



UK Health
Security
Agency

Incubation and infectious period of influenza A (H5) in non-human mammals

A rapid evidence summary

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Main messages

1. The purpose of this rapid evidence summary was to identify and summarise the available evidence on the infectious period (the timeframe in which an individual may transmit the infection to others) and incubation period (the time between contracting an infection and symptom onset) of influenza A (H5) in non-human mammals (search up to 15 May 2024) ([1 to 8](#)).
2. Eight studies were included in this review. Seven studies were experimental animal studies (including ferrets, guinea pigs, dogs, and cats), where non-human mammals were inoculated with H5 influenza, and a total of 46 healthy non-human mammals were exposed between one and 2 days later to the infected animals to examine transmission ([1 to 7](#)). One study was an observational study reporting on an outbreak of H5N1 influenza among 147 tigers in Thailand ([8](#)).
3. Six of the 7 experimental studies reported on infectious period of H5 influenza by repeat testing of healthy, exposed non-human mammals ([1 to 6](#)). One experimental study ([7](#)) and the one observational study ([8](#)) provided evidence for the incubation period.
4. In 6 of the experimental studies reporting on infectious period, the time from exposure to testing positive for H5 influenza for non-human mammals was between 2 and 8 days, although most non-human mammals tested positive 5 or fewer days after exposure ([1 to 6](#)). The time from exposure to the last positive test was between 4 and 12 days across the 6 studies, although not all studies continued to test until there were no more positive tests, meaning some non-human mammals could have tested positive for longer.
5. The 2 studies reporting on the incubation period suggested the incubation period of H5 influenza was around 3 days for 147 tigers ([8](#)), and 3 to 4 days for one cat ([7](#)).
6. In the experimental studies inoculating non-human mammals with more than one strain of H5 influenza, there were differences in the proportion of non-human mammals testing positive and the time to first and last positive tests. This may be due to chance given the low number of non-human mammals examined, but this may also suggest different strains of H5 influenza could have different infectious periods.
7. The studies included a variety of non-human mammal species, and there were differences in how the contact non-human mammals were exposed to the inoculated non-human mammals, which may have contributed to differences in the results between studies.
8. Overall, there was limited evidence estimating both the infectious period and the incubation period of influenza A (H5) in non-human mammals, with evidence from 46 non-human mammals exposed to inoculated non-human mammals (many of the exposed non-human mammals did not become infected) for the infectious period (time from exposure to first and last positive test), and evidence from up to 147 tigers and one cat for the incubation period.

Purpose

The purpose of this rapid evidence summary was to identify and summarise the available evidence on the infectious period and incubation period of influenza A (H5) in non-human mammals.

There was one review question:

1. What are the infectious period and incubation periods of influenza A (H5) in non-human mammals?

Methods

A rapid evidence summary was conducted, following streamlined systematic methods to accelerate the review process (9). A literature search was undertaken to look for all relevant studies, published or available as preprint, up to 15 May 2024. Full details of the search are available in the protocol in [Annexe A](#).

Screening on title and abstract was undertaken in duplicate by 2 reviewers for 10% of the eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and checked by a second.

A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are provided in the protocol in [Annexe A](#).

There was one deviation from the protocol:

- non-human mammals that were inoculated with H5 influenza were excluded, as their infectious and incubation periods would likely be different to non-human mammals exposed to H5 influenza naturally

For this review, the definitions used were:

- infectious period: the timeframe when an individual may transmit the infection to others
- incubation period: the time between contracting an infection and symptom onset

Only studies of the H5 sub-type of influenza A were included.

Evidence

In total, 3,374 primary studies were screened at title and abstract, and 55 studies were screened at full text. Of these, 8 studies were included ([1 to 8](#)). The PRISMA diagram showing the flow of studies through this review is available in [Annexe B](#). Studies excluded on full text screening are available with the reasons for exclusion in [Annexe C](#).

Seven studies were experimental animal studies, where non-human mammals were inoculated with H5 influenza, and healthy non-human mammals were exposed between one and 2 days later to the infected non-human mammals to examine viral transmission ([1 to 7](#)). One study was an observational study reporting on an outbreak of H5N1 influenza among tigers ([8](#)).

Four studies were conducted in China ([3, 5 to 7](#)), one study in the US ([4](#)), one study in Thailand ([8](#)), and 2 studies did not state the location ([1, 2](#)). Other than the observational study of infected tigers, which was conducted in 2004 ([8](#)), no other study reported the study time period. Four studies were conducted with ferrets ([1 to 4](#)), 2 studies with guinea pigs ([5, 6](#)), one study with cats exposed to dogs ([7](#)), and one study with tigers ([8](#)).

Six of the 7 experimental studies reported on how many non-human mammals tested positive for H5 influenza after exposure to an infected non-human mammal, as determined by regular testing ([1 to 6](#)). One experimental study ([7](#)) and the one observational study ([8](#)) provided evidence for the incubation period.

Experimental studies

All 7 experimental studies inoculated non-human mammals with H5 influenza, and between one and 2 days later exposed a total of 46 healthy non-human mammals to the infected non-human mammals to examine transmission ([1 to 7](#)). All studies then tested the healthy, exposed non-human mammals for H5 influenza every 2 days for an amount of time. All healthy, exposed non-human mammals were tested, regardless of whether they had previously tested positive. The studies typically reported the number of positive tests on each day, rather than reporting on which non-human mammals were positive on which days, so the total number of non-human mammals testing positive overall was not known. These results give an indication of how long after exposure non-human mammals start testing positive for H5 influenza (time from exposure to first positive test), and how long after exposure non-human mammals can potentially test positive (time from exposure to last positive test). This is an estimate of the infectious period for non-human mammals, though a positive test does not necessarily indicate that a non-human mammal is infectious.

Only studies where at least one transmission event was reported were included, and evidence was only reported in this review from study groups with at least one transmission event. Six

experimental studies provided evidence for the infectious period ([1 to 6](#)), and one study provided evidence for the incubation period ([7](#)). Study characteristics are presented in [Table D.1a](#) for studies of ferrets, [Table D.1b](#) in studies of guinea pigs, and [Table D.1c](#) in studies of cats and dogs.

Infectious period

Studies in ferrets

Herfst and others inoculated 4 ferrets with H5N1 influenza, and exposed 4 healthy ferrets to aerosols from the inoculated ferrets ([1](#)). The exposed ferrets were tested for H5N1 positivity every other day after exposure, from days one to 11. One of the 4 exposed ferrets (25%) tested positive 3 days after exposure, 3 tested positive at 5 and 7 days after exposure (75%), one tested positive 9 days after exposure (25%), and no ferrets tested positive 11 days after exposure.

Imai and others inoculated 15 ferrets with 3 different strains of H5 influenza, and exposed 15 healthy ferrets to aerosols from the inoculated ferrets ([2](#)). The exposed ferrets were tested for H5 positivity every other day after exposure, from days one to 7. For the first strain of H5 influenza, 3 healthy ferrets were exposed to 3 inoculated ferrets, and all tested positive 3, 5, and 7 days after exposure (100%). For the second strain, 6 healthy ferrets were exposed to 6 inoculated ferrets, with one testing positive 5 days after exposure (16.7%), and 2 testing positive 7 days after exposure (33.3%). For the third strain, 6 healthy ferrets were exposed to 6 inoculated ferrets, with 2 testing positive 3 days after exposure (33.3%), 3 testing positive 5 days after exposure (50%), and 4 testing positive 7 days after exposure (66.7%).

