Title

Revisiting the role of swine on the risk of Japanese Encephalitis Virus (JEV) transmission in the United States: a rapid systematic review of the literature

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Contributions of the authors

Natalia Cernicchiaro is the guarantor. Study protocol was initially drafted by Vanessa Veloso (VV), Andrea Dixon (AD), and Natalia Cernicchiaro (NC), and all authors provided feedback. Vanessa Veloso will conduct the search and deduplication of references obtained during the primary search strategy. Vanessa Veloso will independently perform the relevance screening of primary databases and Madison Evje (ME) will independently perform the relevance screening of grey literature; Christy Hanthorn (CH) will serve as second reviewer for VV, and VV will serve as second reviewer for ME (resolving conflicts and checking excluded and unclear references). Note that VV and ME will not perform the relevance screening in duplicate, but concurrently (VV will screen the primary databases, and ME will perform hand search and grey literature search and screening). VV, NC, SE, CH, Taylor McAtee (TM), and Ashley Thackrah (AT), 03.13.23 will independently, and concurrently, conduct the data extraction (i.e., data extraction will be performed in duplicate). ~~Natalia Cernicchiaro will conduct the risk of bias assessment.~~ 03.13.23 (RoB will not be conducted as indicated later in RoB-section) Vanessa Veloso will conduct identification and characterization of knowledge gaps, data synthesis, and manuscript preparation. VV, CH, NC, and AD will identify, develop and/or modify all necessary tools for this rapid review (i.e., relevance screening tool, data extraction tool, ~~risk of bias tool~~03.13.23, and knowledge gap identification tool). All authors will read and provide feedback on the original

and subsequent versions of the manuscript. A final version of the manuscript will be submitted for publication after approval of all study contributors.

Sponsor, support & funding sources

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Background 04.04.23 (Changes in wording of the Background section are not indicated with an underline or strikethrough since they do not affect the proposed research materials & methods).

Japanese Encephalitis (JE) is an emerging, zoonotic disease caused by the Japanese encephalitis virus (JEV), which is transmitted primarily by *Culex* species mosquitoes (particularly *Culex tritaeniorhynchus*). The JEV maintains its life cycle between mosquitoes and vertebrate hosts, primarily pigs and wading birds (Le Flohic et al., 2013). In humans, JEV infection causes inflammation of the brain (encephalitis) as well as fever, headache, respiratory distress, gastrointestinal pain, confusion, seizures, and, in some cases, death (Fischer et al., 2012; Hills et al., 2014). The global incidence of JE is uncertain. Effectiveness and quality of JE surveillance in endemic countries vary (Jayatilleke et al. 2020), as does availability of diagnostic testing throughout the world. Between 50,000 and 100,000 JE cases per year are estimated to occur in endemic countries (WHO, 2006; Campbell et al., 2011, Quan et al., 2020). Among all clinical cases, children under the age of 10 comprise the majority affected (WHO, 2006).

Whereas less than 1% of the cases are accompanied by symptoms, 30% of the symptomatic cases are fatal (Campbell et al., 2011). Being untreatable and incurable, once introduced in a community, JE can lead to devastating economic and health impacts.

The United States (US) is considered a susceptible region with great potential for JEV introduction. The availability of competent vectors, susceptible maintenance hosts (avian), intensive travel and trade activities to and from JEV-affected countries, areas with similar climatic and environmental conditions to countries where the virus is epidemic, and large populations of susceptible, amplifying hosts (domestic and feral pigs), makes the US suitable for JEV emergence. In fact, the US is the world's third-largest producer and consumer of pork and pork products (ERS, USDA 2022). The importance of the swine industry to the US economy and the sizeable naïve pig populations, magnify the severity of a potential viral incursion. As pigs are considered the main amplifying host of JEV, an extensive review of the literature and identification of knowledge gaps will assist researchers, stakeholders, and policy makers with effort prioritization, development of precautionary intervention measures, and evaluation of disease control measures. Although current conditions have not been favorable for JEV to establish in the US, increases in international trade and globalization, as well as changes in climate and land use, and reductions in pesticide use, can contribute to its rapid and wide geographical spread (Oliveira et al., 2018). A good understanding of the role of swine as an amplifying host for this virus is critical to public health authorities when planning prevention and preparedness measures.

Objectives

A rapid systematic review of the literature, referred to as a rapid review (RR) for the rest of the document, will be implemented as per the Cochrane group (Garritty et al., 2021) guidelines 04.04.23 (additional/complementary wording), with the ultimate goal of investigating the role of swine on the risk of JEV transmission in the US, and to identify knowledge gaps that may serve as a guide for future research efforts, 04.04.23 (change in wording) the objectives of this review are: 1) to gather and summarize available scientific literature on the role of swine (~~with emphasis on the role of feral swine~~ domestic and feral 04.04.23 (change in wording)) in the transmission of the JEV and 2) to identify knowledge gaps and potential areas amenable for future research, using a rapid review of the literature 04.04.23 (change in wording).

Therefore, this rapid review will seek to 03.23.23 address several questions ~~the following questions as they are~~ 04.04.23 (change in wording) related to both domestic and feral pigs, including 04.04.23 (change in wording): 1) What is the role of swine in the transmission of JEV?; 2) What is the JEV seroprevalence in pigs (domestic and feral)?; 3) Are there differences in JEV transmission depending on the type of swine operations (e.g., confined commercial or research vs. opened commercial or research vs. semi-opened commercial or research vs. subsistence farming)?; 4) Are there differences in JEV transmission depending on the size of the swine operations?; 5) Are there differences in JEV transmission depending on the location of the swine operations (e.g., urban vs peri-urban vs rural; proximity to bodies of water)?; 6) What are the most important routes of infection/transmission in swine?; 7) Are there differences in swine transmission and/or pathophysiology among JEV genotypes (including differences in infectiousness, lesions, clinical signs)?; 8) Are there management or biosecurity/hygiene procedures that are associated with susceptibility of JEV introduction/transmission (e.g., quarantine, segregation, personnel standard procedures, animal-sourcing, truck trafficking procedures, testing, mosquito trapping, in-house

surveillance/testing)?; 9) What surveillance efforts have been put in place worldwide (e.g., use of bird or pig sentinels, mosquito trapping)?; 10) What is the speed with which JEV spreads throughout a population (i.e., reproductive number/ratio (R_0) for JEV); 11) What have been the most successful preparedness response strategies (e.g., vaccine banks, diagnostic tests, trained veterinarians, other strategic measures that allow a quick response) deployed in other countries for reducing JEV prevalence/transmission?; 12) Are there differences among pig breeds/genetic makeup that are known to influence swine herd susceptibility to JEV transmission?; 13) Is there a difference in JEV susceptibility based on the sex and/or age category of pigs?; 14) Regarding immunization status, to other viruses besides JEV, is there any cross-protection with other viruses?; 15) Which JEV vaccines are available for use in swine?; 16) What vaccines are the most effective for swine?; 17) What is the sensitivity/specificity of diagnostic tests available for detection of JEV in swine?; 18) Can JEV be found/transmitted/introduced via pork products? Other non-planned a priori outcomes related to JEV in swine species were extracted from the literature when identified as pertinent to the study objectives 04.04.23 (complementary statement to clarify the methodology).

