

APPROVED

By Jan Sargeant at 11:54 am, May 14, 2018

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Protocol for a scoping review of Influenza A viruses infecting swine or directly related to swine.

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

Section/topic	#	Checklist item
Identification	1a	Protocol for a Scoping Review of Influenza A viruses infecting swine or directly related to Swine
Update	1b	We are aware of no previous scoping reviews on this topic.
Registration	2	This review protocol will be posted in advance of study commencement on the University of Guelph Atrium and on the Website Systematic Reviews for Animals & Food (SYREAF) http://www.syreaf.org/contact/
Contact	3a	Sheila Keay ¹ , Zvonimir Poljak ¹ , Annette O'Connor ² , Robert Friendship ¹ , Terri O Sullivan ¹ and Jan Sargeant ^{1,3} ¹ Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, Canada ² Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames, Iowa, USA ³ Centre for Public Health and Zoonoses, Ontario Veterinary College, University of Guelph, Guelph, Canada Corresponding author: SK: University of Guelph, Ontario Veterinary College, Guelph, Ontario, Canada. skeay@uoguelph.ca
Contributions	3b	Protocol written by SK, JS and ZP with contributions by AOC, RF and TOC.
Amendments	4	No previous versions have been published.

Section/topic	#	Checklist item
Sources	5a	Study funding provided by the Ontario Veterinary College Fellowship- Guelph Ontario, Canada, Ontario, and the Ministry of Agriculture Food and Rural Affairs (OMAFRA), Guelph Ontario, Canada KTT Growing Forward 2
Sponsor	5b	Ontario Veterinary College, OMAFRA
Role of sponsor/ funder	5c	The Ontario Veterinary College and OMAFRA played no role in the protocol development, review or execution beyond approval of overall concept when allocating financial support.
Rationale	6	<p>Influenza A viruses are endemic in swine populations, a global zoonotic concern, and associated with economically significant disease in food animal production. Global partnerships (Star-IDAZ 2014, USDA 2014, European Food Safety Authority 2015, WHO 2017) have conducted gap analyses on Animal Influenza Research and set research agendas for various species. To date, however, an explicit inventory of the broad areas of accumulated research on Influenza A viruses in swine or directly related to swine (IAV-S), constructed in compliance with syntheses standards for literature mapping (Arksey and O'Malley 2005), is not available.</p> <p>In particular, a baseline descriptive categorization of the available body of evidence on priority components of infectious disease control and management research, once available to stakeholders at all levels of swine production, may facilitate, communication, innovation, acceptance, and compliance with investigative and intervention strategies over broad geopolitical areas (Morris 2015).</p>
Objectives	7	The purpose of this scoping review is to provide an explicitly organized summation and categorization of study characteristics of the body of available research evidence and review documents on Influenza A viruses of swine (IAV-S), where swine and applicability to swine is the primary focus. From this, a determination will be made if the bodies of research on IAV-S vaccines, and on other risk factors and interventions warrant a systematic review and possible meta-analyses.
Eligibility criteria	8	The scoping review will not include studies where the primary objective is study of IAV-S in non-swine species (e.g. IAV-S zoonotic studies are excluded).

Section/topic	#	Checklist item
		<p>Citation type: Inclusive of reviews, white papers/working papers/policy documents, conference proceedings (as identified below), primary research papers, and editorials/commentaries in scientific journals.</p> <p>Study type: All study types</p> <p>Geographic location: Any geographic location</p> <p>Dates: Citations will be limited to publication in 1990 or later. Several substantial diagnostic, production, and disease events occurred during the 1990s affecting the swine industry and approaches to understanding the role of IAV-S in swine production, including, substantial expansion and restructuring globally of swine production, emergent of new endemic subtypes of IAV-s in swine populations, improved understanding of the role of co-morbidities, and rapid expansion and development of 'omics', Big Data, and mathematical modelling applications. All of which signalled increased interest in surveillance and characterization of IAV-S sub-types, behaviour, and intervention in swine herds, and a step change in swine infectious disease management practices.</p> <p>Language: All English language publications and citation abstracts will be eligible. See supplemental materials Table 1 for a listing of parameters and parameter definitions.</p>
Information sources	9	<p>Grey Literature Search:</p> <p>Manual search will be conducted of the following websites for white papers, working reports, policy papers, NGO reports, Association reports, or issue papers.</p> <ul style="list-style-type: none"> • The European Surveillance Network for Influenza in Pigs (ESNIP1,2and 3) projects reported on CORDIS (European Commission Community Research and Development Information Service) <ul style="list-style-type: none"> ○ https://cordis.europa.eu/project/rcn/97365_en.html ○ http://www.esnip.ugent.be/ ○ http://www.esnip.ugent.be/page4/page4.html ○ https://www.wur.nl/en/show/ESNIP-3-European-surveillance-network-for-influenza-in-pigs-3.htm ○ https://cordis.europa.eu/projects/home_en.html • OFFLU – the joint OIE-FAO Network of expertise on animal influenza <ul style="list-style-type: none"> ○ http://www.offlu.net/index.php?id=51