Sun and others inoculated 6 ferrets with 2 different strains of H5N6 influenza, and exposed 6 healthy ferrets to direct contact with the inoculated ferrets ([3](#)). The exposed ferrets were tested for H5N6 positivity every other day after exposure, from days 2 to 12. For the first strain, 3 healthy ferrets were exposed to 3 inoculated ferrets, with all 3 testing positive 4, 6, 8, and 10 days after exposure (100%), and 2 still testing positive 12 days after exposure (66.7%). For the second strain, 3 healthy ferrets were exposed to 3 inoculated ferrets, with all 3 testing positive 2, 4, 6, 8, and 10 days after exposure (100%), and one still testing positive 12 days after exposure (33.3%).

Yen and others inoculated 2 ferrets with H5N1 influenza, and exposed 4 healthy ferrets to direct contact with the inoculated ferrets ([4](#)). The exposed ferrets were tested for H5N1 positivity every other day after exposure, from days 2 to 12 days. One ferret (25%) tested positive on 8 and 12 days after exposure, and a different ferret tested positive 6 days after exposure, but all other tests were negative.

Studies in guinea pigs

Cui and others inoculated 6 guinea pigs with 2 different strains of H5N6 influenza, and exposed 6 healthy guinea pigs to direct contact with the inoculated guinea pigs (5). The exposed guinea pigs were tested for H5N6 positivity every other day after exposure from days 2 to 8. For the first strain, 3 healthy guinea pigs were exposed to 3 inoculated guinea pigs, with one testing positive 2 and 4 days after exposure (33.3%). For the second strain, 3 healthy guinea pigs were exposed to 3 inoculated guinea pigs, with all 3 testing positive 2, 4, 6, and 8 days after exposure (100%).

Gao and others inoculated a total of 6 guinea pigs with 2 different strains of H5N1 influenza, and exposed 6 healthy guinea pigs to direct contact with the inoculated guinea pigs (6). The exposed guinea pigs were tested for H5N1 positivity every other day after exposure from days 2 to 14. For the first strain, 3 healthy guinea pigs were exposed to 3 inoculated guinea pigs, with all 3 testing positive 4, 6, and 8 days after exposure (100%), and one still testing positive 10 and 12 days after exposure (33.3%). For the second strain, 3 healthy guinea pigs were exposed to 3 inoculated guinea pigs, with 2 testing positive 4 days after exposure (66.7%), all 3 testing positive 6, 8, and 10 days after exposure (100%), and 2 still testing positive 12 days after exposure (66.7%).

Incubation period

Hai-xia and others inoculated 3 dogs with H5N2 influenza, and exposed 5 healthy cats to the inoculated dogs (7). It is unclear if the cats were routinely tested for H5N2 influenza, although viral samples were collected for 14 days. However, one of the 5 cats (20%) developed influenza symptoms 3 to 4 days after exposure.

Observational studies

One observational study provided evidence for the incubation period of H5N1 influenza (8). The study characteristics are presented in [Table D.1d](#).

Thanawongnuwech and others reported on the incubation period of H5N1 influenza in tigers at a zoo in Thailand in 2004 (8). The study reported that the outbreak likely started when the tigers ate infected chicken. In total, 147 tigers either died from H5N1 influenza or were euthanised to try to prevent transmission to healthy tigers. The authors estimated the incubation period to be about 3 days, and suggested there may have been tiger to tiger transmission.

Summary

In 6 studies, the time from exposure to the first non-human mammal testing positive for H5 influenza was between 2 and 8 days, although the majority of non-human mammals tested positive 5 or fewer days after exposure. The time to the last positive test in each study was

between 4 and 12 days after exposure across the 6 studies, although not all studies continued to test until there were no more positive tests, meaning some non-human mammals could have tested positive for longer.

The 2 studies reporting on the incubation period suggested the incubation period of H5 influenza was around 3 days for tigers, and 3 to 4 days in one cat.

In the experimental studies inoculating non-human mammals with different strains of H5 influenza, there were differences between studies in the proportion of non-human mammals testing positive and the time from exposure to first and last positive tests. The studies experimented or reported on a variety of non-human mammals, and there were differences in how the healthy non-human mammals were exposed to the inoculated non-human mammals, which could have contributed to differences in results between studies.

Limitations

This rapid evidence summary used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but a search of other sources was not conducted (such as websites of public health organisations), so it is possible relevant evidence may have been missed.

Limitations of the reported evidence included a limited number of studies, number and variety of species of non-human mammals, and strains of H5 influenza. Additionally, all experimental studies were undertaken in controlled conditions, possibly affecting the generalisability of the summary findings to exposure to H5 influenza in the wild and other non-laboratory settings.

Additionally, there was no formal risk of bias assessment of the included studies which limited the interpretation of the findings. However, important limitations of the evidence have been highlighted in the report, including most evidence being from experimental studies in laboratories only, and the limited amount of evidence due to both small number of studies and the number and variety of species of non-human mammals within those studies.

Evidence gaps

There was limited evidence for the infectious period of influenza A (H5) in non-human mammals, with a total of 46 non-human mammals exposed to inoculated non-human mammals, many of which did not become infected. All studies looked at time from exposure to first and last positive tests for H5 influenza, and test positivity does not necessarily indicate infectiousness.

There was also limited evidence estimating the incubation period of influenza A (H5) in non-human mammals, with all available evidence coming from an outbreak in up to 147 tigers, and a single infected cat.

Conclusion

Overall, there was limited evidence estimating both the infectious period and the incubation period of influenza A (H5) in non-human mammals, with evidence from 46 non-human mammals exposed to inoculated non-human mammals (many of which did not become infected) for the infectious period (time from exposure to first and last positive test amongst all non-human mammals), and evidence from up to 147 tigers and one cat for the incubation period.

Across 6 studies, the reported time from exposure to testing positive for H5 influenza for non-human mammals was between 2 and 8 days, although most non-human mammals tested positive 5 or fewer days after exposure. The time from exposure to the last positive test was between 4 and 12 days across the 6 studies, although not all studies continued to test until there were no more positive tests, meaning some non-human mammals could have tested positive for longer. In the experimental studies inoculating non-human mammals with different strains of H5 influenza, there were differences between studies in the proportion of non-human mammals testing positive and the time from exposure to first and last positive tests. Additionally, the studies experimented or reported on a variety of non-human mammals, and there were differences in how the contact non-human mammals were exposed to the inoculated non-human mammals, which may have contributed to differences in the results between studies.

The 2 studies reporting on the incubation period suggested the incubation period of H5 influenza was around 3 days for tigers, and 3 to 4 days in one cat.

Overall, there was limited evidence estimating both the infectious period and the incubation period of influenza A (H5) in non-human mammals, and the results of this evidence may not be generalisable to all non-human mammals in all settings.

