the study target population a close representation of the national population concerning age and sex?	1	
	Was data collected directly from the subjects (as opposed to a proxy)?	1	
Population representativeness	Was the sampling frame a true or close representation of the target population?	1	
	Was some form of random selection used to select the sample, or was a census undertaken?	**3**	
	a. Without reporting the method of recruitment of study participants or the selection of study sites	0	
	b. Convenience samples without randomly selecting study participants (e.g., archived specimens from clinical labs, patients in a single centre, blood donors)	1	
	c. Randomly selected samples in communities or patients from multiple healthcare settings	2	
	d. Multistage/stratified samples from communities or universal samples from multiple healthcare settings	3	
	Was the likelihood of nonresponse bias minimal?	2	
	a. < 70%	0	
	b. 70–80%	1	
	c. > 80%	2	
Laboratory Assay	Was the study instrument that measured the parameter of interest shown to have validity and reliability?	4	
	Approval or validation by National Regulatory Authority	1	
	Validation before assay for surveillance	1	
	Confirmation of assay methods	2	

Note: # Validation assay for serology without virus neutralization assay (VNA), plaque-reduction neutralization test (PRNT) and microneutralization assay; * Validation assay with neutralization tests for seroprevalence studies and internal controls for molecular testing. ^ only applicable for seroprevalence studies.

Indicators	Parameters	Max. Score	Given score
	Was the same mode of data collection and sample analysis used for all subjects and all samples?	1	
Reporting outcome	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	1	
	Correction for age or sex	1	
	Correction for testing performance (sensitivity and specificity) ^	1	

Note: # Validation assay for serology without virus neutralization assay (VNA), plaque-reduction neutralization test (PRNT) and microneutralization assay; * Validation assay with neutralization tests for seroprevalence studies and internal controls for molecular testing. ^ only applicable for seroprevalence studies.

Data Synthesis for the Meta-analysis

For seroprevalence studies, we aimed to extract the true seropositive cases by multiplying the test performance-adjusted seroprevalence by the number of participants tested for each study. We will extract additional data on test characteristics for different serological assays based on independent internal or external evaluation, published diagnostic testing papers and manufacturers' reported data. In this case, we will use the primary assay considered for reporting outcomes. The true prevalence from the apparent incidence reported from seroprevalence studies will be estimated in a Bayesian framework using RUSCAN. The test sensitivity (se) and specificity (sp) will be specified independently. The specifications we use in the framework are outlined as follows:

$y \sim$ binomial (n, psample)

$p_{sample} = p \times se + (1-p) \times (1-sp)$

y_{sp} = binomial (n_{sp}, sp)

y_{se} = binomial (n_{se}, se)

where p_{sample} is the probability of seeing a positive sample, y is the number of positives observed, n is the sample size, and se and sp are the sensitivity and specificity of the test, respectively. If there is limited or unavailable information on the assay sensitivity and specificity, we will exclude the study from the main findings section.

For surveillance studies, we extracted the number of patients positive for the infection and the total sample tested. For repeated cross-sectional studies, we will calculate the sum of the total number of participants who provided specimens and the total number of positive individuals during the whole study period. For a longitudinal study (cohort) reporting on the incidence of arboviruses over time, we will extract the number/count of individuals who tested positive throughout follow-up but not the episodes of

infections, if any. There will be no sample size restrictions during the data synthesis, provided appropriate justification is given.

Meta-Analysis

We will use generalized linear mixed models (GLMMs) with 95% Clopper–Pearson confidence intervals to perform the meta-analysis with logit transformations via a two-step method. GLMMs directly model the (sero)prevalence with binomial likelihoods and fully account for within-study uncertainties. Heterogeneity will be assessed with I^2 (returns as 'percentage' heterogeneity as a function of tau (τ), which estimates the percentage of total variation due to heterogeneity across studies). We considered the following variables as prespecified sources of heterogeneity and explored them in subgroup and multivariate meta-regression analyses:

- Population group
- Epidemic timelines
- African region (North, South, East, West and Central)
- Disease burden level
- Quality of the studies included in the meta-analysis

We will perform sensitivity analyses based on the graphical display of heterogeneity (GOSH) plots, replicating the results after excluding influential studies from the analysis. Publication bias will be assessed with Egger's test. The "meta", "metafor" and "dmetar" packages implemented in R version 4.3.0 (2023-04-21 ucrt) will be used for this analysis.

Data presentation

Evidence will be presented in tables and forest plots. A narrative summary will proceed with the result presentation with detailed descriptions of how the results relate to the objectives of the review. We will report the findings following the PRISMA 2020 reporting guidelines for systematic reviews [35].

