Systematic review

1. * Review title.

Give the title of the review in English

Systematic Review of Rift Valley Fever Virus (RVFV) Epidemiology and Transmission in Africa and the Arabian Peninsula 1999-present

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

N/A

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

13/11/2020

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

30/06/2021

5. * Stage of review at time of this submission.

Tick the boxes to show which review tasks have been started and which have been completed. Update this field each time any amendments are made to a published record.

Reviews that have started data extraction (at the time of initial submission) are not eligible for inclusion in PROSPERO. If there is later evidence that incorrect status and/or completion date has been supplied, the published PROSPERO record will be marked as retracted.

This field uses answers to initial screening questions. It cannot be edited until after registration.

The review has not yet started: No

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Charles King

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Dr King

7. * Named contact email.

Give the electronic email address of the named contact.

chk@cwru.edu

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

Center for Global Health and Diseases, Case Western Reserve University School of Medicine, 2109 Adelbert Road, BRB 422, Cleveland OH 44106 USA

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

1-216-368-3667

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Coalition for Epidemic Preparedness Innovations (CEPI), Oslo, Norway. (www.cepi.net)

Organisation web address:

https://cepi.net/

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record.**

Dr Charles King. Case Western Reserve University, Cleveland Ohio
Professor A. Desiree LaBeaud. Department of Pediatrics, Stanford University, Stanford, California
Dr Keli Gerken. Department of Pediatrics, Stanford University, Stanford, California

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

Charles King Consulting. Funded by Coalition for Epidemic Preparedness Innovations (CEPI), Oslo, Norway.

(www.cepi.net)

Grant number(s)

State the funder, grant or award number and the date of award

Project CEPI #202032-NO.

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

The review team declare that they have no known conflicts of interest.

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

Dr Janusz Paweska. National Institute for Communicable Diseases of the National Health Laboratory Service
Dr George Warimwe. Oxford University, Oxford
Dr Brian Bird. University of California at Davis, California
Dr Baptiste Dungu. Onderstepoort Biological Products
Dr Jeroen Kortekaas. Wageningen Bioveterinary Research,
Dr Henshaw Mandi. Coalition for Epidemic Preparedness Innovations, Oslo
Dr Roice Fulton. Coalition for Epidemic Preparedness Innovations, Oslo
Dr Gabrielle Breugelmans. Coalition for Epidemic Preparedness Innoivations, Oslo
Dr Paul Oloo. Coalition for Epidemic Preparedness Innovations, UK
Dr Maina L'Azou Jackson. Coalition for Epidemic Preparedness Innovations, UK

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

To characterize the present day epidemiology of Rift Valley fever virus (RVFV) infection and disease to answer the following research question: Can RVF vaccine efficacy be established via a conventional efficacy trial?

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

Computerized publication databases will be searched for relevant literature using the search criteria 'Rift Valley fever', 'RVF', 'prevalence', 'incidence', 'sero*', 'epidemiology', 'disease outbreaks', 'transmission', 'risk assessment OR risk factor', 'mortality OR complications', 'strain OR lineage', 'genetics', 'disease reservoirs', 'population surveillance', 'socioeconomic factors', 'floods OR El Nino', 'forecasting', 'spatio-temporal', and 'modeling'. To maximize inclusion of data from Hispanophone, Francophone, and Lusophone African countries, we will not restrict the language of publication. For greatest inclusion, we will search PubMed, EMBASE, Web of Science, African Journals Online, The Cumulative Index to Nursing and Allied Health Literature (CINAHL), The Scientific Electronic Library Online (SciELO), Elsevier ScienceDirect, ResearchGate, and the ProMed listserv site. The time frame will be limited to 1999-2020. Not all journals are indexed within these online systems. We have found that a secondary yield of relevant studies can be obtained by checking the reference lists of papers that are selected for inclusion in the review, and by using Google Scholar and ScienceDirect to check for 'Papers like this' and 'Papers that cite this paper' for leads to additional published studies. Investigators and public health leaders in endemic countries will be contacted for 'grey literature' available in government reports and regional summaries of cases. Unpublished survey data and pre-publication reports will be sought by contacting our established network of RVF collaborators at African and other international research centers (e.g., ILRI, NASA, WHO). Governmental outbreak and surveillance data will be sought from MoH reports, WHO Disease outbreak news, OIE reports, WHO Weekly Epidemiological Records, the WHOLIS database, the AFENET network for field investigations and other FETPs, and reports from Centers of Disease Control (the US CDC, ECDC, and ACDC). Where possible, the lead authors of these reports will be contacted for additional epidemiological data. Searches will be re-run prior to the final analysis.