Acknowledgment

We would like to thank colleagues within the Clinical and Public Health Response division who either reviewed or input into aspects of the review.

Disclaimer

UKHSA's rapid reviews and evidence summaries aim to provide the best available evidence to decision makers in a timely and accessible way, based on published peer-reviewed scientific papers, and papers on preprint servers. Please note that the reviews and summaries:

- use accelerated methods and may not be representative of the whole body of evidence publicly available
- have undergone an internal independent peer review but not an external peer review
- are only valid as of the date stated on the review

In the event that this review or summary is shared externally, please note additionally, to the greatest extent possible under any applicable law, that UKHSA accepts no liability for any claim, loss or damage arising out of, or connected with the use of, this review or summary by the recipient or any third party including that arising or resulting from any reliance placed on, or any conclusions drawn from, the review or summary.

References

1. Herfst S and others. '[Airborne transmission of influenza A/H5N1 virus between ferrets.](#) Science 2012: volume 336, issue 6088, pages 1534 to 1541
2. Imai M and others. '[Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets](#)' Nature 2012: volume 486, issue 7403, pages 420 to 428
3. Sun H and others. '[Highly Pathogenic Avian Influenza H5N6 Viruses Exhibit Enhanced Affinity for Human Type Sialic Acid Receptor and In-Contact Transmission in Model Ferrets](#)' Journal of Virology 2016: volume 90, issue 14, pages 6235 to 6243
4. Yen HL and others. '[Inefficient transmission of H5N1 influenza viruses in a ferret contact model](#)' Journal of Virology 2007: volume 81, issue 13, pages 6890 to 6898
5. Cui H and others. '[Pathogenicity and Transmissibility of Clade 2.3.4.4h H5N6 Avian Influenza Viruses in Mammals](#)' Animals 2022: volume 12
6. Gao Y and others. '[Identification of amino acids in HA and PB2 critical for the transmission of H5N1 avian influenza viruses in a mammalian host](#)' PLoS Pathogens 2009: volume 5, issue 12, page e1000709
7. Hai-xia F and others. '[Interspecies transmission of canine influenza virus H5N2 to cats and chickens by close contact with experimentally infected dogs](#)' Veterinary Microbiology 2014: volume 170, issue 3, pages 414 to 417
8. Thanawongnuwech R and others. '[Probable tiger-to-tiger transmission of avian influenza H5N1](#)' Emerging Infectious Diseases 2005: volume 11, issue 5, pages 699 to 701
9. Tricco AC and others. '[Rapid reviews to strengthen health policy and systems: A practical guide](#)' 2017

Annexe A. Protocol

Review question

There is one review question:

1. What are the infectious period and incubation period of influenza A (H5) in non-human mammals?

Only studies of non-human mammals with the H5 sub-type of influenza A will be included.

This evidence summary will summarise evidence (search up to 15 May 2024) on the incubation and infectious periods of influenza A (H5) in non-human mammals.

For this review, the definitions used are:

- infectious period: the timeframe when an individual may transmit the infection to others
- incubation period: the time between contracting an infection and symptom onset

Inclusion and exclusion criteria are shown in [Table A.1](#).

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	All non-human mammals, including, but not limited to: <ul style="list-style-type: none"> • domestic mammals • non-domestic mammals • ungulates 	All humans, animals other than non-human mammals
Settings	All settings	
Context		
Intervention or exposure	Laboratory-confirmed Influenza A (H5)	Other influenza Other infectious diseases
Outcomes	Any measure of incubation period of influenza A (H5) Any measure of infectious period of influenza A (H5): <ul style="list-style-type: none"> • transmission period • culture positivity over time • serial interval and generation time • time to peak viral load 	

	Included	Excluded
	<ul style="list-style-type: none"> time to viral clearance viral load over time 	
Language	English	
Date of publication	Up to 15 May 2024	
Study design	Interventional trials, including: <ul style="list-style-type: none"> randomised controlled trials non-randomised controlled trials one-arm trials quasi-experimental studies laboratory studies of non-human mammals Observational studies: <ul style="list-style-type: none"> cohort studies case-control studies cross-sectional studies case reports and series 	<ul style="list-style-type: none"> systematic or narrative reviews cross-over trials opinion pieces modelling studies ecological studies
Publication type	Published and preprint	<ul style="list-style-type: none"> guidelines conference abstracts letters or correspondence editorials any grey literature

Identification of studies

We will search Ovid Medline and Embase, Global Health, and Web of Science Preprint Citation Index for studies published up to 15 May 2024.

Screening

Screening on title and abstract will be undertaken in duplicate by 2 reviewers for at least 10% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion with a third reviewer.

Screening on full text will be undertaken by one reviewer and checked by a second.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information will include country, setting, study design, outcomes measures, non-human mammals (species and number), study period, results and any relevant contextual data (such as timing or level of transmission at the time of the study). This will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

Risk of bias of included studies will not be assessed in this rapid evidence summary due to time constraints.

Synthesis

Where studies present data in a consistent format, a narrative synthesis will be produced to interpret the findings. The number of studies, the number of non-human mammals in each study, effect size and variance across studies will be summarised and presented. Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Search strategy

Database: Ovid MEDLINE(R) ALL (1946 to 14 May 2024)

1. Influenza in Birds/ (8786)
2. influenza a virus, h5n1 subtype/ (6745)
3. influenza a virus, h5n2 subtype/ (469)
4. influenza a virus, h5n6 subtype/ (3)
5. influenza a virus, h5n8 subtype/ (301)
6. Influenza A virus/ or Influenza, Human/ (74239)
7. or/1-6 (79623)
8. exp Canidae/ or exp Mustelidae/ or exp Caniformia/ or exp Dolphins/ or exp Porpoises/ (376991)
9. exp Ruminants/ or exp Swine/ or exp Sheep/ or exp Goats/ or Livestock/ or exp Animal Husbandry/ (763047)
10. exp Feliformia/ or exp Lagomorpha/ (486760)
11. Farmers/ or exp Agriculture/ (132024)
12. exp Artiodactyla/ or exp Perissodactyla/ (824618)
13. exp Animals, Domestic/ (41860)

