Title

Assessment of data on vector and host competence for Japanese encephalitis virus: A systematic review update of Oliveira et al. 2018

Authors

Andrea L. Dixon, Center for Outcomes Research and Epidemiology, Department of Diagnostic Medicine and Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS, USA, aldixon@vet.k-state.edu

Stephen Edache, Center for Outcomes Research and Epidemiology, Department of Diagnostic Medicine and Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS, USA, edache@vet.k-state.edu

Ana R. S. Oliveira, School of Veterinary Medicine, University of California-Davis, Davis, CA, USA, anaoliv@ucdavis.edu

Vanessa De Aguiar Veloso, Center for Outcomes Research and Epidemiology, Department for Diagnostic Medicine and Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS, USA, veloso@vet.k-state.edu

Natalia Cernicchiaro, Center for Outcomes Research and Epidemiology, Department of Diagnostic Medicine and Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS, USA,* ncernic@vet.k-state.edu

Contact information

*Corresponding author: ncernic@vet.k-state.edu; Natalia Cernicchiaro, Kansas State University, College of Veterinary Medicine, Department of Diagnostic Medicine and Pathobiology, Coles Hall 332, 1620 Denison Ave., Manhattan, KS, 66506

Contributions of the authors

Natalia Cernicchiaro is the guarantor. Study protocol was initially drafted by VV, AD, and NC, and all authors provided feedback. AD will conduct the search and deduplication. AD and SE will conduct screening and respective data extraction. AO performed the original systematic review and will conduct the ROB. AD will conduct data synthesis.

Sponsor, support & funding sources

Financial support was provided by the Swine Health Information Center (SHIC) and the College of Veterinary Medicine at Kansas State University. Sponsors did not have any role in the design or implementation of the study.

Rationale

Japanese Encephalitis (JE) is an emerging, zoonotic disease transmitted primarily by *Culex* species mosquitoes (particularly *Culex tritaeniorhynchus*) carrying the flavivirus Japanese encephalitis virus (JEV). Japanese encephalitis virus maintains its life cycle between mosquitoes and vertebrate hosts, primarily pigs and wading birds (Le Flohic et al., 2013). JE is an untreatable and incurable disease that, in humans, can result in inflammation of the brain (encephalitis) causing fever, headache, respiratory signs, gastrointestinal signs, confusion, seizures, coma, and, in some cases, death (Fischer et al., 2012; Kliegman et al., 2015).

The United States (US) is considered a susceptible region with great potential for JEV introduction, given the availability of competent insect vectors, susceptible maintenance (avian) hosts, large populations of susceptible, amplifying hosts (domestic and feral pigs), intensive travel and trade activities to and from JEV-affected countries, and areas with similar climatic and environmental conditions to countries where the virus is epidemic. To investigate the risk of JEV introduction and establishment, Oliveira and colleagues performed a risk assessment (Oliveira et al., 2019) supported by a systematic review of vector and host competency for JEV (Oliveira et al., 2018).

Although Oliveira et al. (2019) found the risk of introduction of JEV in the US through entry of infected mosquitoes via airplanes to be very high, the risk of establishment was considered negligible; yet, increases in international trade and globalization, as well as changes in climate and land use, and the recent incursion of a new JEV genotype into areas previously free from disease, as observed in Australia with the invasion and expansion of JEV (Genotype IV) in the eastern and southeastern states, warrants the need for an update of the review and risk assessment. The objective of this review is to update the systematic review (Oliveira et al., 2018) on host and vector competence of transmission of the Japanese encephalitis virus.

Objectives

The primary objective of this study is to update the systematic review by Oliveira et al. (2018) by conducting a systematic review comprising the appraisal of scientific literature published from 2016 to 2022 on host and vector competence for the transmission of JEV. The research question is: what information is available on vector and host competency and abundance for JEV transmission arising from peer-reviewed published literature from 2016 to 2022?

Registration and amendments

This protocol has been drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P) and will be made publicly available within the K-Rex database (K-Rex/CORE collection). *Post hoc* changes made to the protocol will be recorded and posted as an updated version in the same database. Any changes in the original protocol will be accompanied by a footnote indicating the date of change, and the rationale. Added content will be displayed with an underline and deleted text will be shown with a strike through.

