



UK Health
Security
Agency

Incubation and infectious period of influenza A (H5)

A rapid evidence summary

Contents

Main messages	3
Purpose.....	4
Methods	4
Evidence	5
Health inequalities.....	8
Limitations.....	8
Evidence gaps	9
Conclusion	9
Acknowledgment.....	9
Disclaimer	10
References.....	11
Annexe A: Protocol	12
Annexe B: Excluded full texts.....	20
Annexe C: Data extraction table	23
About the UK Health Security Agency	27

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) (search up to 26 April 2024), including 11 studies in total.
2. One retrospective cohort study of 8 cases estimated the probable range of the infectious period to be between 5 and 13 days ([2](#)), and one retrospective cohort study of 11 secondary cases estimated serial interval to be 8 days (range: 2 to 11 days) ([1](#)). The case series that presented evidence for human-to-human transmission reported that the 2 index cases likely infected 3 secondary cases (individuals infected through direct contact with an index case) 3 to 5 days after their symptom onset ([9](#), [10](#)).
3. Three retrospective cohort studies including up to 59 cases (assuming no overlap in cases between studies) ([2 to 4](#)) and 7 case series and case reports including up to 30 cases (assuming no overlap in cases between studies) ([5 to 11](#)) were identified that provided evidence for the incubation period of H5 influenza.
4. Almost all cases were exposed to poultry prior to symptom onset, although there was evidence of human-to-human transmission in several cases ([2](#), [9](#), [10](#)).
5. Estimates of the incubation period varied between 2 and 10 days across studies, although in the 2 retrospective cohort studies estimating the mean and median incubation periods, the mean was estimated as 3.3 days ([3](#)) and a median as 5 days ([4](#)).
6. Overall, there was very limited evidence estimating the infectious period and limited evidence estimating the incubation period of influenza A (H5). Additionally, almost all cases were identified in Asia between 2003 and 2014, potentially limiting generalisability of the results to a contemporary UK population, as both the circulating H5N1 influenza virus and demographics of potential cases may be different in ways that could affect the infectious and incubation periods.

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).

There was one review question:

1. What are the infectious period and incubation period of influenza A (H5) in humans?

Methods

A rapid evidence summary was conducted, following streamlined systematic methods to accelerate the review process ([12](#)). A literature search was undertaken to look for all relevant studies, published or available as preprint, up to 26 April 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. Studies excluded on full text screening are available with the reasons for exclusion in [Annexe B](#).

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 were no deviations from the protocol.

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

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
- serial interval: time interval between symptom onset of the index and secondary cases

Evidence

In total, 1,434 primary studies were screened at title and abstract, and 31 studies were screened at full text. Of these, 6 studies were included ([3 to 5](#), [7](#), [8](#), [11](#)). Five additional relevant studies were identified from reviews and other included studies ([1](#), [2](#), [6](#), [9](#), [10](#)), so in total 11 studies were included in this review ([1 to 11](#)).

Four studies were retrospective cohort studies with between 8 and 27 cases with H5N1 influenza ([1 to 4](#)), 6 studies were case series of between 2 and 8 cases with H5N1 influenza ([5 to 10](#)), and one study was a case report of a case with H5N6 influenza ([11](#)). All studies were conducted between 2003 and 2014. Four studies were conducted in China ([3](#), [4](#), [10](#), [11](#)), 2 studies in Thailand ([6](#), [9](#)), 2 studies in Indonesia ([1](#), [2](#)), one study in Bangladesh ([5](#)), one study in Turkey ([8](#)), and one study in Vietnam ([7](#)).

Ten studies presented evidence for the incubation period ([2 to 11](#)), one study presented evidence for the infectious period ([2](#)), and one study presented evidence for the serial interval (the time between symptom onset in an index case and a secondary case infected by the index case, used as evidence to inform the infectious period) ([1](#)). All studies reported on cases with known exposure to poultry, although 4 studies also included cases with likely human-to-human transmission ([1](#), [2](#), [9](#), [10](#)).

As multiple studies reported on cases identified in China, Indonesia, and Thailand at similar times, it is possible there is overlap in cases between studies. If there was no overlap between studies, there would be a total of 89 cases included in this report for the incubation period, 8 cases for the infectious period, and 11 cases for the serial interval.

Infectious period

One retrospective cohort study estimated the infectious period ([2](#)), and one retrospective cohort study estimated the serial interval ([1](#)). Study characteristics are presented in [Table C.1a](#).

Aditama and others reported on 11 secondary cases with confirmed or probable H5N1 influenza in infection clusters with inconclusive exposure to a zoonotic source of virus (no reported information on age or sex of cases) in Indonesia between 2005 and 2009 ([1](#)). All index cases had confirmed H5N1 influenza, and for probable secondary cases, the index case had confirmed H5N1 influenza. The median interval between illness onset of serial cases was estimated to be 8 days (range: 2 to 11 days).