14. exp *Mammals/ (402407)
15. or/8-14 (1885722)
16. 7 and 15 (8988)
17. ((flu or influenza* or H5* or ah5*) adj5 (fox or foxes or otter* or seal* or dolphin* or porpois* or bush dog* or sea lion*)).tw,kf. (75)
18. ((flu or influenza* or H5* or ah5*) adj5 (cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk)).tw,kf. (5395)
19. ((flu or influenza* or H5* or ah5*) adj5 (rabbit* or mink or cat or cats or dog or dogs)).tw,kf. (505)
20. ((flu or influenza* or H5* or ah5*) adj5 (mammal* or ungulate* or domestic animal*)).tw,kf. (664)
21. ((flu or influenza* or H5* or ah5*) and scaveng*).tw,kf. (239)
22. ((flu or influenza* or H5* or ah5*) adj5 (feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*)).tw,kf. (428)
23. ((cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk or fox or foxes or otter* or seal* or dolphin* or porpois* or bush dog* or sea lion* or rabbit* or mink or cat or cats or dog or dogs or mammal* or ungulate* or domestic animal* or feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*) and (H5* or ah5* or flu or influenza*)).ti. (4737)
24. (HPAIV or AIV).tw,kf. (3274)
25. "A/tern/South Africa/300/77(H5N3)".tw,kf. (0)
26. "A/Ethiopia/300/77(H5N4)".tw,kf. (0)
27. "A/turkey/Ontario/7732/66(H5N9)".tw,kf. (12)
28. "A/chick/Scotland/59(H5N1)".tw,kf. (0)
29. or/17-28 (10777)
30. 16 or 29 (16879)
31. ((Transmis* or transmit* or infectious* or isolation or shed* or case or cases or isolat*) adj5 (duration* or time* or length* or period* or peak*)).tw,kf. (141946)
32. ((PCR positiv* or Viral proliferat*) adj5 (duration* or time* or length* or period* or peak*)).tw,kf. (491)
33. cycl* threshold*.tw,kf. (2927)
34. CT value*.tw,kf. (5586)
35. (peak* adj1 (vir* load* or vir* concentrat*)).tw,kf. (429)
36. (Viral Load/ or exp Disease Transmission, Infectious/) and exp Time/ (9477)
37. serial interval*.tw,kf. (455)
38. "chain* of transmission".tw,kf. (646)
39. ((clearance* or "viral load*" or (virus adj2 amount*) or (virus adj2 level*)) adj5 (duration* or time* or length* or period*)).tw,kf. (10606)
40. incubat*.tw,kf. (349419)
41. Infectious Disease Incubation Period/ (411)

42. Time Factors/ (1232750)
43. (latent or latency).tw,kf. (198502)
44. Latent Infection/ (214)
45. (time adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. (66833)
46. (period adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. (17069)
47. (asymptom* adj5 (duration or period or length*)).tw,kf. (2216)
48. (generation adj3 time).tw,kf. (5886)
49. (transmission or infectious).ti. (142884)
50. exp *Disease Transmission, Infectious/ (45248)
51. Disease Vectors/ (8566)
52. or/31-51 (2126304)
53. 30 and 52 (1903)

Database: Embase (1974 to 14 May 2024)

1. exp avian influenza/ or "influenza a virus (h5n1)"/ or "influenza a virus (h5n2)"/ or "influenza a virus (h5n3)"/ or "influenza a virus (h5n8)"/ (11631)
2. influenza/ or influenza a virus/ or influenza a/ or influenzavirus a/ (89301)
3. or/1-2 (97971)
4. exp canidae/ or exp mustelidae/ or exp caniformia/ or exp toothed whale/ (322819)
5. exp bovine/ or exp pig/ or exp sheep/ or exp goat/ or exp livestock/ or exp animal husbandry/ (420487)
6. exp feliformia/ or exp lagomorph/ (167228)
7. exp agricultural land/ or agricultural worker/ (50994)
8. exp Artiodactyla/ (368105)
9. exp Perissodactyla/ (83171)
10. exp domestic animal/ (24751)
11. exp *mammal/ (1233965)
12. or/4-11 (2044507)
13. 3 and 12 (7880)
14. ((flu or influenza* or H5* or ah5*) adj5 (fox or foxes or otter* or seal* or dolphin* or porpois* or bush dog* or sea lion*)).tw,kf. (71)
15. ((flu or influenza* or H5* or ah5*) adj5 (cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk)).tw,kf. (6113)
16. ((flu or influenza* or H5* or ah5*) adj5 (rabbit* or mink or cat or cats or dog or dogs)).tw,kf. (499)
17. ((flu or influenza* or H5* or ah5*) adj5 (mammal* or ungulate* or domestic animal*)).tw,kf. (672)
18. ((flu or influenza* or H5* or ah5*) and scaveng*).tw,kf. (322)
19. ((flu or influenza* or H5* or ah5*) adj5 (feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*)).tw,kf. (470)

20. ((cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk or fox or foxes or otter* or seal* or dolphin* or porpois* or bush dog* or sea lion* or rabbit* or mink or cat or cats or dog or dogs or mammal* or ungulate* or domestic animal* or feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*) and (H5* or ah5* or flu or influenza*)).ti. (4808)
21. (HPAIV or AIV).tw,kf. (3594)
22. "A/tern/South Africa/300/77(H5N3)".tw,kf. (0)
23. "A/Ethiopia/300/77(H5N4)".tw,kf. (0)
24. "A/Ethiopia/300/77(H5N4)".tw,kf. (0)
25. "A/chick/Scotland/59(H5N1)".tw,kf. (0)
26. or/14-25 (11824)
27. 13 or 26 (18058)
28. ((Transmis* or transmit* or infectious* or isolat* or shed* or case or cases) adj5 (duration* or time* or length* or period* or peak*)).tw,kf. (203341)
29. ((PCR positiv* or Viral proliferat*) adj5 (duration* or time* or length* or period* or peak*)).tw,kf. (649)
30. cycl* threshold*.tw,kf. (3842)
31. CT value*.tw,kf. (8851)
32. (peak* adj1 (vir* load* or vir* concentrat*)).tw,kf. (681)
33. (virus load/ or exp disease transmission/) and exp time/ (6649)
34. "serial interval*".tw,kf. (503)
35. chain of transmission.tw,kf. (509)
36. ((clearance* or "viral load*" or (virus adj2 amount*) or (virus adj2 level*)) adj5 (duration* or time* or length* or period*)).tw,kf. (15280)
37. incubat*.tw,kf. (430251)
38. incubation time/ or time factor/ or exp latent infection/ (120473)
39. (latent or latency).tw,kf. (247182)
40. (time adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. (108642)
41. (period adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. (25469)
42. (asymptom* adj5 (duration or period or length*)).tw,kf. (3199)
43. (generation adj3 time).tw,kf. (6434)
44. (transmission or infectious).ti. (145231)
45. exp *disease transmission/ (42774)
46. exp disease carrier/ (55030)
47. or/28-46 (1294151)
48. 27 and 47 (2043)
49. limit 48 to conference abstract (284)
50. 48 not 49 (1759)

Database: Global Health (1910 to 14 May 2024)