Registration and amendments

This protocol has been drafted, using the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P). This protocol will be made publicly available within the K-Rex repository (K-Rex/CORE collection). *Post hoc* changes made to the protocol will be recorded and posted as an updated version in the same repository. 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

For the "primary" search, the sources of evidence must include peer-reviewed papers, written in English, and containing information regarding the role of domestic and/or feral swine in the transmission of JEV. For the "grey literature" search, the sources of evidence may or may not be peer-reviewed, must be written 04.04.23 (additional wording) in English, and include information regarding the role of feral swine in the transmission of JEV. We will use a POS (Population, Outcome, Study design) framework for both primary and grey literature searches with no time restrictions, as depicted in Table 1 and Table 2, respectively.

Table 1. Eligibility criteria for the **primary database search** (does not include grey literature search).

Population (P)	Swine (domestic (*Sus domesticus)* and feral (*Sus scrofa*)) of all ages, sexes, and breeds
Outcome (O)	Transmission efficiency, infectiousness, susceptibility to infection, incubation time, duration of viremia, routes of transmission, physiopathology, economic/productivity (reproductive) impacts, vaccine efficacy, diagnostic test performance, pathogen/genotype characteristics (pathogenicity, virulence, ~~infectivity~~ infectiousness 04.04.23 (change in wording for consistency), etc.), among others.

Study design (S)	No restriction.
Language	English
Location	No restriction
Time period	No restriction
Type of evidence	Peer-reviewed articles, and government reports

Table 2. Eligibility criteria for the **grey literature** search.

Population (P)	Feral swine (*Sus scrofa*) of all ages, sexes, and breeds
Outcome (O)	Transmission efficiency, ~~infectiousness~~ infectivity 04.04.23 (change in wording for consistency), susceptibility to infection, incubation time, duration of viremia, routes of transmission, physiopathology, economic/productivity (reproductive) impacts, vaccine efficacy, diagnostic test performance, pathogen/genotype characteristics (pathogenicity, virulence, infectivity, etc.), among others.
Study design (S)	No restriction.
Language	English
Location	No restriction
Time period	No restriction
Type of evidence[£]	Theses, technical reports, APHIS reports

[£]Include articles by Vienna Brown, USDA National Wildlife Research Center (https://www.aphis.usda.gov/aphis/ourfocus/wildlifedamage/programs/nwrc), and USDA Current Research Information System (CRIS; https://cris.nifa.usda.gov/).

Several rapid review approaches will be incorporated to expedite different steps of the process. For accelerating the eligibility assessment of the studies, we will ~~The following rapid review (RR) approaches will be incorporated to expedite the eligibility assessment of the studies~~ 04.04.23 (change in wording): 1) *Limit the number of outcomes focusing on those most important for decision-making* (outcomes of interest will be defined based on stakeholder group interests)

(Garrity et al., 2021), and 2) *Limit inclusion criteria to only English language publications* (Nussbaumer-Streit et al., 2020). Nussbaumer-Streit et al. (2020) reported that this approach had minimal effect on overall conclusions when applied on clinical interventions; however, the authors advise to consider the subject carefully (i.e., topics that are expected to have relevant literature in other languages beside the chosen one).

Information sources

Identification of potentially relevant literature will be performed using the databases described in Table 3.

Table 3. Databases, interface used, and dates encompassed for the rapid review.

Database	Interface	Dates included
Web of Science Core Collection; KCI-Korean Journal Database; MEDLINE; SciELo Citation Index	Web of Science	1950 - 2022
Scopus	Scopus, Elsevier	1920 - 2022

The following RR approaches will be incorporated to expedite the identification of relevant literature: 1) *Limit the number of electronic databases searched* (Garrity et al., 2021). Nussbaumer-Streit et al. (2020) evaluated the effect of various abbreviated search approaches on the overall conclusions of evidence synthesis and concluded that combining at least one

electronic database with a search of reference lists or a second database provides a solid base for decision-making in most cases. MEDLINE was the only exception where the combination with reference lists was not sufficient. 2) *Hand search of reference lists that were deemed relevant by reviewers and after consultation with experts* (Royle and Waugh, 2003). Royle and Waugh (2003) concluded that a more selective approach to database searching is a viable approach to expedite reviews and save resources.

Before defining the primary databases and based on recommendations from Garrity et al. (2021), we performed a pilot search using Web of Science 04.20.23 (acronym definition) (WOS), Scopus, and Center for Agriculture and Biosciences 04.20.23 (acronym definition) (CAB) to evaluate the total number of references yielded with the proposed search strategy (described in the Search strategy section) in each database, the overlapping of results among those 3 databases (WOS, Scopus, and CAB), and the relevance of results. The two selected databases were the ones with less overlap, that yielded a great number of relevant references.

Search strategy

Primary databases (Table 4) searches will be performed by one reviewer (VV), using the following search terms: “Japanese encephalitis”, “Japanese B encephalitis”, “viral encephalitis”, “JE”, “JEV”, “summer encephalitis”, “viral meningitis”, “Russian autumnal encephalitis”, “swine”, “pork”, “sow”, “gilt”, “piglet”, “barrow”, “hog”, “pig”, “boar”, “*Sus domesticus*”, and “*Sus scrofa*”.

A grey literature search will be conducted based on expert guidance to address the role of swine, but specifically feral swine, in the transmission of JEV. The grey literature search will be specified based on the filtering allowances of each database, but guided by the following search

terms: “Japanese encephalitis”, “Japanese b encephalitis”, “JEV”, “JE”, “summer encephalitis”, “viral encephalitis”, “viral meningitis”, “Russian autumnal encephalitis”, “swine”, “boar”, “hog”, “pig”, “pork”, “sow”, “gilt”, “piglet”, “barrow”, “wild”, “feral”, “game”, “free range”, “ranging”, “free-roaming”, “sus scrofa”, “undomesticated”, and “non-domesticated”. Tables 4 and 5 describe results obtained from specific search strategies implemented in ~~Web of Science~~ WOS 04.20.23 (acronym defined prior) and Scopus, and when searching grey literature (respectively).

Table 4. Results obtained from Web of Science (WOS) and Scopus using the search strategy, and different combinations, on August 09, 2022.

Database [§]	Keyword search	Results
WOS	3: #1 AND #2	618
	2: ((((((((((TS=(swine)) OR TS=(pig)) OR TS=(hog)) OR TS=(boar)) OR TS=(pork)) OR TS=("sus scrofa")) OR TS=("sus domesticus")) OR TS=(barrow)) OR TS=(gilt))) OR TS=(piglet)) OR TS=(sow))	
	1: (((((((TS= ("Japanese encephalitis")) OR TS= ("Japanese b encephalitis")) OR TS=(JEV)) OR TS=(JE)) OR TS= ("summer encephalitis")) OR TS= ("viral encephalitis")) OR TS= ("viral meningitis")) OR TS= ("Russian autumnal encephalitis")	

Scopus	TITLE-ABS-KEY ("Japanese encephalitis" OR "Japanese b encephalitis" OR "JEV" OR "je" OR "summer encephalitis" OR "viral encephalitis" OR "viral meningitis" OR "Russian autumnal encephalitis" OR "viral encephalitis") AND (swine OR boar OR hog OR pig OR pork OR "sus scrofa" OR "sus domesticus" OR sow OR piglet OR gilt OR barrow)	2,545

214 § TS = Search for topic terms in the following fields within a record. Search in title, abstract, author keywords, and
215 keywords Plus®. TITLE-ABS-KEY = Search for topic terms in the title, abstract, and keywords.

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Table 5. Results obtained from grey literature and hand search, in August 2022.