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

see item 16 above, which will be available on PROSPERO

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Rift Valley fever virus (RVFV) infection is categorized as a neglected tropical disease due to the fact that RVFV disproportionately affects resource-limited semi-nomadic herding communities, is poverty promoting, and has long-lasting sequelae. Additionally, RVF is expanding its range, threatening other areas of the world as an emerging infectious disease; notably, both Europe and the United States have the necessary vectors and livestock reservoirs to sustain autochthonous RVFV transmission. The severity of RVFV manifestation, its devastating economic and public health effects, and its potential to be sustained in new regions make the study of RVFV transmission and disease a high priority, and the prevention of RVFV infections an essential goal for global health.

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Inclusion: Residents of all ages in Africa, the Arabian Peninsula, and Indian Ocean islands where RVF has been reported to occur. Infections among regional livestock and wildlife will also be included. The primary focus will be on population-based survey data. However, location-specific case reports will be included in spatiotemporal analysis. Exclusion: Laboratory-based studies and intervention trials among experimental animals in controlled settings will be excluded.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

This systematic review will collate observational data from recent reports on Rift Valley fever outbreaks among humans and animals, as well as on interepidemic transmission. Where available, data on differential risk factors will be abstracted and used to identify locations and sub-populations at highest risk for RVFV infection and related disease. Examples for humans include occupation, age group, gender, exposure to animals and animal products, mosquito exposure, and location. For animals, these include species, location, domestication status, and herding practices.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

In determining which exposures (listed above) are more significantly associated with acute RVFV infection, our analysis will compare those who have clinical or laboratory evidence of acute infection to control subjects without infection who live in the same study locations. A subset analysis of exposure-related risk for severe disease can also be done to compare those with and without severe RVF symptoms among those with documented acute viral infection, and risk of death can likewise be compared among this group.

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Observational studies including, case series, cross-sectional surveys, cohort, and case-control studies will be included, with priority to population-based surveys and surveillance data. Because of the current limitations for case finding in many countries, well documented case reports and case series with confirmed diagnoses will also be considered for inclusion. Qualitative evidence from past vaccine experience and efforts at outbreak predictions will be collated and presented alongside the review of quantitative data.

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

Development of a safe and effective human vaccine for Rift Valley fever virus (RVFV) is now considered a priority. RVFV is a mosquito-borne zoonotic pathogen that poses a significant risk to human health in endemic regions of Africa, the Indian Ocean, and the Middle East. Epizootics usually precede epidemics and can result in large-scale abortion storms in local livestock populations. These consecutive RVFV outbreaks in human and animal populations result in significant economic damage from trade embargos and significant livestock losses in affected areas. Recent data also demonstrate that RVFV can be transmitted to humans during interepidemic periods.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

The primary outcome of the review will be to determine the spatial and temporal distribution of human and animal outbreaks of Rift Valley fever virus infections during the period 1999--present

* Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

We will derive summary odds ratios and risk ratios for clinical RVF according to specific exposures and age, sex, location, and occupation categories

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state ‘None’ or ‘Not applicable’ as appropriate to the review

a. Determine the age-, sex- and social status-related risk levels for RVFV infection.b. Determine relative risk for RVFV infection based on occupation and specific exposures to insect vectors and vertebrate animal, including human-to-human transmission.c. Identify locations where different circulating lineages of RVFV

have been identified.d. Catalogue presumed animal reservoirs and evidence on animal transmission dynamics.e. Catalogue current surveillance systems in place for detection and reporting RVF outbreaks.

* Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

as for item 24

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Recovered studies will be independently screened for inclusion/exclusion by each of two experienced project reviewers. In case of disagreement or uncertain status of the study, the third member of the research team will review and decide whether to include the study in the analytic portion of the review. Study data will then be abstracted by the reviewers and recorded in a purpose-built database that will house the needed details for the planned CEPI-requested analyses. The data table will include all the following variables, which will be input, and coded (where appropriate), and made searchable via a user-friendly computer display that presents the variables in more easily readable screen format. All entries will be independently confirmed by a second reviewer. Sub-tables will be embedded in the database to capture details for individual livestock and animal species, different human occupations, and SES categories, when these are provided by a paper under review. Where possible, subject and location descriptors will be coded from free text into standardized categories to facilitate later statistical analysis. These will be made available in pull-down selection menus included as ‘lookup’ tables in the database master file. Inclusion of the Yes/No or True/False variables will facilitate the creation of Boolean selection query tables for later subgroup analysis. Subgroup query tables are then regularly updated as new data are entered during the review process. On a periodic basis, the master file and query tables can be exported into Excel format for interim reports. These, in turn, can later be imported into statistical software for more advanced analysis as specified in the study protocol’s statistical analysis plan.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

The study reviewers will provide an estimate of risk of study bias using the abridged Liverpool Quality Appraisal Tool (LQAT) to score individual study design and performance characteristics of the included surveys. This scoring tool is more suited to observational and non-interventional studies, which will form the bulk of studies to be included in the systematic review. The LQAT provides a summary risk of bias score based on subscores for selection bias, response bias, allocation bias, follow-up bias, methods of risk factor exposure determination, outcomes assessment bias, and whether potential confounding factors were

assessed and adjusted for in the individual study's analysis. Scoring will be done independently by each of two reviewers from the core study team. In case of disagreement or uncertain status of the study, the third member of the research team will review and decide the final score.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