1. avian influenza a viruses/ or avian influenza viruses/ or avian influenza/ (6628)
2. exp canidae/ or exp mustelidae/ or exp dogs/ or exp phocoenidae/ or exp dolphins/ or exp otters/ (67363)
3. exp bovidae/ or exp pigs/ or exp sheep/ or exp goats/ or exp livestock/ or exp animal husbandry/ (230522)
4. farming/ or livestock farming/ or exp farmers/ (18439)
5. exp felidae/ or exp lagomorpha/ (64269)
6. exp ungulates/ (529)
7. exp domestic animals/ (109184)
8. exp mammals/ (3681070)
9. or/2-8 (3744554)
10. 1 and 9 (5793)
11. (HPAIV or AIV).tw,hw. (1287)
12. ((flu or influenza* or H5* or ah5*) adj5 (fox or foxes or otter* or seal* or dolphin* or porpois* or bush dog* or sea lion*)).tw,hw. (41)
13. ((flu or influenza* or H5* or ah5*) adj5 (cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk)).tw,hw. (5000)
14. ((flu or influenza* or H5* or ah5*) adj5 (rabbit* or mink or cat or cats or dog or dogs)).tw,hw. (319)
15. ((flu or influenza* or H5* or ah5*) adj5 (mammal* or ungulate* or domestic animal*)).tw,hw. (465)
16. ((flu or influenza* or H5* or ah5*) and scaveng*).tw,hw. (274)
17. ((flu or influenza* or H5* or ah5*) adj5 (feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*)).tw,hw. (524)
18. ((cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk or fox or foxes or otter* or seal* or dolphin* or porpois* or bush dog* or sea lion* or rabbit* or mink or cat or cats or dog or dogs or mammal* or ungulate* or domestic animal* or feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*) and (H5* or ah5* or flu or influenza*)).ti. (2119)
19. "A/tern/South Africa/300/77(H5N3)".tw,hw. (0)
20. "A/Ethiopia/300/77(H5N4)".tw,hw. (0)
21. "A/Ethiopia/300/77(H5N4)".tw,hw. (0)
22. "A/chick/Scotland/59(H5N1)".tw,hw. (0)
23. or/11-22 (7396)
24. 10 or 23 (11412)
25. ((Transmis* or transmit* or infectious* or isolat* or shed* or case or cases) adj5 (duration* or time* or length* or period* or peak*)).tw,hw. (47524)

26. ((PCR positiv* or Viral proliferat*) adj5 (duration* or time* or length* or period* or peak*)).tw,hw. (348)
27. (cycl* threshold* or CT Value*).tw,hw. (3189)
28. (peak* adj1 (vir* load* or vir* concentrat*)).tw,hw. (211)
29. (viral load/ or exp disease transmission/) and exp time/ (559)
30. latent infections/ or incubation duration/ or time/ (9605)
31. "serial interval*".tw,hw. (291)
32. chain of transmission.tw,hw. (335)
33. ((clearance* or "viral load*" or (virus adj2 amount*) or (virus adj2 level*)) adj5 (duration* or time* or length* or period*)).tw,hw. (3732)
34. incubat*.tw,hw. (80100)
35. (latent or latency).tw,hw. (34302)
36. ((time or period) adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,hw. (14501)
37. (asymptom* adj5 (duration or period or length*)).tw,hw. (511)
38. (generation adj3 time).tw,hw. (1063)
39. (transmission or infectious).ti. (54217)
40. exp disease vectors/ (67067)
41. or/25-40 (291361)
42. 24 and 41 (1286)

Web of Science Preprints

TS=(((flu or influenza* or h5 OR H5N* or ah5*) NEAR/4 (fox or foxes or otter* or seal* or dolphin* or porpois* or "bush dog*" or "sea lion*"))) OR TS=(((flu or influenza* or h5 OR H5N* or ah5*) NEAR/4 (cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk))) OR TS=(((flu or influenza* or h5 OR H5N* or ah5*) NEAR/4 (rabbit* or mink or cat or cats or dog or dogs))) OR TS=(((flu or influenza* or h5 OR H5N* or ah5*) NEAR/4 (mammal* or ungulate* or "domestic animal*"))) OR TS=(((flu or influenza* or h5 OR H5N* or ah5*) and scaveng*)) OR TS=((HPAIV or AIV)) OR TS=("A/tern/South Africa/300/77(H5N3)" OR "A/Ethiopia/300/77(H5N4)" OR "A/turkey/Ontario/7732/66(H5N9)" OR "A/chick/Scotland/59(H5N1)") OR TS=(((flu or influenza* or H5* or ah5*) NEAR/4 (feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*)) OR TI=((cow or cows or cattle or bovine or bovid or sheep or pig or pigs or sow or swine or horse* or goat* or livestock or farm* or deer or elk or fox or foxes or otter* or seal* or dolphin* or porpois* or bush dog* or sea lion* or rabbit* or mink or cat or cats or dog or dogs or mammal* or ungulate* or domestic animal* or feline* or felidae or feliform* or canine* or canidae or caniform* or Mustelid* or ruminant* or lagomorph* or Artiodactyl* or Perissodactyl*) and (H5* or ah5* or flu or influenza*))