Eligibility criteria

The eligibility criteria will follow those set out in the original review, except the time frame will be restricted to 2016 to present.

Table 1. Relevance screening criteria for inclusion and exclusion of articles – adapted from Table 1 Oliveira et al. (2018).

	Inclusion criteria	**Exclusion criteria**
Language	English	Other than English
Time period	2016 to 2022	Published before 2016
Types of evidence	Peer-reviewed articles	Non-peer reviewed articles, conference proceedings, thesis dissertations, and other non-peer reviewed publications
Location	Any country	-
Vector AND/OR Host Competence to JEV		
	Inclusion criteria	**Exclusion criteria**
Population (P)	Vectors (mosquitoes, other insects) and/or Hosts (vertebrate hosts)	Vectors other than insects and non-vertebrate hosts.
Outcomes and outcome measures (O)	Transmission efficiency, feeding patterns, host preference, infectiousness, susceptibility to infection, incubation time, duration of viremia	Vector and/or host competence for other Flaviviruses transmitted by ticks[a]
Study type (S)	Challenge trial (laboratory and field), field studies (e.g., trapping, capture), observational or experimental studies	Non-primary research (thesis) and literature reviews

[a] Tick-borne flaviviruses such as the causative agents of tick-borne encephalitis, Kyasanur Forest disease, Alkhurma disease or Omsk hemorrhagic fever, but other mosquito borne Flaviviruses (West Nile, St. Louis Encephalitis, yellow fever, dengue fever, and Zika) were included.

Information sources

To best replicate the original search, we will search the same electronic databases (Web of Science and Pubmed), as well as Scopus to capture the following privately searched journals: The American Journal of Tropical Medicine and Hygiene, Journal of the American Mosquito Control Association, Journal of Medical Entomology, and Vector-Borne and Zoonotic Diseases. The Armed Forces Pest Management Board will be searched separately. Table 2 describes the electronic databases that will be searched, the interface used, and the time frame.

Table 2. Electronic databases, interface used, and time frames for the search.

Database	Interface	Dates included
Web of Science Core Collection; KCI-Korean Journal Database; MEDLINE; SciELo Citation Index	Web of Science	2016 – 2022
PubMed	National Library of Medicine	2016 – 2022
Scopus	Scopus, Elsevier	2016 – 2022
The Armed Forces Pest Management Board	The Armed Forces Pest Management Board	2016 – 2022

Search strategy

We will utilize the searches from the original paper for the previously searched electronic databases (WOS, PubMed, and the Armed Forces Pest Management Board) and create a separate search based on these search terms for Scopus. AD will perform the search. Table 3 reports the search strategies for each electronic database from Oliveira et al. (2018), Supplementary Materials Appendix 1.

Table 3. Search strategy for each electronic database using the search strategy from Oliveria et al. (2018) – S1 appendix.

Database[§]	**Keyword search**[*]
WOS	TS: ((Japanese encephalitis OR viral encephalitis OR JE OR JEV) AND vector competence AND mosquito AND host competence)
PubMed	All Fields: (Japanese AND encephalitis) AND ((vector OR host) competence)[£]
Scopus	TITLE-ABS-KEY((vector AND competence) OR (mosquito AND vector AND competence) OR (host AND competence)) AND (TITLE-ABS-KEY("japanese encephalitis" OR (viral AND encephalitis) OR "je" OR "jev")
Armed Forces Pest Management Board	Find results in AFPMB website (http://www.afpmb.org/content/search-afpmborg) with all the words: Japanese Encephalitis

[*] All searches were limited to the timeframe 2016-2022 and to the English language.
[§] TS = Search for topic terms in the following fields within a record. Search in title, abstract, author keywords, and keywords Plus®. TITLE-ABS-KEY = Search for topic terms in the title, abstract, and keywords.
[£] This search string differs from the original - "mosquitoes" was replaced by "(vector OR host) AND competence)" - as this better captured the information we were interested in.

Data management

AD will export the database results as Research Information Systems (RIS) files into the systematic review software, Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). Database results will be de-duplicated using the Covidence de-duplication tool. AD and SE will perform the title and abstract screening and data extraction in Covidence. Following the relevance screening of the titles and abstracts, the full-texts of the relevant papers will be imported into Zotero (Corporation for Digital Scholarship, Virginia, USA), and then uploaded into Covidence using the bulk upload function.