Section/topic	#	Checklist item
		<ul style="list-style-type: none"> ○ http://www.oie.int/en/our-scientific-expertise/offlu-the-animal-influenzas-network/ • STAR-IDAZ- the Strategic Alliances for the Cooperation of Research on the Major Infectious Diseases of Animals and Zoonoses. <ul style="list-style-type: none"> ○ http://www.star-idaz.net/ • The European Association of Porcine Health Management website http://www.eaphm.org/ • The American Association of Swine Practitioners (AASV) website https://www.aasv.org/aasv/about.html • The Swine Disease Eradication Center – The University of Minnesota https://www.vetmed.umn.edu/centers-programs/swine-program/research/industry-advisory-board • The Swine Health Information Center - https://www.swinehealth.org/ <p>Key International Collaborative Reports: References from the following reports and Systematic Review will be hand checked for inclusiveness of electronic bibliographic output.</p> <ul style="list-style-type: none"> • USDA - In 2014 the USDA gathered the Animal Influenza Countermeasures Working Group (AICWG) to produce a workshop report Animal Influenza Viruses Gap Analysis. <ul style="list-style-type: none"> ○ https://www.ars.usda.gov/ARSUserFiles/np103/SymposiumWorkshopsMeetings/NVS%20-%20Animal%20Influenza%20Viruses%20Countermeasures%20Group%20Report%20April%202014.pdf • EFSA - The European Food Safety Authority published an event report – Workshop on Research Gap Analysis in Animal Influenza, January 2015. <ul style="list-style-type: none"> ○ https://www.efsa.europa.eu/en/supporting/pub/787e-0 • OFFLU and STAR-IDAZ – A consultation to Develop a Global Animal Influenza Research Agenda, Paris 2014 <ul style="list-style-type: none"> ○ http://www.offlu.net/fileadmin/home/en/publications/pdf/300714/OFFLU_STAR-IDAZ_Executive_Summary_final.pdf

Section/topic	#	Checklist item
		<ul style="list-style-type: none"> • Epidemiological features of influenza circulation in swine populations: A systematic review and meta-analysis (Baudon et al. 2017) (217 references) <p>Conference Proceedings/Abstracts: The following conference proceedings/ abstracts will be hand-searched:</p> <ul style="list-style-type: none"> ▪ The International Society for Influenza and other Respiratory Virus Diseases (ISIRV) – https://isirv.org/site/. Conference proceedings are in powerpoint format and will be screened for follow-up on research presented as ‘in progress’. <ul style="list-style-type: none"> ○ ISIRV conference events: https://isirv.org/site/index.php/upcoming-event i. Options for the Control of Influenza (9 to date)– held every three years they are the largest international scientific conferences exclusively devoted to influenza prevention, control and treatment, including seasonal flu and pandemic preparedness ii. Neglected Influenza Viruses (3 to date) – within a ‘One Health’ theme, explores the latest data on surveillance and disease investigation, virus transmission and control, clinical and experimental virology, and emerging issues and new developments related to swine, equine, canine and other nonhuman/non-avian influenza viruses ▪ The AASV maintains a searchable digital library of proceedings from the prominent swine conferences through the American Association of Swine Veterinarians website (Swine Information Library http://www.aasv.org/library/swineinfo/). Selected proceedings as noted below will be search using the key word ‘influenza’ Resources available on this site include proceedings from: <ul style="list-style-type: none"> ○ AASV Annual Meeting (1999-2018) ○ AASV Pre-Conference Seminars (2007-2018) ○ International Pig Veterinary Society Congress (2000, 2002, 2004, 2006, 2008, 2010, 2012, 2014, 2016) ▪ The following conference proceedings, also included in the AASV swine information library, will be excluded from the review. The Lemman conference now published proceedings as power

Section/topic	#	Checklist item										
		<p>point presentation only versus text, and the others are smaller regional presentations and do not share the national and international attendance of the AASV annual meetings.</p> <ul style="list-style-type: none"> ○ Allen D. Lemman Swine Conference (1998-2017) ○ George A. Young Swine Health and Management Conference (1999-2012) ○ International Symposium on Swine Disease Eradication (2001-2002, 2004) ○ ISU Swine Disease Conference for Swine Practitioners (1999-2017) <p>▪ The European Symposium of Porcine Health Management (2018 is the 10th symposium). Conference abstracts, although available online, are limited to 300 words. They will be excluded from the search.</p> <p>Bibliographic Database Search Strategy and vendor interfaces (platforms):</p> <table border="1" data-bbox="595 772 1839 1353"> <thead> <tr> <th data-bbox="595 772 1218 820">Platform (vendor interface)</th> <th data-bbox="1218 772 1839 820">Database</th> </tr> </thead> <tbody> <tr> <td data-bbox="595 820 1218 906">CAB Direct</td> <td data-bbox="1218 820 1839 906">CAB Abstracts and Global Health-1973-current and others</td> </tr> <tr> <td data-bbox="595 906 1218 1182">NCBI (National Center for Biotechnology Information) website</td> <td data-bbox="1218 906 1839 1182">PubMed – includes MEDLINE (National Library of Medicine biomedical database of citations and abstracts indexed using MeSH thesaurus)) -also includes in-process and other non-indexed citations (books, manuscripts and articles supplied ahead of print)</td> </tr> <tr> <td data-bbox="595 1182 1218 1268">Web of Science (The Science Citation Index, Clarivate Analytics, 1864-current)</td> <td data-bbox="1218 1182 1839 1268">(multiple)</td> </tr> <tr> <td data-bbox="595 1268 1218 1353"></td> <td data-bbox="1218 1268 1839 1353">Agricola (USDA National Agricultural Library 1970-Current)</td> </tr> </tbody> </table>	Platform (vendor interface)	Database	CAB Direct	CAB Abstracts and Global Health-1973-current and others	NCBI (National Center for Biotechnology Information) website	PubMed – includes MEDLINE (National Library of Medicine biomedical database of citations and abstracts indexed using MeSH thesaurus)) -also includes in-process and other non-indexed citations (books, manuscripts and articles supplied ahead of print)	Web of Science (The Science Citation Index, Clarivate Analytics, 1864-current)	(multiple)		Agricola (USDA National Agricultural Library 1970-Current)
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		<table border="1"> <tr> <td data-bbox="598 284 1216 336"></td> <td data-bbox="1216 284 1834 336"></td> </tr> <tr> <td data-bbox="598 336 1216 421">ProQuest</td> <td data-bbox="1216 336 1834 421">Dissertations & Theses A&I: Health & Medicine Full Text (1998-2018)</td> </tr> </table>			ProQuest	Dissertations & Theses A&I: Health & Medicine Full Text (1998-2018)
ProQuest	Dissertations & Theses A&I: Health & Medicine Full Text (1998-2018)					
Search strategy	10	<p>Search stings will be developed and formatted for selected bibliometric platforms with support from a University of Guelph librarian with expertise and experience in systematic review methods. Example search string formatted for Web of Science: TS=(pork OR swine OR Sus scrofa OR pig\$ OR piglet\$ OR piglets OR gilt\$ OR boar\$ OR sow\$ OR hog\$ OR weaner\$ OR feeder\$ OR finisher\$ OR "market-weight" OR porcine NOT "guinea pig\$") AND TS=("influenza*" OR "IAV" OR "Influenza A virus\$" OR "swine influenza" OR "swine flu" OR "swine influenza virus" OR "SIV" OR "H3N2" OR "H1N1" OR "H1N2 " OR "H3N1" OR "H2N3")</p> <p>(pork OR swine OR "Sus scrofa" OR pig* OR piglet* OR piglets OR gilt* OR boar* OR sow* OR hog*OR weaner* OR feeder* OR finisher* OR "market-weight" OR porcine NOT "guinea pig*")</p> <p>("influenza*" OR IAV OR "Influenza A virus*" OR "swine influenza" OR "swine flu" OR "swine influenza virus" OR "SIV" OR "H3N2" OR "H1N1" OR "H1N2 " OR "H3N1" OR "H2N3")</p>				
Data management	11a	<p>All citations will be downloaded (or if necessary, manually added) to EndNote reference management software (© 2018 Clarivate Analytics) for deduplication. De-duplicated citations will be downloaded to Distiller-SR software package for eligibility screening and categorization (© 2018 Systematic Review and Literature Review Software by Evidence Partners).</p>				
Selection process	11b	<p>Eligibility screening will be at the title/abstract level with review of the full text if necessary. All relevance screening and data extraction will be done in duplicate using forms constructed in Distiller SR. Discrepancies will be discussed by both reviewers and if not resolved a third reviewer will arbitrate for resolution.</p> <p>The level 1 relevance screening form will be pre-tested on a sampling of 200 papers.</p>				