Database	Keyword search	Results[0]
USDA APHIS[1]	"Feral swine" "Japanese encephalitis"	1,881
CDC[2]	ALL THIS WORD: Japanese encephalitis ANY OF THESE WORDS: feral wild undomesticated free-range ranging roaming swine pig hog boar pork	7,266
USDA NWRC[3]	6: “Japanese encephalitis” AND feral AND boar (n = 2) 5: “Japanese encephalitis” AND wild AND boar (n = 2) 4: “Japanese encephalitis” AND feral AND pig (n = 1) 3: “Japanese encephalitis” AND wild AND pig (n = 4) 2: “Japanese encephalitis” AND wild AND swine (n = 7) 1: “Japanese encephalitis” AND feral AND swine (n = 7)	330

USDA CRIS[4]	"Japanese encephalitis" AND (feral; wild; "free range"; ranging; "free roaming"; game; undomesticated) AND (swine; pig; boar; hog; pork; "sus scrofa")	1,249
Articles by Vienna Brown[5]	(“Japanese encephalitis”, “Japanese b encephalitis”, “JEV”, “JE”, “summer encephalitis”, “viral encephalitis”, “viral meningitis”, “Russian autumnal encephalitis”, “viral encephalitis”) OR ((“swine”, “boar”, “hog”, “pig”, “pork”) AND (“wild”, “feral”, “game”, “free range”, “ranging”, “free roaming”, “sus scrofa”, and “undomesticated”))	33
Reference lists of Wildlife Health Australia[6]	(“Japanese encephalitis”, “Japanese b encephalitis”, “JEV”, “JE”, “summer encephalitis”, “viral encephalitis”, “viral meningitis”, “Russian autumnal encephalitis”, “viral encephalitis”) OR ((“swine”, “boar”, “hog”, “pig”, “pork”) AND (“wild”, “feral”, “game”, “free range”, “ranging”, “free roaming”, “sus scrofa”, and “undomesticated”))	92

USDA APHIS = United States Department of Agriculture, Animal and Plant Health Inspection Service; CDC = Centers for Disease Control and Prevention; USDA NWRC = United States Department of Agriculture, National Wildlife Research Center; USDA CRIS = United States Department of Agriculture, Current Research Information System.

[0] Resulting number for each source is reported before de-duplication of references

[1]Keyword search will be conducted within each database, using the website search option.

https://www.aphis.usda.gov/aphis/home/

[2]Seearch was performed using the “advanced search” option-fields

[3]Wildlife Services Digital Collection (https://nwrc.contentdm.oclc.org/digital/collection/NWRCPubs1); the wild- synonyms "game", "free range", "ranging", "free-roaming", "undomesticated", and "non-domesticated" did not find any result.

[4]Search term string was entered in "Full text Terms" field-option, using "Subfile option" as "(Any)". https://cris.nifa.usda.gov/cgi-bin/starfinder/99451/crisassist.txt

[5] Articles by Vienna Brown include: 1) Brown VR, Bowen RA, Bosco-Lauth AM. Zoonotic pathogens from feral swine that pose a significant threat to public health. Transbound Emerg Dis. 2018 Jun;65(3):649-659. 2) Brown, V. R., Marlow, M. C., Maison, R. M., Gidlewski, T., Bowen, R., & Bosco-Lauth, A. (2019). Current status and future recommendations for feral swine disease surveillance in the United States. Journal of animal science, 97(6), 2279-2282.

3) Brown, V. R., Marlow, M. C., Gidlewski, T., Bowen, R., & Bosco-Lauth, A. (2020). Perspectives on the past, present, and future of feral swine disease surveillance in the United States. Journal of Animal Science, 98(8), skaa256.

[6]The reference list of the review article was searched for titles referring to Japanese encephalitis in wild pigs and all above mentioned synonyms.

Data management

A single reviewer (VV) will export results from the databases as Research Information Systems (RIS) files and deduplicate the reference list using Covidence AI (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). Following relevance screening, full-text pdfs from relevant reference lists will be searched, downloaded, and saved in a single folder by an undergraduate student-worker (ME). Full-text pdf files will be named based on the first Covidence ID number, first author's last name, and publication year ~~(first authors having multiple publications in the same year will have the year followed by a unique letter~~ 03.13.23 (same first author and year of publication still have different Covidence ID, letters were unnecessary) (e.g., 764 - Simpson

2020; 765 - Simpson 2022). Full-text pdfs available online will be ~~imported into Zotero (Corporation for Digital Scholarship, Virginia, USA), and then~~ 03.13.23 (this step was not required to upload pdf files into Covidence) uploaded into Covidence using the bulk upload function (VV), or manually uploaded for those not available online (ME). 03.13.23 [full text pdfs acquired via k-state library services were uploaded manually (ME)].

Relevance Screening/Selection process

The selection process of articles obtained through 04.04.23 (additional wording) the primary databases (Table 4) will be performed according to the following steps:

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

#2: Deduplication. Duplicated references will be removed using Covidence's deduplication tool.

#3: Primary relevance screening tool development. A screening tool comprised of a flow chart will be designed based on the POS and the current study objectives. The tool will be piloted using 150 randomly selected abstracts (sorted by author in Covidence), which will be reviewed by two reviewers (VV and CH) concurrently 04.04.23 (additional wording) and ~~adjusted/edited~~ amended 04.20.23 (change in wording) as necessary to improve clarification of the relevance criteria. If major edits (i.e., change in meaning) 04.20.23 (clarification of what would be considered major edits) are incorporated, an additional round of screening will be performed in another set of 50 randomly chosen abstracts. This process will be repeated until the clarity of the relevance criteria is deemed sufficient by the reviewers (VV and CH; at least 80% agreeability 04.20.23 (clarification of methodology)). Once the relevance screening tool is finalized, all articles will be screened using the finalized screening tool.

#4: Primary relevance screening tool calibration. The proposed primary relevance screening tool will be tested for ~~clarity~~ agreeability of the reviewers and clarity of the tool ~~utility~~. ~~and utility~~ 03.13.23 (This sentence was misconstrued for its intended meaning). For the test exercise, ~~a pair of reviewers~~ two 04.20.23 (change in wording) (VV and CH) will independently review a random sample of 20% of the total ~~titles and abstracts~~ references 04.20.23 (change in wording) and assess eligibility. 04.04.23 (This sentence was misconstrued for its intended meaning) ~~Reviewers' agreeability when using the primary relevance screening tool, as well as the tools' clarity will be evaluated.~~ ~~04.04.23 (Re-wording)~~ Reviewers will compare their results and discuss any differing decisions or questions that arose during the screening. The primary relevance screening tool will be used in its current form only if > 80% agreement is achieved between reviewers. If this threshold is not met, then the primary relevance screening tool will be amended based on reviewers' 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 screening. Once a final version of the relevance screening tool is decided upon, VV and CH will complete the title and abstract screening. During this step, one reviewer will evaluate each reference (VV) and a second reviewer will check excluded references for ~~inconsistencies~~ agreement 04.20.23 (change in wording) (CH). Articles that are ambiguous as to whether they fit the eligibility criteria will be 04.20.23 (additional wording for clarification) deemed "unclear" by the primary reviewer (VV)04.20.23 will be re-evaluated by the second reviewer (CH). Only articles deemed "unclear" by both reviewers during the primary screening will undergo a supplementary screening (full text screening). Supplementary screening will be performed by the second reviewer (CH) using the full text article and the same relevance tool as the primary screening. Disagreements between the second and primary reviewer on "excluded" and "unclear"

articles will be indicated by the second reviewer with a note explaining the reason for disagreement. Disagreements will be resolved via consensus between the two reviewers (VV and CH). If consensus cannot be achieved, then a third reviewer (NC) will be consulted. Studies included in the primary relevance screening will move directly to data extraction, as well as those deemed "unclear" during the first relevance screening and subsequently identified as relevant after the supplementary relevance screening. References that moved to the supplementary screening phase or extraction phase can still be excluded if deemed not relevant. References excluded during the supplementary screening or extraction phase will receive a tag with the reason for exclusion.