Relevance Screening/Selection process

The selection process will be performed according to the following steps:

#1: Citation retrieval. Citations from the search strategy will be downloaded as RIS and then uploaded into Covidence as described on Data management section.

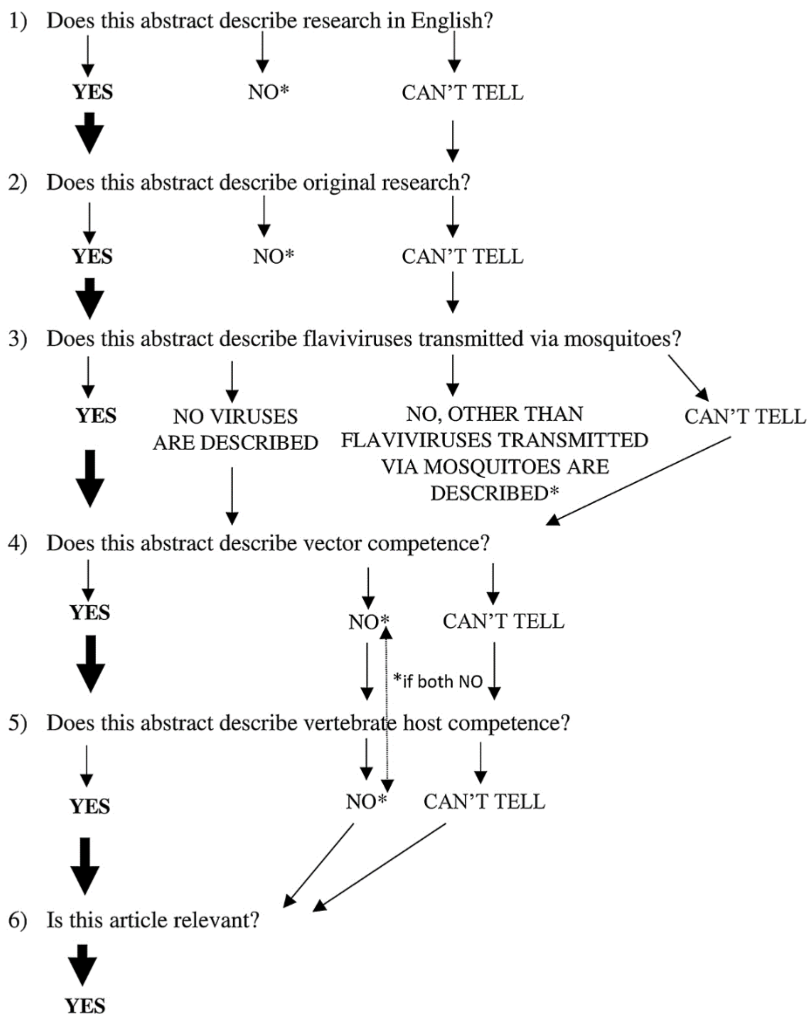
#2: Deduplication. Duplicated references will be removed using Covidence's de-duplication tool.

#3: Relevance screening tool-development. The screening tool comprised of a flow chart (Figure 1 below from Oliveira et al. 2018) will be used.

#4: Relevance screening tool calibration. The proposed primary relevance screening tool will be tested for clarity and utility. For the test exercise, a pair of reviewers (AD, SE) will independently review a random sample of 20% of the total titles and abstracts. Reviewers will compare their results and discuss any differing decisions or questions that arose during the screening. The agreement of the two reviewers will be calculated and if there is at least 80% agreement, the version of the screening tool in question will be utilized for the final relevance screening. If this threshold is not met, then the relevance screening tool will be amended based on reviewer recommendations, and another iteration of screening will be performed to another set of 25 citations; this process will continue until at least 80% agreement is achieved.

#5: Title and Abstract Screen. Once a final version of the relevance screening tool is decided upon, AD and SE will complete the title and abstract screen in duplicate. If it is unclear from the title and abstract if the article is relevant, the article in question will undergo a second full-text review. Otherwise, all relevant articles will move onto data extraction. Any relevant literature reviews will be set aside, and the reference list hand-searched to identify any missing publications, from within the time frame of 2016-2022, that were missed by the search.