Section/topic	#	Checklist item
		<p>All citations screened at level 1 as 'unclear' will be forwarded to a second level full text screening for relevance.</p> <p>All relevant conference proceedings and primary research citations will be forwarded for full text screening for relevance and data extraction (for 'charting of results').</p> <p>Reasons for exclusion will captured for all citations.</p> <p>Relevance screening questions:</p> <p>Scoping review inclusion criteria as listed below is topically widely permissive. In the case of an excessively high number of identified relevant citations, deviance from the protocol will include additional screening questions at the title/abstract level to narrow the scope of the review to control/prevention strategies.</p> <p>First level screening of title/abstract:</p> <ol style="list-style-type: none"> 1. Is this report/study/document primarily about Influenza A virus in swine (IAV-S) where swine or direct applicability to swine is the primary focus? If yes, proceed to Q2. If no, screen out. If unclear proceed to full text second level screening. 2. Is the full body text (beyond title/abstract) available in English? If yes, proceed to Q3. If no, screen out. If unclear proceed to full text second level screening. 3. Is the citation a conference proceeding or primary research? <ul style="list-style-type: none"> ○ If unclear proceed to full text second level screening. ○ If yes, keep citation for full text screening and data extraction. ○ If no, what is the document type? <ul style="list-style-type: none"> □ Review. If yes, identify the review type (as indicated by the authors in the title/abstract): <ul style="list-style-type: none"> ▪ Systematic Review without a meta-analysis ▪ Systematic Review and Meta-analysis ▪ Meta-analysis only

Section/topic	#	Checklist item
		<ul style="list-style-type: none"> ▪ Narrative or traditional review ▪ Unclear □ Report (White paper, working report, policy paper, NGO reports, Association reports, issue papers, guidelines). □ Editorial or commentary. □ Other
Data collection process	11c	<p>All relevant citations will be full text screened and data extracted in duplicate using forms pre-constructed in Distiller-SR. Discrepancies will be discussed by both reviewers and arbitrated for resolution if necessary by a third reviewer.</p> <p>Data extraction forms will be pre-tested on a sampling of 10 selected papers for assessment of question clarity and reviewer training for screening tool.</p>
Data items	12	<p>Second level full text screening using the same first level screening question will be done for all citations identified as relevant or 'unclear' at the title/abstract level:</p> <p>Data entry for charting of results: The extraction form will be populated with entries for each of the following questions for all relevant citations. <u>(See Supplemental Table 1. For definitions of terms)</u></p> <p>1. What is the primary author affiliation? (select all that apply)</p> <ul style="list-style-type: none"> □ University □ Pork production company (commercial producer) □ Independent Research Consultant or Professional □ Allied industry (i.e. pharmaceutical, breeding stock, industry association, etc.) □ National or sub-national government organizations □ International governmental organizations □ Non-governmental organizations □ Professional organizations