Discussion

Generally, systematic reviews and meta-analyses collect all possibly available evidence, designs, and reviews and combine the results from these studies for analysis based on their quality [40]. In this review, we provide comprehensive snapshots of DENV, ZIKV, CHIKV, WNV, RVFV and YFV investigations and a meta-analysis of the results to provide an epidemiological inventory, with useful findings for risk mapping and future prevention and control programs in Africa.

This review provides transparent and reproducible steps as well as the introduction of new concepts for analysing information from observational studies in line with standard reporting guidelines [35]. The methodology involves careful and expert appraisal of evidence in terms of its quality to maximize the accuracy of our report. The results of this review will include an estimate and description of the burdens of DENV, ZIKV, CHIKV, WNV, RVFV and YFV infections in Africa. This will highlight the need and advocate

for interventions for controlling outbreaks. Second, the results will provide an estimate of the trend in the etiology of infections to inform stakeholders regarding the effectiveness of control and prevention interventions. Third, the review estimates and describes potential outbreaks of arboviruses to inform the need for enhanced infection prevention rapid response systems in Africa. The findings of this review will be shared via professional networks and a drafted manuscript for publication in a peer-reviewed journal.

Abbreviations

cDNA: complementary deoxyribonucleic acid

CHIKV: Chikungunya virus

DARE: Design, Assay and Reporting Evaluation

DENV: Dengue virus

MeSH: Medical Subject Headings

RVFV: Rift Valley fever virus

WHO: World Health Organization

WNV: West Nile virus

YFV: yellow fever virus

ZIKV: Zika virus

Declarations

Ethics approval and consent to participate

Not Applicable

Consent for publication

Not Applicable

Availability of data and materials

Not Applicable

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

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Not Applicable

References

1. Gudo, E.S., et al., *Seroepidemiological studies of arboviruses in Africa.* 2018: p. 361-371.
2. Agboli, E., et al., *Arbovirus Epidemiology: The Mystery of Unnoticed Epidemics in Ghana, West Africa.* 2022. **10**(10): p. 1914.
3. Braack, L., et al., *Mosquito-borne arboviruses of African origin: review of key viruses and vectors.* Parasites & Vectors, 2018. **11**(1): p. 29.
4. Buchwald, A.G., et al., *Aedes-borne disease outbreaks in West Africa: A call for enhanced surveillance.* Acta Tropica, 2020. **209**: p. 105468.
5. Ushijima, Y., et al., *Surveillance of the major pathogenic arboviruses of public health concern in Gabon, Central Africa: increased risk of West Nile virus and dengue virus infections.* 2021. **21**(1): p. 1-11.
6. Klein, R.S., *Encephalitic Arboviruses of Africa: Emergence, Clinical Presentation and Neuropathogenesis.* Front Immunol, 2021. **12**: p. 769942.
7. Stoler, J., et al., *Deconstructing "malaria": West Africa as the next front for dengue fever surveillance and control.* 2014. **134**: p. 58-65.
8. Agboli, E., et al., *Mosquito-associated viruses and their related mosquitoes in West Africa.* 2021. **13**(5): p. 891.
9. Ali, I.M., et al., *Arboviruses as an unappreciated cause of nonmalarial acute febrile illness in the Dschang Health District of western Cameroon.* PLoS Negl Trop Dis, 2022. **16**(10): p. e0010790.
10. Sanou, A.S., et al., *Building laboratory-based arbovirus sentinel surveillance capacity during an ongoing dengue outbreak, Burkina Faso, 2017.* 2018. **16**(S1): p. S-103-S-110.
11. WHO-TDR, *Surveillance and control of arboviral diseases in the WHO African Region: assessment of country capacities*. 2022, World Health Organization on behalf of the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.
12. CDC, *Arboviral diseases, neuroinvasive and nonneuroinvasive*. 2015, Centers for Disease Control and Prevention.