Non-peer-reviewed articles on JEV and feral swine will be excluded from primary relevance screening with a "grey literature" tag. Excluded references containing "grey literature" tags will be evaluated using the grey literature relevance screening process. A similar screening process will be carried out for non-peer-reviewed articles. One reviewer will evaluate each reference (ME) and a second reviewer will check excluded references for agreement (VV). Articles deemed "unclear" by the primary reviewer (ME) will be re-evaluated by the second reviewer (VV). Disagreements between the second and primary reviewer will be resolved via consensus between the two reviewers (VV and ME). If consensus cannot be achieved, then a third reviewer (NC, or CH) will be consulted. 04.04.23 (statement to clarify the grey literature screening process)

The selection process of the grey literature and hand search (Table 5) will be performed according to the following steps:

#1: A search strategy will be defined according to each electronic source based on search resources/restrictions available in each electronic database.

#2: Results obtained from each combination of words in each database will be screenshot and saved as a record of search terms used and resulting references obtained.

#3: The relevance screening of grey literature/hand search (i.e., governmental organizations databases, reference list of reference review articles) will be performed by accessing the relevance of titles first. Only titles that include either JEV (or synonymous), or wild swine (or synonyms) will be further investigated for relevance, using the full text file.

#4: Relevant literature will be downloaded and included for data extraction.

Data extraction

Data extraction will be performed in ~~Covidence~~ Excel 11.20.23 (changed due to the complexity of the data being extracted and Covidence's lack of capacity to extract several outcomes per reference), using a custom-built data collection form. The data extraction form will be assessed via a calibration exercise, similar to the one performed for the relevance screening tool. After achieving 80% agreement during the calibration exercise, and upon refinement of the data extraction tool, full-text articles will be evaluated for extraction in duplicate, and independently by teams of two reviewers ~~two reviewers~~ (VV, CH, SE, NC, AT, TM) 03.13.23. Unresolved discrepancies will be resolved by a third available reviewer (VV, CH, SE, NC, AT) 03.13.23. Full-text articles can still be excluded during the data extraction process (if deemed irrelevant during extraction phase by both reviewers 03.13.23). Exclusion of studies that moved to the extraction phase will be performed by entering "no" into the "inclusion" column, and the corresponding reason for exclusion into the "Exclusion reason" column of the data extraction tool. ~~moving the study back to screening when choosing the Covidence built-in option "Move study to full text review", then the article will be double-tagged with a 1) reason for exclusion, and 2) "retracted-during-extraction" tags.~~ 3.13.23 (Covidence was

not used for the data extraction process) The following RR approaches will be incorporated to expedite data extraction: ~~1) *Limit data extraction to a minimal set of required data items, and limit the outcomes to cost-effectiveness* (Tricco et al., 2015);~~ 3.13.23 (a great number of outcomes on JEV and swine were extracted with the intent to understand the role of swine in JEV transmission) ~~2) *Use standardized data extraction form piloted elsewhere* (Wollscheid and Tripney, 2021);~~ 3.13.23 (Data extraction tool was custom-built to meet our research objectives, which included a great amount of outcomes of interest) 3) *Use data from existing SR to reduce time spent on data extraction; however, the methodological and reporting quality of the existing SR will be assessed* (Hamel et al., 2020; Martyn-St James et al., 2017). When comparing the accuracy of extracting data from an existing SR versus extracting from the primary studies, Martyn-St James et al. (2017) concluded that data in existing reviews were highly accurate, and findings and conclusions did not differ between methods.

Data items

All variables for which data will be sought will be defined (such as POS items~~, funding sources,~~3.13.23 (not extracted) location), including prioritization of main and additional outcomes (with rationale), any pre-planned data assumptions and simplifications (Table 6). Experts and/or stakeholders in the topic area will be involved in early stages of the project to ensure the included outcomes are relevant.

Table 6. List of data items that will be extracted from the included reference list of studies

Data item	Description

Number	Study ID number as identified in Covidence (same reference number used for relevance screening).
Study	For articles describing multiple studies, repeat the reference information in the row below and differentiate the studies by attributing different numerical identifications for each trial within a publication.
Title	Exact title of publication.
Row descriptor	Row designation to help organize the extraction by row (extractor help column).
Authors	Name of all authors as shown in Covidence extraction section.
Publication year	Year of publication.
Journal	Journal of publication.
Source	Indicate if the article was obtained via primary electronic search ("DB") or hand search/grey literature ("HS").
Outcome	Identify the outcome investigated by the reference being extracted (e.g., “mortality", "morbidity", "seroprevalence", "diagnostic test efficacy", "vaccine efficacy", "viremia", "biosecurity", "surveillance", "incubation period"). If multiple outcomes, use one row per outcome (multiple rows for the same study for each outcome). Report "NA" if the reference has no outcome to extract and thus will be excluded.
Include	Does this reference contain extractable data? "yes", or "no". If "no", define the reason for exclusion in "Exclusion reason"; if "yes", enter "NA" for "Exclusion reason".
Exclusion reason	Reason for "no" in "Include"- category [e.g., foreign language, wrong outcome, wrong population, wrong publication type (i.e., non-peer-reviewed), wrong study type (non-systematic reviews)]. If the reference is excluded, enter "." for the remaining row cells.
Status	Indicate the reference status in the extraction process as: extracted, pending, or excluded.
Comments A	Comments to clarify one or more entries made in this section (reference information).
Population	Identify the study population as "domestic swine", "feral swine", "miniature pigs", "pork meat", "porcine cells", "unspecified swine", "sentinel pigs", "other". If “other”, define in the Comments B section. If author mention "pigs from farms", pigs will be assumed to be "domestic swine".
Population ID	Identify each study population within a reference by entering different numbers to different populations.
Cluster ID	If clustering is present, identify the different clusters by attributing a different ID number (one per row if outcome is provided by cluster, e.g., province 1, province 2, or farm 1, farm 2), or identify number of clusters per outcome (if outcome is provided as average of all clusters identify how many are included in the average, e.g., 18 provinces).

Repeated measures	If repeated measures are present, identify the unit followed by a number (e.g., hour 1, hour 2, day 1, day 2, month 1, month 2). If no repeated measure is present, enter "NA".
Sex	Identify the sex of the study population as "male", "female", or "both" (both sexes are present). Use “NR” if not reported, or "NA" if not applicable (e.g., pork meat).
Breed	Animal breed as reported by authors. Use "NR" if not reported, or "NA" if not applicable (e.g., pork meat, feral swine, porcine cells).
Age	Define age category at start of study period as reported by authors (i.e., age in months, weeks, or "stillborn", "newborn", “nursing piglets”, "weaned piglets", "barrow", "gilt", "sows", "boar"). Enter "multiple" if multiple age categories, "NR" if not reported or cannot tell, or "NA" if not applicable. Use multiple rows (one per category) if the authors reported outcome per age category.
Comments B	Comments to clarify one or more entries made in this section (population section).
Year cond.	Year the study was conducted. Use "NR" if not reported.
Month cond.	Month the study was conducted. Use "NR" if not reported.
Season cond.	Season the study was conducted (as reported by authors). Use "NR" if not reported.
Country	Country where the study was conducted. Use "NR" if not reported.
State/province	State or province where the study was conducted. Use "NR" if not reported.
City/district	City or district where the study was conducted. Use "NR" if not reported.
Region	Region where the study was conducted (as described by authors). Use "NR" if not reported.
Comments C	Comments to clarify one or multiple entries made in this section (study location characteristics).
Type of study tab	Identify the tab where the study will be directed for further extraction as "observational", "experimental", "case-study", systematic review ("SR"), modeling ("MO"), or meta-analysis ("MA").
Study design	Study design as reported by authors (e.g., *in vitro*, survey, case-control, cohort, cross-sectional, etc.), or "NR" if not reported.
Objective	Study objectives as stated by the author. Use "NR" if not reported.
Comments D	Comments to clarify one or more entries made in this section (study design).
Experimental exposure	Identify exposure type as "natural" or "challenge". Use "NR" if not reported or cannot tell.
Exp. comparative analysis	Enter "yes" for studies designed for comparative analysis, or "no" if there is no comparison (i.e., surveillance, prevalence studies). if no, enter "NA" for Exp. Comparator.