Section/topic	#	Checklist item
		<ul style="list-style-type: none"> <input type="checkbox"/> Other <input type="checkbox"/> Unclear/Not-stated <p>2. What country/ region is the primary author affiliated with? *(non-EU-28 countries are lumped into regions if they are not a global top 10 producer)</p> <ul style="list-style-type: none"> <input type="checkbox"/> China <input type="checkbox"/> Viet Nam <input type="checkbox"/> South Korea <input type="checkbox"/> Philippines <input type="checkbox"/> Other Asian countries <input type="checkbox"/> European Union-28 <input type="checkbox"/> Russian Federation <input type="checkbox"/> Other European countries <input type="checkbox"/> United States <input type="checkbox"/> Mexico <input type="checkbox"/> Canada <input type="checkbox"/> Brazil <input type="checkbox"/> Other Central/South American countries <input type="checkbox"/> Oceania <input type="checkbox"/> Africa <p>3. What is the study setting (select all that apply)?</p> <ul style="list-style-type: none"> <input type="checkbox"/> <i>In silico</i> <input type="checkbox"/> <i>In vitro</i> <input type="checkbox"/> <i>ex vivo</i> <input type="checkbox"/> <i>in vivo</i> <p>4. What type of observations are used?</p> <ul style="list-style-type: none"> <input type="checkbox"/> Theoretical <input type="checkbox"/> Empirical

Section/topic	#	Checklist item
		<ul style="list-style-type: none"> <input type="checkbox"/> Both <input type="checkbox"/> Unclear <p><u>For Q4 responses for the observation type as 'empirical':</u></p> <p>What is the study design approach?</p> <ul style="list-style-type: none"> <input type="checkbox"/> Descriptive <input type="checkbox"/> Analytic (Hypothesis testing) - experimental <input type="checkbox"/> Analytic (Hypothesis testing) observational <input type="checkbox"/> Unclear <p>5. What is the unit of study/ test population or level of study?</p> <ul style="list-style-type: none"> <input type="checkbox"/> Viral molecules (gene, protein, metabolite, mRNA, lipids) <input type="checkbox"/> Host Molecules (gene, protein, metabolite, mRNA, lipids) <input type="checkbox"/> Whole Virus <input type="checkbox"/> Host cells (swine) <input type="checkbox"/> Host tissues (swine) <input type="checkbox"/> Individual pig level <input type="checkbox"/> Groups/ pens/ rooms/ or batches of animals on a production site/ farm operation level <input type="checkbox"/> Regional or National <input type="checkbox"/> Unclear <p>6. What is the primary categorical focus of the document?</p> <ul style="list-style-type: none"> <input type="checkbox"/> Virus characterization (exclusive of host interaction) <input type="checkbox"/> Development or validation of laboratory methods and diagnostics <input type="checkbox"/> Pathology/pathophysiology and immunology (Virus-host interaction <u>exclusive</u> of vaccine focus) <input type="checkbox"/> Infection dynamic and transmission parameter studies

Section/topic	#	Checklist item
		<ul style="list-style-type: none"> <input type="checkbox"/> Surveillance, monitoring, disease prevalence or incidence studies (Does not include phylogeny or molecular epidemiologic studies) <input type="checkbox"/> Phylogeny (molecular epidemiology) <input type="checkbox"/> Risk Factors or Interventions including Vaccine Development and Evaluation <input type="checkbox"/> Cost of disease (economics) <input type="checkbox"/> Other <input type="checkbox"/> Unclear <p>For Q6 responses for study focus as 'risk factors and interventions':</p> <ul style="list-style-type: none"> i. What is the consideration of vaccines in this study? <ul style="list-style-type: none"> <input type="checkbox"/> Intervention/ risk factor focus is ONLY IAV vaccine development or evaluation. <input type="checkbox"/> Intervention/risk factor focus is multiple inclusive of IAV vaccine development/evaluation AND one or more other interventions/risk factors. <input type="checkbox"/> Intervention/risk factor focus does NOT include IAV vaccine development/evaluation <input type="checkbox"/> Unclear ii. For studies identified in (i.) above involving swine IAV vaccine development and evaluation, what is the type of vaccine study? <ul style="list-style-type: none"> <input type="checkbox"/> 'Bench top' and studies in non-swine species <input type="checkbox"/> Challenge studies <u>in swine</u> <input type="checkbox"/> Natural exposure studies in swine <input type="checkbox"/> Unclear <p>7. What is the funding source for the document? (select all that apply)</p> <ul style="list-style-type: none"> <input type="checkbox"/> University(s) <input type="checkbox"/> Pork production company (commercial producer) <input type="checkbox"/> Allied industry and industry associations (i.e. pharmaceutical, breeding stock, feed company, etc.)

Section/topic	#	Checklist item
		<ul style="list-style-type: none"> <input type="checkbox"/> National or sub-national government <input type="checkbox"/> International governmental organizations <input type="checkbox"/> Non-governmental organizations <input type="checkbox"/> Professional organizations <input type="checkbox"/> Other <input type="checkbox"/> Unclear/ Not stated
Outcomes and prioritization	13	<p>PRISMA flowchart of study selection process.</p> <p>Descriptive summary inclusive of frequency tables summing quantities of citations categorized for each question.</p> <p>Identification of percentage of relevant conference proceedings omitted due to subsequent publication of findings in a peer reviewed journal (i.e. conference proceedings omitted at deduplication phase).</p>
Risk of bias in individual studies	14	N/A for scoping studies.
Synthesis		N/A for scoping studies.
		N/A for scoping studies.
		N/A for scoping studies.
	15	<p>Listing of identified review articles by type (as screened out at the relevance screening step)</p> <p>Tabling of citations identified as conference proceedings and primary research papers by extracted data for each question (Questions 1-7)</p> <p>Bar graph presentations of categorical focus by type of study design.</p> <p>Bubble plots of number of studies per categorical focus by year of publication.</p>
Meta-bias(es)	16	N/A for scoping studies.

Section/topic	#	Checklist item
Confidence in cumulative evidence	17	N/A for scoping studies.