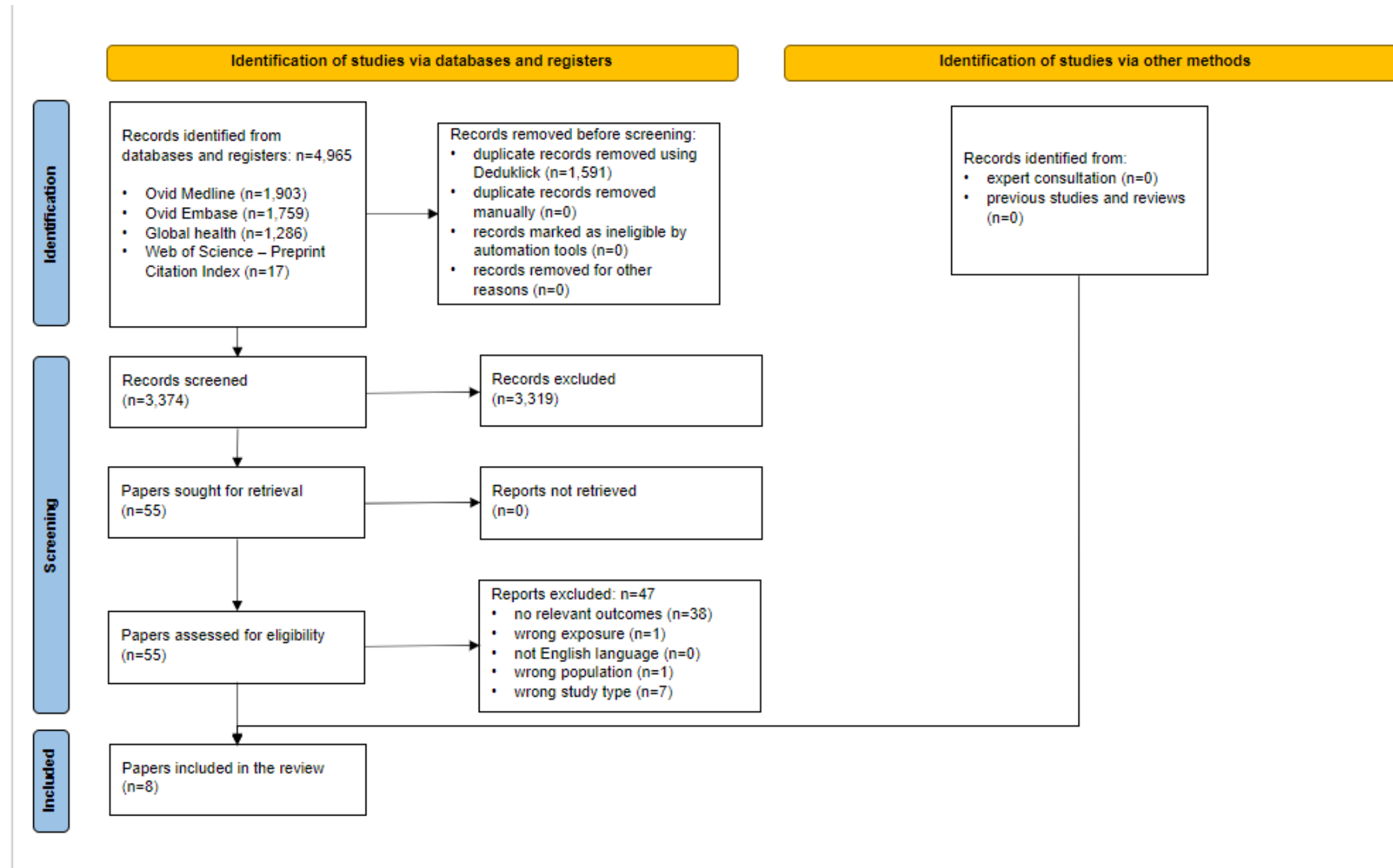
And

TS=(((Transmis* or transmit* or infectious* or isolation or shed* or case or cases or isolat*) NEAR/4 (duration* or time* or length* or period* or peak*))) OR TS=(((PCR positiv* or "Viral proliferat*") NEAR/4 (duration* or time* or length* or period* or peak*))) OR TS=("cycl* threshold*") OR TS=("CT value*") OR TS=((peak* NEAR/0 ("vir* load*" or "vir* concentrat*"))) OR TS=("serial interval*") OR TS=("chain* of transmission") OR TS=((clearance* or "viral load*" or (virus NEAR/2 amount* or (virus NEAR/2 level*)) NEAR/5 (duration* or time* or length* or period*)) OR TS=(incubat*) OR TS=((latent or latency)) OR TS=((time NEAR/4 (asymptom* or symptom* or onset or "clinical presentation"))) OR TS=((period NEAR/4 (asymptom* or symptom* or onset or "clinical presentation"))) OR TS=((asymptom* NEAR/4 (duration or period or length*))) OR TS=((generation NEAR/2 time)) OR TI=((transmission or infectious))

17 results

Annexe B. PRISMA diagram

Figure B.1. PRISMA diagram



Text version for Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 8 studies.

From identification of studies via databases and registers, n=4,965 records identified from databases and registers:

- Ovid Medline (n=1,903)
- Ovid Embase (n=1,759)
- Global health (n=1,286)
- Web of Science – Preprint Citation Index (n=17)

From these, records removed before screening:

- duplicate records removed using Deduplick (n=1,591)
- duplicate records removed manually (n=0)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=3,374 records screened, of which n=3,319 were excluded, leaving n=55 papers sought for retrieval, all of which were retrieved.

Of the n=55 papers assessed for eligibility, n=47 reports were excluded:

- no relevant outcomes (n=38)
- wrong exposure (n=1)
- not English language (n=0)
- wrong population (n=1)
- wrong study type (n=7)

From identification of studies via other methods, records were identified from:

- expert consultation (n=0)
- previous studies and reviews (n=0)

Overall, n=8 papers were included in the review

Annexe C. Excluded full texts

No relevant outcomes (38 studies)

Arruda B and others. ['Divergent Pathogenesis and Transmission of Highly Pathogenic Avian Influenza A\(H5N1\) in Swine'](#) Emerging Infectious Diseases 2024: volume 30, issue 4, pages 738 to 751

Carlson CM and others. ['Transforming growth factor-beta: activation by neuraminidase and role in highly pathogenic H5N1 influenza pathogenesis'](#) PLoS Pathogens 2010: volume 6, issue 10, page e1001136

Chen Y and others. ['Dogs are highly susceptible to H5N1 avian influenza virus'](#) Virology 2010: volume 405, issue 1, pages 15 to 19

Cronk BD and others. ['Infection and tissue distribution of highly pathogenic avian influenza A type H5N1 \(clade 2.3.4.4b\) in red fox kits \(Vulpes vulpes\)'](#) Emerging Microbes & Infections 2023: volume 12, issue 2, page 2249554

Duan M and others. ['In vitro and in vivo protection against the highly pathogenic H5N1 influenza virus by an antisense phosphorothioate oligonucleotide'](#) Antiviral Therapy 2008: volume 13, issue 1, pages 109 to 114

Giese M and others. ['Experimental infection and natural contact exposure of dogs with avian influenza virus \(H5N1\)'](#) Emerging Infectious Diseases 2008: volume 14, issue 2, pages 308 to 310

Herbreteau CH and others. ['Specific polyclonal F\(ab'\)₂ neutralize a large panel of highly pathogenic avian influenza A viruses \(H5N1\) and control infection in mice'](#) Immunotherapy 2014: volume 6, issue 6, pages 699 to 708

Herfst S and others. ['A Dutch highly pathogenic H5N6 avian influenza virus showed remarkable tropism for extra-respiratory organs and caused severe disease but was not transmissible via air in the ferret model'](#) Msphere 2023: volume 8, issue 4

Hiono T and others. ['Experimental infection of highly and low pathogenic avian influenza viruses to chickens, ducks, tree sparrows, jungle crows, and black rats for the evaluation of their roles in virus transmission'](#) Veterinary Microbiology 2016: volume 182, pages 108 to 115

Horwood PF and others. ['Transmission experiments support clade-level differences in the transmission and pathogenicity of Cambodian influenza A/H5N1 viruses'](#) Emerging Microbes & Infections 2020: volume 9, issue 1, pages 1702 to 1711

Kang Y and others. ['Pathogenicity and transmissibility of three avian influenza A \(H5N6\) viruses isolated from wild birds'](#) Journal of Infection 2018: volume 76, pages 286 to 294

Kaplan BS and others. ['Novel Highly Pathogenic Avian A\(H5N2\) and A\(H5N8\) Influenza Viruses of Clade 2.3.4.4 from North America Have Limited Capacity for Replication and Transmission in Mammals'](#) Msphere 2016: volume 1, issue 2, pages Mar to Apr

Kaplan BS and others. ['Absence of clinical disease and contact transmission of HPAI H5NX clade 2.3.4.4 from North America in experimentally infected pigs'](#) Influenza and Other Respiratory Viruses 2017: volume 11, issue 5, pages 464 to 470

Kida H and others. ['Potential for transmission of avian influenza viruses to pigs'](#) Journal of General Virology 1994: volume 75, pages 2183 to 2188

Kim Y and others. ['Pathobiological features of a novel, highly pathogenic avian influenza A\(H5N8\) virus'](#) Emerging Microbes and Infections 2014: volume 3, issue 10, page e75

Lalor PA and others. ['Plasmid DNA-based vaccines protect mice and ferrets against lethal challenge with A/Vietnam/1203/04 \(H5N1\) influenza virus'](#) Journal of Infectious Diseases 2008: volume 197, issue 12, pages 1643 to 1652

Layton RC and others. ['Enhanced immunogenicity, mortality protection, and reduced viral brain invasion by alum adjuvant with an H5N1 split-virion vaccine in the ferret'](#) PLoS ONE [Electronic Resource] 2011: volume 6, issue 6, page e20641