Exp. comparator	Indicate the comparison group (e.g., controls (C), positive-control (PC), negative-control (NC), C&PC, C&NC, PC&NC, C&PC&NC). Use "NR" if not reported or cannot tell, "NA" if not applicable, or "other". If "other", specify in the comments E section.
Intervention	Define the study intervention (e.g., vaccination, metaphylactic antimicrobial (preventive), antimicrobial treatment (curative), feed additive, etc.).
Exp. sample size start	Sample size reported in the study at the beginning of experimental phase; use "NR" if not reported or cannot tell.
Comments E	Comments to clarify one or more entries made in this section [intervention (experimental tab)]. If treatment structure (e.g., one-, two-way factorial) was reported, enter here.
Obs. comparative analysis	Enter "yes" for studies designed for comparative analysis, or "no" if there is no comparison.
Obs. comparator	Indicate the comparison group (e.g., controls, non-exposed, non-diseased). Use "NR" if not reported or cannot tell, "NA" if not applicable (e.g., case-report), or "other". If "other", specify in the comments F section.
Exposure	Define the risk factor/exposure (e.g., vaccination, month, season, region, mosquito abundance, operation type, etc.).
Obs. sample size start	Number of animals comprising the study population at beginning of study period as reported by the authors. Use "NR" if not reported or cannot tell.
Comments F	Comments to clarify entries made in this section [exposure (observational tab)].
Case sample size	Number of animals used as reported by the authors. Use "NR" if not reported.
Comments G	Comments to clarify one or more entries made in this section (case control).
Operation purpose	Operation purpose as "commercial", "education" (research), "subsistence" (backyard), "surveillance" (sentinel pigs), "unspecified farms", "slaughterhouse". Subsistence farming is identified when farm products are intended to meet the needs of themselves and their families. If "subsistence", add any complementary information on management characteristics in the Comments H section, then skip to Site characteristics section. Use "NR" if not reported, or "NA" if not applicable.
Production type	Production type at the farm level, as reported by authors (e.g., "farrow-finish", "farrow-wean", "feeder", "wean-finish", "finish", "seedstock", "breeding", "purebred"). Use "NR" if not reported, or "NA" if not applicable.
Farm size	Farm size as number of animals at maximum capacity (one-time animal capacity). Use "NR" if not reported, or "NA" if not applicable.
Barn size	Number of animals per barn during study period. Use "NR" if not reported, or "NA" if not applicable.
Pen size	Number of animals per pen during study period. Use "NR" if not reported, or "NA" if not applicable.

Facility loc.	Farm location as per author description (e.g., "urban", "rural", "peri-urban"). Use "NR" if not reported, "NA" if not applicable.
Operation type	Type of swine operations reported as: "confined", "semi-opened" (includes at least a roof, maybe half walls, and/or side-nets), or "open". Use "NR" if not reported, or "NA" if not applicable.
Production syst.	Identify the production system as "conventional", "alternative", or "organic". If alternative, expand in Comments H (i.e., antibiotic-free, hormone -free, other). Use "NR" if not reported, or "NA" if not applicable.
Animal turnover	How often new animals are being introduced into the production system in days/months interval. Use "NR" if not reported, or "NA" if not applicable.
Biosecurity procedure	Reported biosecurity/hygiene procedures applied at the farm (e.g., quarantine, segregation, personnel standard procedures, animal-sourcing, conveyance management, testing, mosquito control, in-house surveillance procedure(s), etc.). Use "NR" if not reported, or "NA" if not applicable.
AI	Does the farm use artificial insemination (AI)? "yes", "no", or "NR" if not reported, or cannot tell, or "NA" if not applicable.
Comments H	Comments to clarify one or more entries made in this section (management characteristics). This section should only be used if necessary since it is an open response field.
Multispecies	Are there multiple species raised on the pig production site? "yes", "no", or "NR" if not reported, or cannot tell, "NA" if not applicable. If yes, define in Other Species.
Other species	If "yes" for multispecies, what other animal species are raised on the farm?
Body water proximity	Is the pig production site close to a body of water? "yes", "no", or "NR" if not reported, or cannot tell, "NA" if not applicable. If "yes", specify in Body water type.
Body water type	If "yes" for Body water proximity, specify if "moving salt-water" (ocean), "steady salt-water" (salt-water lake, or swamp), "moving fresh-water" (river, creek), "steady fresh-water" (pond, lake, or fresh-water swamp), "flooded area" (rice paddies). Use "NR" if not reported, or cannot tell, "NA" if not applicable.
Bird presence	Are there birds present in the area? "yes", or "no". If "yes", specify the species in Bird species. Use "NR" if not reported or cannot tell, "NA" if not applicable.
Bird abundance	Was bird abundance reported? If so, extract as "high", "moderate", "low", or "none" based on authors' clue/description (clarify threshold in Comments I if necessary). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Bird species	If "yes" for Bird presence, extract bird species. Use "NR" if not reported or cannot tell, or "NA" if not applicable.

Mosquito presence	Are there mosquitoes in the area? "yes", or "no". If "yes", specify how abundant in Mosquito abundance measure, and Mosquito abundance value (if reported as value), OR Mosquito abundance category (if reported as category). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Mosquito abundance measure	Measure used to report mosquito abundance value. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Mosquito abundance value	Reported mosquito abundance value. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Mosquito abundance cat.	Reported mosquito abundance as category (e.g., "high", "moderate", "low", or "none" based on authors' description (clarify threshold in Comments I if necessary)). Use "NR" if not reported or cannot tell, or "NA" if not applicable (authors reported mosquito abundance numerically, and values were extracted in Mosquito abundance measure and Mosquito abundance value).
Farm site topography	Reported topography of pig production site. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Comments I	Comments to clarify one or more entries made in this section (site characteristics).
Cell line	Cell line name as reported by authors. Use "NR" if not reported, and "NA" if not a cell culture study.
Cell derived	Tissue from which the cell line was derived (e.g., porcine kidney, porcine testis, etc.).
Comments J	Comments to clarify one or more entries made in this section (cell culture characteristics).
JEV strain	JEV strain identification. Use "NR" if not reported, or "NA" if not applicable (e.g., natural exposure).
Comments K	Comments to clarify one or more entries made in this section (JEV strain characteristics).
JEV case definition	List all criteria for author's case definition, such as: diagnostic test, clinical signs, pathological finding, agent isolation and culture, any combination of those, or other(s). Use "NR" if not reported, or "NA" if not applicable.
JEV isolation	Was JEV isolated from positive pigs? "yes", "no", or "NR" if cannot tell.
JEV isolation sample	What sample type was used for the isolation (e.g., meat, blood, brain tissue, saliva)?.
JEV genotype	JEV genotype(s) identified. Use "NR" if not reported.
Diagnostic test	Was diagnostic test used? "yes", "no", or "NR" if cannot tell.
Diagnostic test sample	What sample type was used for the diagnostic test (e.g., blood, brain tissue, saliva, etc.)? Use "NR" if not reported or cannot tell, or "NA" if "no" for Diagnostic test.