References:

Arksey, Hilary, and Lisa O'Malley. 2005. "Scoping Studies: Towards a Methodological Framework." *International Journal of Social Research Methodology: Theory and Practice* 8 (1): 19–32. <https://doi.org/10.1080/1364557032000119616>.

Baudon, Eugénie, Marisa Peyre, Malik Peiris, and Benjamin John Cowling. 2017. "Epidemiological Features of Influenza Circulation in Swine Populations: A Systematic Review and Meta-Analysis." *PLoS ONE* 12 (6): 1–25. <https://doi.org/10.1371/journal.pone.0179044>.

Table 1. Supplemental Materials -Definitions for the IAV-S Scoping Review:

Working definitions and background information applicable to all questions:

The virus:

IAV-S – Influenza A viruses of swine. Also referred to as swine influenza viruses (SIV).

Influenza A viruses are historically identified antigenically (serotyping technology) based on viral surface proteins hemagglutinin (HA- 18 different subtypes) and neuraminidase (NA -9 different subtypes).

Subtypes identified as endemic in swine populations H1N1, H3N2, and H1N2 (occasionally H3N1, H2N3) Enveloped, negative sense, single stranded RNA virus with 8 strand segmented genome

Research analytics:

Molecular biology: The study of the structure and function of molecules and macromolecular systems associated with biological processes, especially the molecular basis of inheritance and protein synthesis (U.S. National Library of Medicine)

Big data: Data gathered horizontally (wide breath of same information on multiple units of study), vertically (deep breadth of multiple information on same unit of study), or both, which is of such high velocity, variety, and volume (the three 'v's) it requires

new technologies and personnel expertise for processing, storage, and for comprehensive analysis (bioinformatics and development of data science) beyond the capability of conventional desktop computing. Traditional database management systems were built for structured data (tabular or relational structures) and are not suited for the mostly unstructured nature of big data and its inherent uncertain veracity (fourth 'v')(Pfeiffer and Stevens 2015). Big data includes sensory and other measurement devices connected through the internet (i.e. Internet of Things , IoT), participatory, crowd sourcing or citizen science mechanisms.

Molecular epidemiology – The use of techniques of molecular biology (used for identification and strain typing) in the study of the distribution and determinants of IAV occurrence in swine populations(Alvarez and Perez 2017).

Next generation sequencing (NGS) – (a.k.a. massively parallel or deep sequencing) – available beginning 2005, performs sequencing of millions of small fragments of DNA in unison. It replaced previous Sanger sequencing technology (time intense, limited scope or genomic detection, required use of secondary dedicated assays to view comprehensive genomic variability). NGS parallel harvests the full spectrum of genomic variation in a single experiment producing large data production per turn and requires bioinformatics analyses for interpretation. NGS in microbiology replaces conventional characterization of pathogens (i.e. morphology, staining properties, and metabolic criteria) with a genomic definition (Behjati and Tarpey 2013). Sequence data may be published in online genetic databases (often collected for surveillance activities). Prominent public genetic databases for influenza virus sequences are GenBank, Global Initiative on Sharing All Influenza Data (GISAID), and the Influenza Research Databases (IRD) (Von Dobschuetz et al. 2015)

'omics' – differentiated scope of molecular biology by implied modern requirement for use of computing and big data (bioinformatics) " Omics is a discipline of science and engineering since the advent of NGS technology for analyzing the interactions and functions of biological information entities in various –ome layers(clusters) of life. The main focus is on: 1) mapping information objects such as genes, proteins, and ligands (binding molecules); 2) finding interaction relationships among the objects; 3) engineering the networks and objects to understand and manipulate the regulatory mechanisms; and 4) integrating various 'omes' and omics subfields." http://omics.org/index.php/Main_Page

Question specific definitions:

1. What is the document type?

Review	An overview of past facts and findings for the purpose of summing and reflecting on available information on a given subject area. Could be a systematic review, meta-analysis, or a narrative or traditional review. If answered yes, please see detailed descriptions of review types in Q. 5 definitions below.
Report (White paper, working report, policy paper, NGO reports, Association reports , issue papers, guidelines)	Published documents which may review subject area literature but secondarily as a supportive discourse for purposeful statements or endorsements of an organization's unified position, agenda, focus of action, or as a contextual statement for recommended guidelines for operation in a subject area. Report usually of substantial structure and may contain an executive summary (i.e. policy or position reports) and often published by the authoring organization.
Conference Proceeding/ Abstracts	Research findings as presented at science based conferences
Primary Research paper	New findings as published in literature.
Editorial or commentary	Authored by those tacitly or explicitly recognized as an authoritative voice on the subject area. Page length is limited and topic coverage is brief opinion or instruction
Other	Citation not fitting with the above listed documents types categories.

2. What kind of review is this document?

Systematic Review without a meta-analysis	For the purpose of this scoping review we will not assess if a review meets criteria of a Systematic Review Rather, citations where the author identifies the review as a 'systematic review' are included in this grouping. This category includes only author identified systematic reviews which do not include a meta-analysis.
Meta-analysis only	Citation author describes combining quantitatively information from multiple primary studies as a 'meta-analyses'.
Systematic Review inclusive of a Meta-analysis	This category includes only those reviews where citation author describes review as a systematic review with a meta-analysis in the title/abstract.

Narrative or traditional review	Citations where authors do not describe the review as a 'systematic review' will be considered narrative or traditional reviews: surveying of existing published facts and findings of a subject area (primary literature) for the purpose of integrating past literature to facilitate digestion and possibly for concluding generalities by an interested audience. The difference from a systematic review process is the absence in a narrative review of an explicit description of the steps taken to reduce risk of bias such as development of study question, inclusion/exclusion criteria, search methods, and assessment of the primary researched for risk of bias (i.e. a lack of process transparency) (Cooper and Hedges 2009).
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3. What is the primary author affiliation (select all that apply)?