Figure 1. Relevance screening chart from Oliveira et al. (2018)



*Stop answering the other questions of the tool – abstract NOT RELEVANT
Arrows in bold represent which answers lead to a RELEVANT paper.

Data extraction

Data extraction will be performed in Covidence, creating a data collection form based on Table 2 form Oliveira et al. (2018). Data extraction will be performed in duplicate by two reviewers (AD and SE).

Data items

Table 4. The data items to be extracted, adapted from Table 2 of Oliveira et al. (2018).

	Data item	**Explanation**
Vectors		
Transmission efficiency[a]	Infection rate	Infection rate is the sum of individual/pool of mosquitoes that are JEV-positive divided by the total number of mosquitoes/pools tested in experimental studies.
	Dissemination rate	Dissemination rate is the proportion of mosquitoes with virus in their legs, irrespective to their infection status (Golnar et al. 2015)
	Transmission rate	Transmission rate is the proportion of mosquitoes with a disseminated infection that transmits the virus during refeeding (Golnar et al 2015)
Host preference	Host species preference	The host species from which the mosquito blood meals originated.
Susceptibility to infection	Proportion of JEV infection	The proportion of JEV infection is the total of positive mosquito pools divided by the total number of pools tested (observational studies)
	Minimum infection rate (MIR)	MIR is the ratio of positive mosquito pools to the total number of mosquitoes in the sample (assumption: only one infected individual is present in a positive pool) (Bustamante and Lord, 2010)
	Maximum likelihood estimate (MLE)	MLE is the proportion (parameter of a binomial distribution) of infected mosquitoes that maximizes the likelihood of pools of a specific size being positive (Bustamante and Lord 2010)
Hosts		
Susceptibility to infection	Proportion of JEV infection	The proportion of positive vertebrate hosts is the sum of positive samples divided by the sum of samples tested

[a]Administration routes included: oral feeding (pledgets/membranes or hosts), intrathoracic inoculation, or vertical transmission (parents infected either intrathoracically or by oral feeding).

Risk of bias assessment (RoB)

RoB assessment will be performed by a third reviewer (either AO or NC) using the previous framework in Oliveira et al. (2018) for experimental (Table 3) and observational studies (Table 4).

Data synthesis

Tables 6-11 of Oliveira et al. (2018) will be updated.

Meta-biases

No meta-analyses will be performed for this update.

References

Bustamante, D.M. and Lord, C.C. 2010. Sources of error in the estimation of mosquito infection rates used to assess risk of arbovirus transmission. *Am J Trop Med Hyg.* Jun;82(6):1172-84. doi: 10.4269/ajtmh.2010.09-0323.

Fischer, M., Hills, S., Lindsey, N. and Staples, J.E., 2010. Japanese encephalitis vaccines; recommendations of the Advisory Committee on Immunization Practices (ACIP).

Golnar, A.J., Turell, M.J., LaBeaud, A.D., Kading, R.C., Hamer, G.L. 2015. Predicting the mosquito species and vertebrate species involved in the theoretical transmission of Rift valley fever virus in the United States. *PLoS Negl. Trop. Dis.* 8 (9): e3163.

Kliegman, R. M., Stanton, B. M., & Geme, J. S. (2015). Nelson textbook of pediatrics, 2-volume set: 20e.

Le Flohic, G., Porphyre, V., Barbazan, P. and Gonzalez, J.P., 2013. Review of climate, landscape, and viral genetics as drivers of the Japanese encephalitis virus ecology. *PLoS neglected tropical diseases*, *7*(9): e2208.

Oliveira, A.R., Strathe, E., Etcheverry, L., Cohnstaedt, L.W., McVey, D.S., Piaggio, J. and Cernicchiaro, N., 2018. Assessment of data on vector and host competence for Japanese encephalitis virus: A systematic review of the literature. *Preventive veterinary medicine*, 154: 71-89.

Oliveira, A.R.S., Piaggio, J., Cohnstaedt, L.W., McVey, D.S., and Cernicchiaro, N. 2019. Introduction of the Japanese encephalitis virus (JEV) in the United States – A qualitative risk assessment. *Transbound Emerg Dis.*, 1-17.