Diagnostic test name	What is the name of the diagnostic test used as reported by the authors? If multiple tests, use one row per diagnostic test. Use "NR" if not reported or cannot tell, or "NA" if "no" for Diagnostic test.
Diagnostic test measure	Unit of measure used to report test results. Use "NR" if not reported, or "NA" if not applicable.
Diagnostic test value	Numeric result of diagnostic test. Use "NR" if not reported, or "NA" if not applicable.
Confirmatory test	Was there any confirmatory test? If yes, name the test, and/or copy and paste any other provided information/clarification.
Clinical signs	Were clinical signs observed/reported? "yes", "no", "NR" if not reported or cannot tell.
Clinical signs manifestation	In vivo clinical signs as described by the authors. Use "NR" if not reported.
Pathological findings	Were pathological findings described by the authors (macroscopy or microscopy)? "yes", "no", "NR" if not reported or cannot tell.
Macroscopy	Macroscopic findings (post-mortem) as described by the authors. Use "NR" if not reported, or "NA" if "no" for Pathological findings.
Microscopy	Microscopic findings (post-mortem) as described by the authors. Use "NR" if not reported, or "NA" if "no" for Pathological findings.
Differential diag.	Was differential diagnostic test used? "yes", "no", or "NR" if cannot tell. If "yes", define what test in Differential diag. test.
Differential diag. test	If "yes" for Differential diag., define what test was used. Use "NR" if not reported or cannot tell, and "NA" if not applicable ("no" for Differential diag.). If multiple differential tests, add a new row for each test.
Differential to	What agent(s) were ruled out with the differential diagnostic test used. Use "NR" if not reported or cannot tell, and "NA" if not applicable ("no" for Differential diag.).
Comments L	Comments to clarify one or more entries made in this section (case definition).
	This section refers to the outcome(s) of the study being extracted
Outcome level	Level at which the outcome was measured (e.g., "in-vitro cell", "in-vivo cell" "animal", "barn", "farm", "county", "region", "state", "province").
Diagnostic test	Name of new diagnostic test being evaluated/compared to diagnostic test defined at case definition section. Use "NA" if not applicable (study did not evaluate/compare diagnostic tests). If multiple diagnostic tests are being evaluated, create one row for each comparison.
Diag. test sample	What sample type is being used for the diagnostic test (e.g., plasma, saliva, brain, placenta, cerebrospinal fluid). If multiple samples are being used, use a new row for each sample. Use "NR" if not reported or cannot tell, or "NA" if not applicable.

Diag. test cross-reactivity	Was cross-reactivity described by the authors for the diagnostic test used? "yes", "no", "NR" if not reported or cannot tell, or "NA" if not applicable (study did not evaluate diagnostic test). If "yes", extract to which viruses cross-reactivity was observed in Cross-reactivity sp.
Cross-reactivity sp.	If "yes" for Diag. Test Cross-reactivity, extract to which viruses cross-reactivity was observed/evaluated. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Diag. test performance measure	Type of performance measurement reported, such as sensitivity, specificity, likelihood ratio, predictive values, and/or other accuracy/correlation measures reported for diagnostic tests being compared. If multiple test metrics were evaluated, enter one per row (use multiple rows). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Diag. test performance value	Reported value of test performance. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Diag. test measure of var.	Measure of variability reported for test performance estimate (e.g., standard error, standard deviation, confidence interval). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Diag. test value of var.	Numerical value of variability reported for diagnostic test performance estimate. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Diag. test p value	Reported p-value for test performance. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Comments M	Comments to clarify one or more entries made in this section (diagnostic test).
Peak virus titer measure	Unit of measure used to report viral peak titer. Use "NR" if not reported, or "NA" if not applicable.
Peak virus titer value	Peak value of virus titer. Use "NR" if not reported, or "NA" if not applicable.
Peak virus titer measure var.	Unit to report measure of variation for peak value of virus titer. Use "NR" if not reported, or "NA" if not applicable.
Peak virus titer value var.	Measure of variation for viral peak titer value. Use "NR" if not reported, or "NA" if not applicable.
Time virus peak measure	Unit of measure for time post infection when viral titer peaked. Use "NR" if not reported, or "NA" if not applicable.
Time virus peak value	Time (value) post infection when viral titer peaked. Use "NR" if not reported, or "NA" if not applicable.
Cytopathic change	Cytopathic changes associated with JEV described by the authors. Use "NR" if not reported, or "NA" if not applicable.
Start time cytopathic change measure	Measure of time used to report time post infection when cytopathic changes started. Use "NR" if not reported, or "NA" if not applicable.

Start time cytopathic change	Time (value) post infection when cytopathic changes started. Use "NR" if not reported, or "NA" if not applicable.
Comments N	Comments to clarify one or more entries made in this section (cell level - study outcomes).
JEV morbidity measure	Define morbidity measure type (e.g., proportion, percentage). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV morbidity value	Reported numerical value of morbidity. Use "NR" if not reported, or "NA" if not applicable.
JEV morbidity calculated	If authors did not report a morbidity value but reported numbers that allow calculation by the reviewer, report the calculated value here (indicate the measure type (e.g., percentage) in the JEV Morbidity Measure section). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV morbidity measure of var.	Reported measure of variability for morbidity (e.g., standard error, standard deviation, confidence interval). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV morbidity value of var	Numerical value of variability reported for morbidity estimate. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV morbidity p value	Reported p-value for morbidity. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV mortality measure	Type of mortality measure reported (e.g., proportion, percentage). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV mortality value	Reported numerical value of mortality. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV mortality calculated	If authors did not report mortality value but reported numbers that allow calculation by the reviewer, report the value here (indicate the measure type (e.g., percentage) in JEV Mortality Measure section). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV mortality measure of var.	Reported measure of variability for mortality (e.g., standard error, standard deviation, confidence interval). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV mortality value of var.	Numerical value of variability reported for mortality. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV mortality p value	Reported p-value for mortality estimate. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Comment O	Comments to clarify one or more entries made in this section (morbidity and mortality).
Seroprevalence measure	Seroprevalence measure type (e.g., percentage, No. of positives per 1,000 pigs). Use "NR" if not reported or cannot tell, or "NA" if not applicable.