Under what affiliation does the primary (first) author list in citation title/abstract? Check all that apply if the author lists multiple affiliations.	
University	
Pork Production Company (commercial producer)	<p>e.g. Commercial and/or corporate production companies with affiliated contract growers, vertically integrated production such as:</p> <p>Global top pork producers: https://www.wattagnet.com/articles/25011-infographic-worlds-top-10-pig-producers</p> <ul style="list-style-type: none"> ○ WH Group, China ○ CP Group, Thailand ○ Wen's Food Group, China ○ Triumph Foods, U.S. ○ BRF, Brazil ○ NongHyup Agribusiness, South Korea ○ Cooperl Arc Atlantique, France, ○ The Maschhoffs, U.S. ○ Seaboard Corp., U.S. ○ Vall Companys Grupo, Spain
Independent Research Consultant or Professional	e.g. Private practitioners (commonly conference proceedings authored by field practitioners in independent practice)

Allied industry (i.e. pharmaceutical, breeding stock, industry association, etc.)	e.g. National Pork Board (Swine Health Information Center) and Pork Check-off funds used for research , various breeding stock companies, pharmaceutical company annual research awarding, etc.
National or sub-national Government organizations	e.g. Canadian Food Inspection Agency, US Department of Agriculture, Ontario Ministry of Agriculture and Food
International governmental organization	E.g. WHO, FAO, EFSA, OIE, STAR-IDAZ. OFFLU
Non-governmental organizations (NGOs)	Any non-profit, voluntary group which is organized on a local, national or international level and working independent of external control or affiliated political parties and generally engaged in work for aid or development. e.g. Veterinarians without borders, Bill and Melinda Gates Foundation, Consultative Group on International Agricultural Research (CGIAR), National Institute for Animal Agriculture (NIAA)
Professional organizations and associations	American Association of Swine Veterinarians, European Association of Porcine Health Management
Other	
Unclear/ Not-stated	

4. What country/ region is the primary author affiliated with?

*(countries lumped into regions if not a global top 10 producer)

China	Does not include Taiwan
Viet Nam	
South Korea	
Philippines	
Other Asian countries (not in the global top 10 pork producers)	Not China, Viet Nam, South Korea, Philippines but inclusive of other Asian countries (including Taiwan) not included in the listing of top 10 global pork producers (in 1000MT CWE) -USDA FAS
European Union-28	Austria, Belgium, Bulgaria , Croatia, Cyprus , Czech Republic, Denmark , Estonia, Finland , France, Germany, Greece, Hungary, Ireland , Italy , Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland , Portugal, Romania, Slovakia, Slovenia, Spain , Sweden, United Kingdom
Russian Federation	

Other European countries not in the global top 10 pork producers	Albania, Armenia. Belarus, Gibraltar, Iceland, Kosovo, Liechtenstein, Macedonia, Norway, Switzerland, Turkey, Ukraine, and Vatican City State
United States	
Mexico	
Canada	
Brazil	
Other Caribbean, Central/South American countries not in the global top 10 pork producers	Central America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama South America (not including Brazil): Venezuela, Argentina, Uruguay, Bolivia, Suriname, Peru, Chile, Paraguay, Colombia, Guyana, Ecuador, French Guiana, Falkland Islands. Caribbean: see https://en.wikipedia.org/wiki/List_of_Caribbean_countries_by_population
Oceania	Australia, New Zealand, Melanesia, Micronesia, Polynesia
Africa	See: https://www.countries-of-the-world.com/countries-of-africa.html

5. What is the study setting?

<i>in silico</i>	<p>Research in which computer-based modeling and analysis tools are developed and utilized to predict and elucidate dynamics of biological systems, their design and control, and their evolution. Can include mathematical models or statistical (epidemiologic models).</p> <p>Examples: Simulation modeling, Agent based , SIR models (Susceptible Infected Recovered), Big data and ‘omic’ analytics such as predictive analytics, phylogenetic , and phylodynamic analyses</p> <p>Mathematical or computer simulation models refer to dynamic disease transmission models where force of infection varies with changes in the prevalence of infectious and susceptible individuals in a population over time.(Dorjee et al. 2013)</p>
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	Statistical models explore associations between outcome and explanatory variables and include issues such as statistical characterization of numerical or categorical data, estimating the probabilistic future behaviour of a system based on past behavior, extrapolation or interpolation of data based on some best-fit, error estimates of observations, or analysis of data or model generated output. https://serc.carleton.edu/introgeo/mathstatmodels/index.html
<i>in vitro</i>	'Within glass' performing a given procedure in a controlled usually in a cultured system outside of the a living organism (pig)
<i>ex vivo</i>	For example studies with harvested tissues outside of the whole organism (pig)
<i>in vivo</i>	Tests performed within the whole living organism(pig) as opposed to a tissue extract or dead organism

6. What type of observations are used?

Theoretical	Does not use data gathered from the real world. Theoretical work can be inspired by real-world phenomena, but it does not involve the gathering or analysis of data from those phenomena; an exploration of what could be, rather than what is, using tools ranging from analytical models to individual-based simulations (Haller 2014)
Empirical	Data gathered from observations from the real world. Empirical work can be defined as the gathering and analysis of data from phenomena observed in the real world. Research for cause and effect relationships are based on data generated through <i>a priori</i> designed studies and spans a range from purely observational field studies to hypothesis-driven experimentation in the laboratory. (Haller 2014)

7. (For studies using empirical observations) What is the study design-approach*?