To inform initiatives for development of a vaccine for RVF prevention, CEPI has asked for recent 1999-present data on RVF epidemiology in Africa and the Arabian Peninsula including the following dimensions:a. National/regional incidence and prevalence over time - reported cases, deaths, attack rates,b. Seropositivity, and case fatality risksc. Age, sex, and other sociodemographic characteristics of the reported casesd. Risk factors and sub-populations at risk (e.g., veterinarians, butchers, herdsmen)e. Transmission mechanisms: direct contact animal-human, vector-borne transmission,f. Human to human (e.g., vertical transmission, blood donation)g. Viral circulation: regional distribution of RVFV lineagesh. Seasonal patterns: recurrencei. Animal reservoirs and animal-mosquito-animal transmission dynamicsj. Characterization of national/regional human and animal ("One Health") RVF/viralhemorrhagic fever surveillance systems: reporting, case definitions, lab ascertainmentThese can be summarized in descriptive tabular and graphical formats with the use of statistical software (SPSS, SAS, SigmaPlot, or other) to present the aggregate results for all included studies. For groupwise comparisons in terms of odds or risk of infection, weighted meta-analysis can be performed with the use of specialized software (Comprehensive Meta-Analysis, Biostat, Inc.) which provides for covariate adjustments by fixed- and random-effects modeling of summary estimates. It will also provide estimates of heterogeneity among studies, and the potential for publication bias, along with funnel plots and forest plots of individual and summary effects found in the included studies.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

Sensitivity analysis is available to examine the global impact of including each individual study, and through testing the differences among specific pre-defined study subgroups based on region, environmental factors, age group, gender, study risk of bias, year of publication. Because RVFV outbreaks are sporadic and focal, often based on episodes of excess heavy rainfall, environmental aspects are important to dissect in the analysis. Also, based on current knowledge of occupational exposures and the influence of adult (vs. childhood) and gender roles in RVFV transmission areas, more precise determination of high risk groups is desired.

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness
No

Diagnostic
No

Epidemiologic
No

Individual patient data (IPD) meta-analysis
No

Intervention
No

Meta-analysis
Yes

Methodology
No

Narrative synthesis
No

Network meta-analysis
No

Pre-clinical
No

Prevention
No

Prognostic
No

Prospective meta-analysis (PMA)
No

Review of reviews
No

Service delivery
No

Synthesis of qualitative studies
Yes

Systematic review
Yes

Other
No

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system

No

Cancer
No

Cardiovascular
No

Care of the elderly
No

Child health
No

Complementary therapies
No

COVID-19
No

Crime and justice
No

Dental
No

Digestive system
No

Ear, nose and throat
No

Education
No

Endocrine and metabolic disorders
No

Eye disorders
No

General interest
No

Genetics
No

Health inequalities/health equity
No

Infections and infestations
Yes

International development
No

Mental health and behavioural conditions
No

Musculoskeletal
No

Neurological
No

Nursing
No

Obstetrics and gynaecology
No

Oral health
No

Palliative care
No

Perioperative care
No

Physiotherapy
No

Pregnancy and childbirth
No

Public health (including social determinants of health)
Yes

Rehabilitation
No

Respiratory disorders
No

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
Yes

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

United States of America

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

N/A

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

N/A

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

In addition to producing a report for the funders of this review, a detailed paper describing the results will be submitted to a leading journal in this field for Open Access publication. Furthermore, should the findings of the review warrant a change in practice, a one page summary report will be prepared and sent to policymakers at the WHO Expert Advisory Group on arboviruses.

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

Systematic review; meta-analysis; Rift Valley fever; Rift Valley fever virus; incidence; prevalence; endemic status; transmission factors; exposure risk; attack rate; mosquito; case fatality risk; human; animal;

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

None

38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.
Please provide anticipated publication date

Review_Completed_published

39. Any additional information.

Provide any other information relevant to the registration of this review.

This review is being undertaken as part of the planning for a randomised trial to determine efficacy of a vaccine against RVF in humans.

Although our protocol is somewhat similar to PROSPERO reviews registered by Anywaine (CRD42019128928 'Systematic review study protocol investigating the clinical manifestations and long-term complications of Rift Valley fever in humans') and Belhadi (CRD42020167306, 'The mortality, prevalence, sequelaes and treatments of viral haemorrhagic fevers: a systematic literature review') the current review has a focused time scale, involves epidemic and inter-epidemic data with a specific focus on RVF infection risk rather than clinical outcomes, and involves documenting disease in both humans and animals according to location and environmental and individual risk factors.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission). List authors, title and journal details preferably in Vancouver format.

N/A

Give the link to the published review or preprint.