Leschnik M and others. ['Subclinical infection with avian influenza A \(H5N1\) virus in cats'](#) Emerging Infectious Diseases 2007: volume 13, pages 243 to 247

Maines TR and others. ['Local innate immune responses and influenza virus transmission and virulence in ferrets'](#) Journal of Infectious Diseases 2012: volume 205, issue 3, pages 474 to 485

Matsuoka Y and others. ['Neuraminidase stalk length and additional glycosylation of the hemagglutinin influence the virulence of influenza H5N1 viruses for mice'](#) Journal of Virology 2009: volume 83, issue 9, pages 4704 to 4708

Noh JY and others. ['Limited pathogenicity and transmissibility of Korean highly pathogenic avian influenza H5N6 clade 2.3.4.4 in ferrets'](#) Transboundary and Emerging Diseases 2018: volume 65, issue 4, pages 923 to 926

Pulit-Penalosa JA and others. ['Pathogenesis and Transmissibility of North American Highly Pathogenic Avian Influenza A\(H5N1\) Virus in Ferrets'](#) Emerging Infectious Diseases 2022: volume 28, pages 1913 to 1915

Pulit-Penalozza JA and others. ['Pathogenesis and Transmission of Novel Highly Pathogenic Avian Influenza H5N2 and H5N8 Viruses in Ferrets and Mice'](#) Journal of Virology 2015: volume 89, issue 20, pages 10286 to 10293

Rabalski L and others. ['Emergence and potential transmission route of avian influenza A \(H5N1\) virus in domestic cats in Poland, June 2023'](#) Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2023: volume 28, issue 31, page 8

Richard M and others. ['Low Virulence and Lack of Airborne Transmission of the Dutch Highly Pathogenic Avian Influenza Virus H5N8 in Ferrets'](#) PLoS ONE [Electronic Resource] 2015: volume 10, issue 6, page e0129827

Romero Tejeda A and others. ['Susceptibility to and transmission of H5N1 and H7N1 highly pathogenic avian influenza viruses in bank voles \(Myodes glareolus\)'](#) Veterinary Research 2015: volume 46, page 51

Shaban S and others. ['Is There Cross-Species Transmission to Pigs of Avian Influenza Virus Within Poultry Farms with Previous Outbreak of Avian Influenza?'](#) African Journal of Biomedical Research 2021: volume 24, pages 333 to 338

Song QQ and others. ['Dog to dog transmission of a novel influenza virus \(H5N2\) isolated from a canine'](#) Veterinary Microbiology 2013: volume 161, issue 3, pages 331 to 333

Stark GV and others. ['Clinical profiles associated with influenza disease in the ferret model'](#) PLoS ONE [Electronic Resource] 2013: volume 8, issue 3, page e58337

Steel J and others. ['Transmission of influenza virus in a mammalian host is increased by PB2 amino acids 627K or 627E/701N'](#) PLoS Pathogens 2009: volume 5, issue 1, page e1000252

Tumpey TM and others. ['Depletion of lymphocytes and diminished cytokine production in mice infected with a highly virulent influenza A \(H5N1\) virus isolated from humans'](#) Journal of Virology 2000: volume 74, issue 13, pages 6105 to 6116

Villanueva-Saz S and others. ['Serological exposure to influenza A in cats from an area with wild birds positive for avian influenza'](#) Zoonoses and Public Health 2024: volume 71, issue 3, pages 324 to 330

Wang X and others. ['Highly pathogenic avian influenza A virus \(H5N1\) can be transmitted in ferrets by transfusion'](#) BMC Infectious Diseases 2014: volume 14, page 192

Wilker PR and others. ['Selection on haemagglutinin imposes a bottleneck during mammalian transmission of reassortant H5N1 influenza viruses'](#) Nature communications 2013: volume 4, page 2636

Wu H and others. ['Novel reassortant influenza A\(H5N8\) viruses in domestic ducks, Eastern China'](#) Emerging Infectious Diseases 2014: volume 20, issue 8, pages 1315 to 1318

Yuan Z and others. ['Serological surveillance of H5 and H9 avian influenza A viral infections among pigs in Southern China'](#) Microbial Pathogenesis 2013: volume 64, pages 39 to 42

Yun NE and others. ['Injectable peramivir mitigates disease and promotes survival in ferrets and mice infected with the highly virulent influenza virus, A/Vietnam/1203/04 \(H5N1\)'](#) Virology 2008: volume 374, issue 1, pages 198 to 209

Zaraket H and others. ['Increased acid stability of the hemagglutinin protein enhances H5N1 influenza virus growth in the upper respiratory tract but is insufficient for transmission in ferrets'](#) Journal of Virology 2013: volume 87, issue 17, pages 9911 to 9922

Wrong exposure (1 study)

Root JJ and others. ['When fur and feather occur together: interclass transmission of avian influenza A virus from mammals to birds through common resources'](#) Scientific Reports 2015: volume 5, page 14354

Wrong population (1 study)

Spackman E and others. ['Characterization of low-pathogenicity H5N1 avian influenza viruses from North America'](#) Journal of Virology 2007: volume 81, issue 21, pages 11612 to 11619

Wrong study type (7 studies)

Ayyalasomayajula S and others. ['A network model of H5N1 avian influenza transmission dynamics in domestic cats'](#) Zoonoses and Public Health 2008: volume 55, issue 8, pages 497 to 506

Burgos S, Burgos SA. ['Reports of Avian Influenza H5N1 in cats and dogs'](#) International Journal of Poultry Science 2007: volume 6, issue 12, pages 1003 to 1005

Looi MK. ['Bird flu: Person with rare strain in US sparks alarm about cow transmission'](#) BMJ 2024: volume 385, page q797

Root JJ. ['What Are the Transmission Mechanisms of Influenza A Viruses in Wild Mammals?'](#) Journal of Infectious Diseases 2020: volume 221, issue 2, pages 169 to 171

Tomori O, Oluwayelu DO. ['Domestic Animals as Potential Reservoirs of Zoonotic Viral Diseases'](#) Annual Review of Animal Biosciences 2023: volume 11, pages 33 to 55

Incubation and infectious period of influenza A (H5) in non-human mammals: a rapid evidence summary

Vahlenkamp TW. ['Influenza in cats and dogs - risk for humans?'](#) European Journal of Companion Animal Practice 2015: volume 25, issue 1, pages 8 to 12

Xiang B and others. ['Wild bird-origin H5N6 avian influenza virus is transmissible in guinea pigs'](#) Journal of Infection 2020: volume 80, pages e20 to e22

Annexe D. Data extraction table

Table D1. Study characteristics of included studies

Table D1a. Study characteristics of experimental animal studies (ferrets)