Descriptive	Includes case-reports, case-series reports, and surveys† designed solely to describe the nature and distribution of outcome events. Answer what, who, were and when but not why and how Comparisons are not made between exposed versus non-exposed, or treated versus not-treated, and no inferences about associations can be made. †surveys designed to collect information about both an outcome and a potential exposure of interest are to be categorized as cross-sectional (analytic observational study whose outcome frequency measure is prevalence)
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Analytic (Hypothesis testing) *– designed to make comparisons between subgroups of study subjects based on exposure or outcome status for the purpose of making statistical associations or inferences between exposures of interest and outcomes of interest. Includes a comparison group.	
Two types: experimental or observational	
Experimental	- includes laboratory (in-house strictly controlled conditions) and controlled field trials (investigator controls allocation of subjects to study groups but study performed under 'real-world' conditions, including randomized controlled trials (RCTs))
Observational	- includes cross-sectional, cohort, case-control, and hybrid studies - disease or condition of interest is naturally occurring and the investigator does not control allocation to interventions or exposures.
Unclear	

*definitions as per (Dohoo, Martin, and Stryhn 2009) **Chapter7**.

8. What is the unit of study/ test population?

Viral molecules (gene, protein, metabolite, mRNA, lipids)	<p>Study of the molecules such as genes, mRNA, proteins, metabolites, and lipids which make up a cell, tissue or organism in specific biologic samples (Horgan and Kenny 2011)</p> <p>Genes: The genetic sequences(s) of the viral genome or parts of the genome is the unit of study. IAV genome is composed of 8 segments which encode for at least 12 proteins.</p> <p>Proteins: general structural components of the virus including for IAV HA, NA, M2, M1, NP, NS1, NS2/NEP, PA, PB1, PB1-F2, PB2 (Sandbulte et al. 2015)</p> <p>Metabolites: a substance produced by viral metabolism or necessary the progress of a metabolic process such as a precursor or sequelae molecule</p>
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	<p>mRNA: messenger RNA –viral mRNA – involved in early viral replication steps in the host cell nucleus. It is translated into viral proteins. Regulation of mRNA is a target of viral systems.</p> <p>lipids: important in composition of viral envelop and plays a role in virus infection.</p>
Host Molecules (gene, protein, metabolite, mRNA, lipids)	<p>Genes: The genetic sequences(s) of the host genome or parts of the genome(with respect to IAV infection or defences) is the unit of study</p> <p>Proteins: can include studies of host cell proteins in response to viral interaction</p> <p>Metabolites: a host cell substance produced by host cell metabolism or necessary the progress of a host cell metabolic process such as a precursor or sequelae molecule</p> <p>mRNA: messenger RNA –host cell mRNA – involved in translation of viral genome into proteins</p> <p>lipids: important in composition of host cell membranes which is site of viral assembly and release from host cells.</p>
Whole Virus	Studies where the whole virus is the primary focus such as hazard characterization studies of viral survival in various environments, or studies of whole viral structures beyond specific protein focus or genome focus.
Host cells (swine)	Studies of the host whole cell on a level of organelles versus molecular level.
Host tissues (swine)	<ul style="list-style-type: none"> - studies of architectural/functional changes at the tissue level -Can include studies on host changes at the tissue level due to infection or sequelae from infections. For example histopathologic studies of tissue damage.
Individual pig level	
Groups/ pens/ rooms/ or batches of animals/production site/ farm operation level	Outdoor production farm(s) or system(s) with pastures or rotational plots where animals are kept as free-range for part or all of their production cycle.
National/ Regional/ Multi-national	An entire country or regionally includes a geographic area at the sub-national or supra-national level defined by some commonality as a region such as trading blocks, data sharing agreements, geographical blocks, disease status, etc.

Unclear	
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9. What is the primary categorical focus of the document?

Virus characterization	Study of the virus exclusive of virus-host interactions (see pathophysiology and immunology below).
Development or validation of laboratory methods and diagnostics	Development or validation of molecular tests, serologic tests, or virus recovery tests for the purpose of virus detection or identification.
Pathology, pathophysiology and immunology* * (excluding vaccine development /evaluation)	<p>Pathophysiology and immunology - <u>inclusive of studies on virus-host interaction</u>- clinical and physiologic changes or processes within individual swine (whole animal, tissue, cellular and/or sub-cellular level) resulting from IAV-S infection including molecular determinants of host specificity, tissue tropism, virulence, viral entry and shedding at the cellular level, and influence of co-infection with other viruses on IAV-S behaviour in swine, swine immunologic responses to the virus and other host physiologic defenses</p> <p>Exclusive of vaccine development/evaluation</p>
Infection dynamic and transmission parameter studies	<p>Studies specifically for the determination of transmission parameters and infection dynamics at the level of pig-to-pig, within group, within farm, within regions.</p> <p>Studies may be of parameters including: incubation period, latent period, subclinical infectious period, clinical infectious period, immunity period, basic reproductive number (R_0), generation interval, contact frequency, transmission probability per contact, transmission coefficients/ rates of infection, etc.</p> <p>Transmission of the IAV-S to swine includes: Vertical transmission – from mother to young Horizontal indirect transmission - transfer to pigs from another species (vector-borne is not considered a mode of IAV transmission) Horizontal direct – close and casual pig-to-pig contact, transfer in semen, air/water, surface contamination exposure (i.e. not cleaning barns between groups)</p>