Seroprevalence value	Reported value of seroprevalence. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Seroprevalence measure of var.	Measure of variability reported for seroprevalence estimate (e.g., standard error, standard deviation, confidence interval). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Seroprevalence value of var	Numerical value of variability reported for seroprevalence estimate. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Seroprevalence p value	Reported p-value for seroprevalence. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
JEV ab titer	Measure of JEV-specific antibody levels (from infected animals). Use "NR" if not reported or cannot tell, or "NA" if not applicable. Can be a range if row is for repeated measures for a group of animals, or if applicable in other circumstances.
Comments P	Comments to clarify one or more entries made in this section (seroprevalence).
JEV R0	Reported JEV basic reproductive number in pigs (r-naught); estimate of JEV contagiousness. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine	Name of vaccine being tested. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine route	Route of vaccine administration. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine Ab titer	Measure of JEV vaccine-specific antibody levels. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine Ab titer day	Days post-vaccine when antibody levels were evaluated. Use "NR" if not reported or cannot tell, or "NA" if not applicable. If over multiple days, please add a row for each day/time.
Vaccine efficacy measure	Type of vaccine performance measure used to report vaccine efficacy. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine efficacy value	Reported numerical value of vaccine efficacy. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine efficacy measure of var.	Measure of variability used to report vaccine efficacy estimate (e.g., standard error, standard deviation, confidence interval). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine efficacy value of var.	Numerical value of variability reported for vaccine efficacy estimate. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Vaccine efficacy p value	Reported p-value for vaccine efficacy estimate. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Route of transmission	Indicate the route of transmission studied if reported as an outcome as "direct-contact" (physical contact between hosts), "indirect-contact" (contact with relatively fresh bodily fluids or tissue), "vector" (animate intermediary), "vehicle" (inanimate intermediary), "challenge", or "vertical"(transplacental transmission). If

	multiple routes were investigated, then enter the study again in a row below. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Transmission type	Indicate the source of transmission as described by the authors (e.g., droplet, direct-contact, indirect-contact, airborne, gastrointestinal, oral-nasal, intravenous (i.e., challenge), vector borne, vehicle borne, vertical, or biological-material (semen, blood, placenta, stillborn)).
Route incubation period	Reported time from infection (challenge) to first clinical signs specific to the route of transmission indicated in Route of Transmission and Transmission Type rows. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Pig viremia orig.	Define the source of viremia as "natural", "challenge", "maternal", "vaccine". Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Pig viremia measure	Type of measure used to report viremia value (e.g., PFU of JEV). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Pig viremia day	Day post infection when viremia was measured. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Pig viremia value	Reported numerical value for viremia. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Pig viremia duration	Duration of viremia in days. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Biosecurity procedures	Biosecurity procedures evaluated in the study (e.g., quarantine, segregation, personnel standard procedures, conveyance management, testing, mosquito control, in-house surveillance). Use "NR" if not reported, or "NA" if not applicable.
Biosecurity Effectiveness measure	Type of biosecurity effectiveness measure reported (e.g., proportion, percentage). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Biosecurity Effectiveness value	Reported numerical value of biosecurity effectiveness. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Biosecurity Effectiveness measure of var.	Reported measure of variability for biosecurity effectiveness (e.g., standard error, standard deviation, confidence interval). Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Biosecurity effectiveness value of var.	Numerical value of variability reported for biosecurity effectiveness. Use "NR" if not reported or cannot tell, or "NA" if not applicable.
Biosecurity effectiveness p value	Reported p-value for biosecurity effectiveness. Use "NR" if not reported or cannot tell, or "NA" if not applicable.

Comments Q	Comments to clarify one or more entries made in this section (outcome).
JEV surveillance strategy	JEV surveillance strategy evaluated in the study (only if reported as an outcome of the study), such as "sentinel pigs", "sentinel birds", "testing pigs", "testing wild-life", "testing birds", "encouraging provider/veterinarian report", "promoting awareness", "laboratory-based surveillance" (group of laboratories recruited by the health department to regularly report specified laboratory results), "adequate case investigation program", "expanding report". Use "NR" if not reported, or "NA" if not applicable.
Effectiveness surveillance	Critical evaluation of the effectiveness of JEV surveillance programs used to detect and monitor JEV in endemic regions. Use "NR" if not reported, or "NA" if not applicable.
JEV regulatory control	Type of JEV regulatory control evaluated in the study. Use "NR" if not reported, or "NA" if not applicable. Use one per row if multiple regulatory controls were evaluated.
Effectiveness regulatory control	Critical evaluation of the effectiveness of the JEV regulatory control. Use "NR" if not reported, or "NA" if not applicable.
JEV outbreak signals	Were there signals/"triggers" that indicated the possibility of JEV introduction? If so, list them here. If none, enter "none". Use "NR" if not reported, or "NA" if not applicable.
Mosquito control strategy	Type of mosquito control strategy to prevent JEV introduction/circulation. Use "NR" if not reported, or "NA" if not applicable. Use one per row if multiple mosquito control strategies were evaluated.
Effectiveness mosquito control	Critical evaluation of the effectiveness of mosquito control strategy to prevent introduction/circulation of JEV. Use "NR" if not reported, or "NA" if not applicable.
Bird control strategy	Type of bird control strategy to prevent JEV introduction/circulation. Use "NR" if not reported, or "NA" if not applicable. If multiple, enter one per row.
Effectiveness bird control	Critical evaluation of the effectiveness of bird control strategy on preventing JEV introduction/circulation. Use "NR" if not reported, or "NA" if not applicable.
JEV economic impact	Economic impact of JEV reported by the authors. Use "NR" if not reported, or "NA" if not applicable.
Comments R	Comments to clarify one or more entries made in this section (critically evaluated outcomes). This section should only be used if necessary since it is an open response field.

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~~**Table 6.** List of data items that will be extracted from the included reference list of studies~~

~~**Data item***~~	~~**Explanation**~~

- Reference information	Title, all authors, first affiliation, journal, volume, pages, and publication date
Type of evidence	Peer-reviewed or not
Type of evidence - peer-reviewed	Primary research (original papers), review, systematic review, N/A
Type of evidence - non-peer-reviewed	Theses, technical reports, other, N/A
Quality of systematic reviews/scoping reviews	Was there an assessment of the quality of evidence (RoB or GRADE)?
Study characteristics	
- Year and season of study	Year and season when the study was conducted, or not reported (NR)
- Country and region	Country and region where the study was conducted. If not reported, reviewers will report the main author's institution location.
- Study type	Reported study design as review, experimental or observational, or not reported (NR)
Study design - observational: type	Reported study design as case-control, cohort, cross-sectional, other
Study design - experimental: type	Reported study design as RCBD, CRD, split-plot, cross-over, latin-square, ND (used in studies with no design/randomization), or NR
Study design - experimental: randomization method (if RCBD or CRD)	If the study design is reported as RCBD, then reported randomization method used for the study, or N/A (if not a randomized study), or NR
Study design - experimental: type of exposure	Reported type: laboratory natural, field natural , Lab challenge, Field challenge, or not reported (NR)
Study design - experimental: preventive intervention	Vaccine, quarantine, mosquito control, testing of new animals, segregation, sanitation, NR, or N/A
Study design - experimental: curative intervention	Management of positive animals (segregation, euthanasia and disposal, other) disposal of contaminated material (placenta, stillborn piglets), treatment of positive animals, NR, N/A
Study design - experimental: treatment structure	Reported treatment structure as one-, two-, three-way factorial, or NR
- Total number of EU	Number of experimental units (unit of replication) used in the study, or NR
- Number of EU/treatments	Number of EU per treatment (replication), or NR
- Blinding	Was the use of blinding reported? Single-blind, double-blind, triple-blind, no, or unclear
- Blinding: level	Data collectors, data collectors & data analysist, NR
Confounding	Is confounding addressed and accounted for? Yes, No, or Unclear
Sample size determination	Is there a sample size determination conducted? (this will address the "imprecision" domain of quality of