13. CDC, *Symptoms and treatment. Dengue*. 2020.
14. Manu, S.K., et al., *Arbovirus circulation among febrile patients at the Greater Accra Regional Hospital, Ghana.* BMC Res Notes, 2019. **12**(1): p. 332.
15. Patterson, J., M. Sammon, and M.J.W.J.o. E.M. Garg, *Dengue, Zika and chikungunya: emerging arboviruses in the New World.* 2016. **17**(6): p. 671.
16. WHO, *Centers for Disease Control and Prevention. Technical guidelines for integrated disease surveillance and response in the African Region, third edition*. 2019.
17. Braack, L., et al., *Developing African arbovirus networks and capacity strengthening in arbovirus surveillance and response: findings from a virtual workshop*. 2023, BioMed Central.
18. Baba, M., J. Villinger, and D.K. Masiga, *Repetitive dengue outbreaks in East Africa: A proposed phased mitigation approach may reduce its impact.* Rev Med Virol, 2016. **26**(3): p. 183-96.
19. Fang, Y., et al., *Epidemiology of Mosquito-Borne Viruses in Egypt: A Systematic Review.* Viruses, 2022. **14**(7).
20. Humphrey, J.M., et al., *Dengue in the Middle East and North Africa: A Systematic Review.* PLoS Negl Trop Dis, 2016. **10**(12): p. e0005194.
21. Mbanzulu, K.M., et al., *Mosquito-borne viral diseases in the Democratic Republic of the Congo: a review.* Parasit Vectors, 2020. **13**(1): p. 103.
22. Mencattelli, G., et al., *Epidemiology of West Nile virus in Africa: An underestimated threat.* PLoS Negl Trop Dis, 2022. **16**(1): p. e0010075.
23. Abdullahi, I.N., et al., *Prevalence Pattern of Chikungunya Virus Infection in Nigeria: A Four Decade Systematic Review and Meta-analysis.* Pathog Glob Health, 2020. **114**(3): p. 111-116.
24. Abdullahi, I.N., et al., *Distribution pattern and prevalence of West Nile virus infection in Nigeria from 1950 to 2020: a systematic review.* Epidemiol Health, 2020. **42**: p. e2020071.
25. Cecilia, H., et al., *Mechanistic models of Rift Valley fever virus transmission: A systematic review.* PLoS Negl Trop Dis, 2022. **16**(11): p. e0010339.
26. Eltom, K., et al., *Dengue Virus Infection in Sub-Saharan Africa Between 2010 and 2020: A Systematic Review and Meta-Analysis.* Front Cell Infect Microbiol, 2021. **11**: p. 678945.
27. Elven, J., et al., *Nonmalarial febrile illness: a systematic review of published aetiological studies and case reports from Africa, 1980-2015.* BMC Med, 2020. **18**(1): p. 279.
28. Mwanyika, G.O., et al., *Dengue Virus Infection and Associated Risk Factors in Africa: A Systematic Review and Meta-Analysis.* Viruses, 2021. **13**(4).
29. Paixão, E.S., et al., *Chikungunya chronic disease: a systematic review and meta-analysis.* Trans R Soc Trop Med Hyg, 2018. **112**(7): p. 301-316.
30. Russo, G., L. Subissi, and G. Rezza, *Chikungunya fever in Africa: a systematic review.* Pathog Glob Health, 2020. **114**(3): p. 136-144.
31. Simo, F.B.N., et al., *Dengue virus infection in people residing in Africa: a systematic review and meta-analysis of prevalence studies.* Sci Rep, 2019. **9**(1): p. 13626.

32. Simo, F.B.N., et al., *Chikungunya virus infection prevalence in Africa: a contemporaneous systematic review and meta-analysis.* Public Health, 2019. **166**: p. 79-88.
33. Wainaina, M., et al., *A systematic review and meta-analysis of the aetiological agents of nonmalarial febrile illnesses in Africa.* PLoS Negl Trop Dis, 2022. **16**(1): p. e0010144.
34. Ward, T., et al., *Dengue data and surveillance in Tanzania: a systematic literature review.* Trop Med Int Health, 2017. **22**(8): p. 960-970.
35. Page, M.J., et al., *PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews.* Bmj, 2021. **372**: p. n160.
36. Polanin, J.R., et al., *Best practice guidelines for abstract screening large-evidence systematic reviews and meta-analyses.* Res Synth Methods, 2019. **10**(3): p. 330-42.
37. Piper, C., *System for the Unified Management, Assessment, and Review of Information (SUMARI).* J Med Libr Assoc, 2019. **107**(4): p. 634-6.
38. Hoffmann, W., et al., *Guidelines and recommendations for ensuring Good Epidemiological Practice (GEP): a guideline developed by the German Society for Epidemiology.* 2019. **34**(3): p. 301-317.
39. WHO, *Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection*. 2020, World Health Organization. p. 1-19.
40. Ahn, E. and H. Kang, *Introduction to systematic review and meta-analysis.* Korean J Anesthesiol, 2018. **71**(2): p. 103-112.