	<p>- Not pig-to-human transmission studies. Not vaccine evaluation/development studies.</p>
<p>Surveillance (and monitoring*),disease incidence or prevalence studies</p>	<p>OIE Terrestrial Animal Health Code – 25/07/2017. “Surveillance is aimed at demonstrating absence of disease or infection, determining the presence or distribution of disease or infection or detecting as early as possible exotic or emerging diseases.”</p> <p>*monitoring is associated with collection of data as per surveillance but without a clear related action plan</p> <p>Types of surveillance include: Surveillance - Epidemiologic reporting of viral spatio-temporal presence or absence (i.e. emergence, re-emergence) , and can be census, random, systematic, convenience, haphazard, purposive, volunteer, event related, participant recommended sampling strategies. Disease Incidence or prevalence studies for detection of disease in a population of animals.</p> <p>Does not include molecular epidemiologic studies (i.e. phylogenetic/ phylodynamic analyses)</p>
<p>Phylogeny</p>	<p>Studies of the evolutionary history of IAV-S. Systems of classification most commonly based on phylogenetic hypotheses of how groups evolved from their common ancestors.</p> <p>Includes also citations on: <u>Phylogenetic analysis</u>: The study of the evolutionary dynamics of IAV and to provide insight into swine IAV genetic diversity using statistical inference models to understand patterns of genome changes(Anderson et al. 2015). <u>Phylodynamic analysis</u>: characterizes the joint evolutionary and epidemic behaviour of viruses using techniques of phylogenetics applied in a dynamic statistical model (Bayesian models) (Alvarez et al. 2016)</p>
<p>Risk factors and Interventions including vaccine evaluation and development studies.</p>	<p>Definition of intervention as adopted from Oxford English Dictionary by FAO/WHO working group on Salmonella control: “as any action of intervening, or ‘stepping in’, or interfering in any affair, so as to affect its course or issue”, within the context of controlling disease (Pienaar E.D., n.d.).</p>

This category includes also studies to identify factors inferred or associated with increasing (risk factors) or decreasing (protective factors or assets) the occurrence of (IAV-S) infection/clinical disease in swine. Interventions can be directed at risk factors, or the absence of an intervention can be a risk factor.

Examples include – protective factors such as products (e.g. vaccines) or programs (e.g. gilt acclimatization) to reduce the risk or impact of infection. Studies can be inclusive of risk management and biosecurity actions taken as standalone interventions or in conjunction with one or more interventions as part of a program or “best operating practices” to limit exposure, transmission and spread at the animal level or higher (i.e. within a production site, between production sites, regions).

Two general types of factors; individual characteristics of the pig (pig level) or those that occur in the environmental and affect groups versus individual pigs (farm/operational/regional level).

Pig level (factors within the pig): age, co-morbidity, reproductive status, immune status.

Production site level (factors within the production site): on-site population size, ownership type (contract, fully owned), production purpose (commercial, breeding stock), site demographic (farrow to finish, sow farm, boar stud, breeder-weaner, nursery, finisher, nursery-finisher, etc.), site animal flow (i.e. all-in/ all-out by site/room/pen, continuous flow, etc.), replacement breeding stock management strategies (quarantine periods, testing, method of acclimatization, etc.), adoption of on-site biosecurity practices, etc.

Operational level (factors of entities outside of the site but directly related to the operations of the farm): operational structure (one-site, multi-site), number of sites in operation, total herd size in operation, herd demographic proportions (breed to slaughter, nursery finishing operation only, breed to wean only, etc.) up-stream (sourcing site) infection status, live animal, deadstock, and feed transportation (dedicated, shared, downtime, washing), proximity to other barns (both within the operation and out site of the operation) , adoption of operational best practices (as industry identified good production practices, HACCP principles), etc.

	Regional level (factors outside the not directly under the control of the operational entity): pig or farm density at different geographic levels, seasonality, regulatory policies/programs, regional disease prevalence, commodity pricing, etc.
Cost of disease (economics)	Economic studies – e.g. estimates of cost of disease, partial budgeting, cost-benefit analyses, risk assessments e.g. (Haden et al. 2012)

10. This question applies to only citations identified (in Q4) as focused on risk factors and interventions: What is the consideration of vaccines in this study?

Intervention/ risk factor focus is ONLY IAV vaccine development or evaluation.	These studies are exclusively IAV vaccine development or evaluation studies and no other risk factors or interventions are included in the study design.
Intervention/risk factor focus is multiple inclusive of IAV vaccine development/evaluation AND one or more other interventions/risk factors.	On farm disease management programs are most often a combination of adoption of multiple actions. In these studies, observations are collected on outcome measures/dependent variables with specific reference to both IAV vaccines and one or more other interventions/risk factors as independent or confounding variables.
Intervention/risk factor focus does NOT include IAV vaccine development/evaluation.	Focus and study design is on one or more non-vaccine (IAV) risk factors or interventions and IAV vaccine use is not considered in the study design as either a confounder or independent variable.

11. For studies identified in (i.) involving swine IAV vaccine development and evaluation, what is the type of vaccine study?

Bench top and trials in non-swine species	Vaccine development and basic research including testing in non-swine trials - vaccine production methods, bench-top and non-swine trials. Expect most if not all of these studies will be conducted in a laboratory setting.
IAV Challenge trials in swine	Vaccine trials in swine - challenge trials (allocation to intervention group and disease exposure are deliberate and under the control of the investigator ('Connor and Sargeant, 2014). These studies would normally only be conducted under highly controlled setting

	where pathogen (IAV) exposure can be limited and controlled. May be trials conducted also for regulatory purposes (i.e. safety/efficacy).
IAV natural exposure in swine	Vaccine trials in swine - natural disease exposure. This would include most observational studies and trials conducted in live swine in research or commercial herds. The difference from challenge trials is that the researcher does NOT deliberately expose the swine to the virus.

12. What is the funding source for the document (select all that apply)?

University(s)	See definitions for Question 1. Author affiliations
Pork Production Company (commercial producer)	
Independent Research Consultant or Professional	
Allied industry and industry associations	
National or sub-national government organizations	
International governmental organization	
Non-governmental organizations	
professional organizations	
Other	
Unclear/Not-stated	

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