	evidence (to add in discussion section). Yes, No, or Unclear
Outcomes	
- JEV case definition	Method used to confirm disease (diagnostic test, clinical signs, other, NR)
JEV case definition: diagnostic test	What diagnostic test was used (ELISA, HIA (hemagglutination inhibition assay) HIA+SNT (seroneutralization test), PCR, RT-PCR, other, NR or N/A
JEV case definition: clinical signs	Combination of clinical signs used to declare as positive JE case, NR or N/A
JEV seroprevalence	Reported prevalence (%, proportion, measures of association, etc.) and test used for prevalence determination; NR, or N/A
JEV morbidity (prevalence based on clinical signs)	%, proportion, etc; NR, or N/A
- Infection rate in swine	Infection rate (also known as "R(t)") is the estimated number of new swine that become infected during a specific time period; NR, or N/A
- Incubation period in swine	The number of days between infection and manifestation of clinical signs; NR, or N/A
- Routes of transmission in swine	The pathway through which JEV enters the organism to infect a susceptible host; NR, or N/A
- Pathological lesions in swine	Anatomical changes caused by the pathological agent during course of disease; NR, or N/A
- Clinical signs in swine	Signs associated with the manifestation of disease; NR, or N/A
- Swine demographics	Sex, age, breed, and genetic markers; NR, or N/A
- JEV immunization status of swine herd	What JEV vaccines were administered to the herd? Commercial name, doses, route of administration; NR, or N/A
- Production size	One time capacity of the entire farm, NR, or N/A.
- Barn size	Total number of animals per barn, NR, or N/A
- Pen size	no of animals/pen, NR, or N/A
- Farm location	Urban, peri-urban, rural, NR, or N/A (as reported by the authors)

- Type of operation	Type of swine operations will be described as: confined commercial or research; opened commercial or research; semi-opened commercial or research; or subsistence farming ("backyard pigs"), NR, or N/A
- Type of production	Farrow to finish, farrow to wean, feeder pig production, wean to finish, seedstock production, or purebred production, NR, or N/A
- Production system	Conventional or alternative/organic (antibiotic-free, and hormone-free raised pigs, other), NR, or N/A
- Biosecurity/hygiene procedures applied at the farm (in general and specific to JEV)	Quarantine, segregation, personnel standard procedures, animal-sourcing, conveyance management , testing, mosquito control, in-house surveillance/testing, NR, or N/A
Effectiveness of farm biosecurity measures	Include measure of effectiveness, NR, or N/A
- JEV surveillance strategies	Mosquito trapping, use of sentinels, etc.; NR, or N/A
- Effectiveness of surveillance	Critical evaluation of the effectiveness of JEV surveillance programs used to detect and monitor JEV in endemic regions; NR, or N/A
- Genotype	I, II, II, IV or V; NR, or N/A
- R0	Reproductive number; estimate of JEV contagiousness; NR, or N/A
- Vaccine efficacy/effectiveness	Degree to which a vaccine prevents disease; NR, or N/A
Type of diagnostic test	Type (antibody, antigen, etc.), name; NR, or N/A
- Diagnostic test performance	Sensitivity, specificity, likelihood ratios, predictive values, and/or other accuracy measures reported for a diagnostic test; NR, or N/A

*RCBD = randomized complete block design; EU = experimental unit; JEV = Japanese encephalitis virus; R0 = R-naught 03.16.23 (this was a preliminary list of data items to be extracted from the included references and it is now being replaced by the final data extraction tool (i.e., after testing, editing, and calibrating)

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343 **Risk of bias assessment (RoB)**

344 Upon determining all relevant articles, an independent reviewer (NC) will evaluate the

345 risk of bias for these articles and document the results. A second reviewer will be available to

346 discuss uncertainties brough up by the primary reviewer. This step will be implemented

347 concurrently with the initiation of the data extraction step. To accelerate this process, we will

348 implement the RR approaches suggested by Garrity et al. (2021) when conduction the RoB

349 rating, which include: 1) limit RoB assessment to only primary outcomes, and 2) use a valid RoB

~~assessment tool specific to the study designs included (https://www.riskofbias.info).~~ 03.16.23 (due to the extent of outcomes extracted and the time constrain for completion of this review, the RoB assessment will not be conducted.

Data synthesis

Methods for summarizing the data around the POS question framework elements with findings grouped by key questions, population of interest, and outcomes, will be implemented. We will use a combination of RR approaches including: 1) *Minimal evidence synthesis (described by Haby et al. (2016) as "a locally prepared, short, contextually framed, narrative report in which the results of the systematic review were described and locally relevant factors that could influence the implementation of evidence-based guideline recommendations were highlighted")*, and 2) *Tabular synthesis of data (for narrative and quantitative data syntheses).*

Identification and characterization of knowledge gaps

We will use a framework (Figure 1; Robinson et al., 2013) developed to systematically identify research gaps from systematic reviews. This framework facilitates the classification of where and why the current evidence falls short and includes two elements: (1) characterization of the gaps and (2) the identification and classification of the reason(s) for the research gap (Robinson et al., 2013).

The PICOS (in our case POS) structure can be used to describe questions or parts of questions inadequately addressed by the evidence synthesized in the RR. The second element of the framework consists of classifying the reasons behind a research gap. For each research gap (row of the worksheet: "Serial no."), the reason(s) that mostly preclude conclusions from being made in the RR will be chosen by the reviewer completing the framework. Reasons for research

gaps will be categorized as per Robinson et al. (2013): A. Insufficient or imprecise information, B. Biased information, C. Inconsistent or unknown consistency, and D. Not the right information (See Figure 1 footnote). Insufficient information (A) will be used when only a limited number of studies or none are identified, or if the sample sizes in the available studies are too small to allow conclusions. Biased information (B) will be concluded based of the aggregate risk of bias (dependent on risk of bias of the individual studies). Consistency (C) will be evaluated based on the effect size directionality of included studies (i.e., inconsistency will be attributed to a research gap when the reported effect sizes of included studies appear to go in opposite directions). Lastly, lack of right information (D) will be assigned to research gaps which result from included studies that are not applicable (e.g., different population, different research setting), do not include/report outcomes of interest for the review, whose duration of study period is insufficient, or other reasons that may be categorized as "D".

In the worksheet table, the reviewer conducting the identification and characterization of the knowledge gap should identify the project name, date of completion, worksheet page number (out of total number of pages), and the key question number. Christy Hanthorn, AT 04.20.23, and VV will work concurrently in the knowledge gaps, each addressing a different research question (i.e., this step will not be conducted in duplicate).

Figure 1. JHU EPC Frameworks Project: Research Gaps Worksheet and Instructions (Original)[+]

<Example Project Name> **Completed by –**

Research Gap Worksheet **Date –**

Page __ of __

Key Question – _____

Serial no.	Reason(s) for gap*	Population (P)	Intervention (I)	Comparison (C)	Outcomes (O)	Setting (S)	Free text of gap	Notes
Ex. 1	B1	Domestic pigs (sow)			seroprevalence	-		Study used wrong diagnostic test
Ex. 2	D1, D4	Feral swine in the US	-	-	-			
Ex 3	A3	Domestic pigs (barrow)			seroprevalence			

*Reasons for Gap: A) Insufficient or Imprecise Information -> A1=No studies, A2=Limited number of studies, A3=Sample sizes too small, A4=Estimate of effect is imprecise

B) Biased Information -> B1=Inappropriate study design, B2=Major methodological limitations in studies

C) Inconsistency or Unknown Consistency -> C1=Consistency unknown (only 1 study), C2=Inconsistent results across studies

D) Not the right information -> D1=Results not applicable to population of interest, D2=Inadequate duration of interventions/comparisons, D3=Inadequate duration of follow-up, D4=Optimal/most important outcomes not addressed, D5=Results not applicable to setting of interest

[+](https://www.ncbi.nlm.nih.gov/books/NBK126708/pdf/Bookshelf_NBK126708.pdf)

Meta-biases (for systematic reviews): Meta-bias will not be implemented in this RR.

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