Yang and others reported on one index case with probable H5N1 influenza and 7 secondary cases with confirmed H5N1 influenza, in Indonesia between 2005 and 2006 (age range: 18 months to 37 years) ([2](#)). The index case was likely exposed to dead poultry but died before testing could confirm infection. H5N1 infection was suspected due to symptoms, history of

contact with diseased poultry and the progression of their illness. The 7 secondary cases were likely the result of human-to-human transmission from the index case. The probable range of the incubation period was estimated to be between 3 and 7 days, and the probable range of the infectious period was estimated to be between 5 and 13 days.

Incubation period

Retrospective cohort studies

Three retrospective cohort studies estimated the incubation period ([2 to 4](#)), Study characteristics are presented in [Table C.1b](#).

Cowling and others reported on 27 cases with confirmed H5N1 influenza and information about dates of recent exposure to live poultry (51% male, median age: 26 years, interquartile range: 19 to 35 years) in China between 2003 and 2013 ([3](#)). The mean incubation period was estimated to be 3.3 days (95% confidence interval: 2.7 to 3.9 days, standard deviation: 1.5 days, 95th percentile: 6.0 days).

Huai and others reported on 24 cases with confirmed H5N1 influenza who had been exposed to sick or dead poultry (16 cases, 25% male, median age: 25 years, age range: 6 to 44 years), or to wet poultry markets (8 cases, 63% male, median age: 30 years, age range: 16 to 41 years), in China (study dates not reported, study published in 2008) ([4](#)). The median incubation period was estimated to be:

- 5 days (range: 2 to 9.5 days) for all 24 cases
- 5 days (range: 2 to 9.5 days) for 18 cases exposed on multiple days
- 5 days (range: 2 to 9 days) for 6 cases with a single known exposure
- 4.3 days (range: 2 to 9 days) for 16 cases exposed to sick or dead poultry only
- 7 days (range: 3.5 to 9 days) for 8 cases exposed to wet poultry markets only

Yang and others, reported above (8 cases of H5N1 influenza in Indonesia between 2005 and 2006), estimated the probable range of the incubation period to be between 3 and 7 days ([2](#)).

Case series and case reports

Seven case series and case reports were included that estimated the incubation period ([5 to 11](#)). Two case series also provided likely times between exposure and symptom onset for 3 cases of likely human-to-human transmission ([9](#), [10](#)). Study characteristics are presented in [Table C.1c](#).

Chakraborty and others reported on 2 cases with confirmed H5N1 or H5 influenza in Bangladesh in 2011 ([5](#)). A 13-month-old girl exposed to chicken had an incubation period of 7 days, and a 31-month-old boy exposed to poultry had an incubation period of 9 to 10 days.

Chotpitayasunondh and others reported on 8 cases with confirmed H5N1 that had direct contact with dead chickens (at least 6 cases were less than 14 years old) in Thailand in 2004 (6). The incubation period was estimated to be 4 days (range: 2 to 8 days).

Hien and others reported on 6 hospitalised cases with confirmed H5N1 influenza exposed to poultry (67% male, age range: 8 to 24 years) in Vietnam between 2003 and 2004 (7). The median incubation period was estimated to be 3 days (interquartile range: 2 to 4 days, range: 2 to 4 days).

Oner and others reported on 8 hospitalised cases with confirmed H5N1 influenza exposed to poultry (37.5% male, median age: 10 years, age range: 5 to 15 years) in Turkey between 2005 and 2006 (8). The mean incubation period was estimated to be 5 days (standard deviation: 1.3 days, range: 4 to 7 days).

Ungchusak and others reported on 3 hospitalised cases with confirmed H5N1 influenza in Thailand in 2004 (9). The first case was an 11-year-old girl who was exposed to dying chickens, who had an incubation period of 3 to 4 days. The second case was a 26-year-old woman, only exposed to the first case (and so there was likely human-to-human transmission 5 days after symptom onset in the first case), with an incubation period of 3 days. The third case was a 32-year-old woman, exposed to the first case (and so there was likely human-to-human transmission 5 days after symptom onset in the first case), with a likely incubation period of 7 to 9 days. The third case also had exposure to dying chickens 18 days before symptom onset, so there may have been zoonotic transmission with a long incubation period, but human-to-human transmission was considered more plausible.

Wang and others reported on 2 cases with confirmed H5N1 influenza in China in 2007 (10). The first case was a 24-year-old man exposed at a poultry market, with an incubation period of 6 days. The second case was a 52-year-old man, with suspected human-to-human transmission from multiple exposures to the first case (3 to 5 days after symptom onset in the first case), and a likely incubation period of 4 to 5 days (possible range: 3 to 6 days).