Study	Country, time period	Population	Outcomes
Herfst 2012 (1)	Not stated, Not stated	4 ferrets inoculated with H5N1 influenza (HA Q222L,G224S PB2 E627K), 4 uninfected aerosol exposed ferrets	Positivity for H5N1 influenza virus of aerosol exposed ferrets: <ul style="list-style-type: none"> • 1 day after exposure: 0 of 4 ferrets (0%) • 3 days after exposure: 1 of 4 ferrets (25%) • 5 days after exposure: 3 of 4 ferrets (75%) • 7 days after exposure: 3 of 4 ferrets (75%) • 9 days after exposure: 1 of 4 ferrets (75%) • 11 days after exposure: 0 of 4 ferrets (0%)
Imai 2012 (2)	Not stated, Not stated	3 ferrets inoculated with H5 HA influenza (rgCA04), 3 uninfected aerosol exposed ferrets	Positivity for H5 HA influenza virus of aerosol exposed ferrets: <ul style="list-style-type: none"> • 1 day after exposure: 0 of 3 ferrets (0%) • 3 days after exposure: 3 of 3 ferrets (100%) • 5 days after exposure: 3 of 3 ferrets (100%) • 7 days after exposure: 3 of 3 ferrets (100%)
		6 ferrets inoculated with H5 HA influenza (HA(N158D/N224K/Q226L)/CA04), 6 uninfected aerosol exposed ferrets	Positivity for H5 HA influenza virus of aerosol exposed ferrets: <ul style="list-style-type: none"> • 1 day after exposure: 0 of 6 ferrets (0%) • 3 days after exposure: 0 of 6 ferrets (0%) • 5 days after exposure: 1 of 6 ferrets (16.7%) • 7 days after exposure: 2 of 6 ferrets (33.3%)
		6 ferrets inoculated with H5 HA influenza HA(N158D/N224K/Q226L/T318I)/CA04, 6 uninfected aerosol exposed ferrets	Positivity for H5 HA influenza virus of aerosol exposed ferrets: <ul style="list-style-type: none"> • 1 day after exposure: 0 of 6 ferrets (0%) • 3 days after exposure: 2 of 6 ferrets (33.3%) • 5 days after exposure: 3 of 6 ferrets (50%) • 7 days after exposure: 4 of 6 ferrets (66.7%)
Sun 2016 (3)	China, Not stated	3 ferrets inoculated with H5N6 influenza (A/goose/Eastern China/S0513/2013), 3 uninfected direct contact ferrets	Positivity for H5N6 influenza virus of direct contact ferrets: <ul style="list-style-type: none"> • 2 days after exposure: 0 of 3 ferrets (0%) • 4 days after exposure: 3 of 3 ferrets (100%) • 6 days after exposure: 3 of 3 ferrets (100%) • 8 days after exposure: 3 of 3 ferrets (100%) • 10 days after exposure: 3 of 3 ferrets (100%) • 12 days after exposure: 2 of 3 ferrets (66.7%)
		3 ferrets inoculated with H5N6 influenza (A/duck/Eastern China/S0711/2014), 3 uninfected direct contact ferrets	Positivity for H5N6 influenza virus of direct contact ferrets: <ul style="list-style-type: none"> • 2 days after exposure: 3 of 3 ferrets (100%)

Study	Country, time period	Population	Outcomes
			<ul style="list-style-type: none"> 4 days after exposure: 3 of 3 ferrets (100%) 6 days after exposure: 3 of 3 ferrets (100%) 8 days after exposure: 3 of 3 ferrets (100%) 10 days after exposure: 3 of 3 ferrets (100%) 12 days after exposure: 1 of 3 ferrets (33.3%)
Yen 2007 (4)	US, Not stated	2 ferrets inoculated with H5N1 influenza (A/Vietnam/JP36-2/05), 4 uninfected direct contact ferrets	Positivity for H5N1 influenza virus of direct contact ferrets: <ul style="list-style-type: none"> 2 days after exposure: 0 of 4 ferrets (0%) 4 days after exposure: 0 of 4 ferrets (0%) 6 days after exposure: 1 of 4 ferrets (25%) 8 days after exposure: 1 of 4 ferrets (25%) 10 days after exposure: 0 of 4 ferrets (0%) 12 days after exposure: 1 of 4 ferrets (25%) (same ferret as day 6)

Table D1b: Study characteristics of experimental animal studies (guinea pigs)

Study	Country, time period	Population	Outcomes
Cui 2022 (5)	China, Not stated	3 guinea pigs inoculated with H5N6 influenza (A/chicken/Hebei/HB1905/2019), 3 uninfected direct contact guinea pigs	Positivity for H5N6 influenza virus of direct contact guinea pigs: <ul style="list-style-type: none"> 2 days after exposure: 1 of 3 guinea pigs (33.3%) 4 days after exposure: 1 of 3 guinea pigs (33.3%) 6 days after exposure: 0 of 3 guinea pigs (0%) 8 days after exposure: 0 of 3 guinea pigs (0%)
		3 guinea pigs inoculated with H5N6 influenza (A/chicken/Hebei/HB1907/2019), 3 uninfected direct contact guinea pigs	3 of 3 direct contact guinea pigs (100%) were positive for H5N6 influenza virus at 2, 4, 6, and 8 days after exposure
Gao 2009 (6)	China, Not stated	3 female guinea pigs inoculated with H5N1 influenza (A/duck/Guangxi/35/01), 3 female uninfected direct contact guinea pigs	Positivity for H5N1 influenza virus of direct contact guinea pigs: <ul style="list-style-type: none"> 2 days after exposure: 0 of 3 guinea pigs (0%) 4 days after exposure: 3 of 3 guinea pigs (100%) 6 days after exposure: 3 of 3 guinea pigs (100%) 8 days after exposure: 3 of 3 guinea pigs (100%) 10 days after exposure: 1 of 3 guinea pigs (33.3%) 12 days after exposure: 1 of 3 guinea pigs (33.3%) 14 days after exposure: 0 of 3 guinea pigs (0%)
		3 female guinea pigs inoculated with H5N1 influenza (A/Bar-headed goose/Qinghai/3/05), 3 female uninfected direct contact guinea pigs	Positivity for H5N1 influenza virus of direct contact guinea pigs: <ul style="list-style-type: none"> 2 days after exposure: 0 of 3 guinea pigs (0%) 4 days after exposure: 2 of 3 guinea pigs (66.7%) 6 days after exposure: 3 of 3 guinea pigs (100%) 8 days after exposure: 3 of 3 guinea pigs (100%)

Study	Country, time period	Population	Outcomes
			<ul style="list-style-type: none"> • 10 days after exposure: 3 of 3 guinea pigs (100%) • 12 days after exposure: 2 of 3 guinea pigs (66.7%) • 14 days after exposure: 0 of 3 guinea pigs (0%)

Table D1c: Study characteristics of experimental animal studies (cats and dogs)

Study	Country, time period	Population	Outcomes
Hai-xia 2014 (7)	China, Not stated	3 dogs inoculated with H5N2 influenza (CA/SD/JT01/09), 5 uninfected exposed cats	1 of 5 cats (20%) developed influenza symptoms 3 to 4 days after exposure

Table D1d: Study characteristics of observational animal studies (tigers)

Study	Country, time period	Population	Outcomes
Thanawongnuwech 2005 (8)	Thailand, 2004	Up to 147 tigers with H5N1 influenza (A/Tiger/Thailand/CU-T3/04 and A/Tiger/Thailand/CU-T7/04)	Incubation period estimated to be around 3 days

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