Zhang and others reported on a 5-year-old girl with confirmed H5N6 influenza exposed to poultry in China in 2014 (11). The incubation period was between 2 and 5 days (there were multiple exposures before symptom onset).

Summary

There was extremely limited evidence estimating the infectious period of influenza A (H5) cases. One study of 8 cases estimated the probable range of the infectious period to be between 5 and 13 days, and one study of 11 secondary cases estimated the median interval between illness onset of serial cases in infection clusters with inconclusive exposure to a zoonotic source of virus to be 8 days (range: 2 to 11 days). Additionally, in the case series

presenting evidence for human-to-human transmission, the 2 index cases likely infected the other 3 cases 3 to 5 days after their symptom onset.

There was also limited evidence estimating the incubation period of influenza A (H5) cases (a maximum of 89 cases if there was no overlap between studies). Most cases were exposed to poultry prior to symptom onset, although there was evidence of human-to-human transmission in some cases. Estimates of the incubation period varied between 2 and 10 days across studies. In the 2 retrospective cohort studies estimating the mean and median incubation periods, the mean was estimated as 3.3 days (3) and the median as 5 days (4).

Health inequalities

Many cases reported in the case series and case reports were children, although there was no substantial difference between the incubation periods of children compared with the retrospective cohort studies. Most studies included proportionately more adult cases, although the sample sizes of all studies were small. Almost all cases were exposed to H5 influenza from poultry, typically in domestic settings or from wet poultry markets, with some evidence of human-to-human transmission. This indicates potential inequalities associated with rurality and deprivation. No further conclusions about health inequalities could be made from the limited evidence.

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.

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 case reports or case series only and the limited amount of evidence due to both small number of studies and cases within those studies.

Evidence gaps

There was limited evidence estimating the incubation period of influenza A (H5), and almost all evidence came from Asia between 2003 and 2014, potentially limiting generalisability of the results to a contemporary UK population, as both the circulating H5N1 influenza virus and demographics of potential cases may be different in ways that could affect the infectious and incubation periods.

There was extremely limited evidence estimating the infectious period of influenza A (H5). For most included studies, there could be no estimates of the infectious period as almost all transmission was from poultry, not from other humans. In 3 studies with likely human-to-human transmission where the index cases were reported on separately ([2](#), [9](#), [10](#)), the index cases died shortly after symptom onset (6 to 10 days after symptom onset).

Conclusion

Overall, there was very limited evidence estimating the infectious period and limited evidence estimating the incubation period of influenza A (H5), with a maximum of 8 cases for the infectious period, 11 cases for the serial interval, and 89 cases for the incubation period. Most cases were exposed to poultry prior to symptom onset, although there was evidence of human-to-human transmission in several cases. Almost all cases were identified in Asia between 2003 and 2014, potentially limiting generalisability of the results to a contemporary UK population, as both the circulating H5N1 influenza virus and demographics of potential cases may be different in ways that could affect the infectious and incubation periods.

One study of 8 cases estimated the probable range of the infectious period to be between 5 and 13 days, and one study of 11 secondary cases estimated the median interval between illness onset of serial cases in infection clusters with inconclusive exposure to a zoonotic source of virus to be 8 days (range: 2 to 11 days). Additionally, in the case series presenting evidence for human-to-human transmission, the 2 index cases likely infected the other 3 cases 3 to 5 days after their symptom onset.

Estimates of the incubation period varied between 2 and 10 days across studies, although in the 2 retrospective cohort studies estimating the mean and median incubation periods, the mean was estimated as 3.3 days and the median as 5 days.

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 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:

- 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 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 by the recipient or any third party including that arising or resulting from any reliance placed on, or any conclusions drawn from, the review.

References

1. Aditama TY and others. '[Avian influenza H5N1 transmission in households, Indonesia](#)' PloS One 2012: volume 7, issue 1, article e29971
2. Yang Y and others. '[Detecting human-to-human transmission of avian influenza A \(H5N1\)](#)' Emerging Infectious Diseases 2007: volume 13, issue 9, pages 1,348 to 1,353
3. Cowling BJ and others. '[Comparative epidemiology of human infections with avian influenza A H7N9 and H5N1 viruses in China: a population-based study of laboratory-confirmed cases](#)' Lancet 2013: volume 382, issue 9887, pages 129 to 137
4. Huai Y and others. '[Incubation period for human cases of avian influenza A \(H5N1\) infection, China](#)' Emerging Infectious Diseases 2008: volume 14, issue 11, pages 1,819 to 1,821
5. Chakraborty A and others. '[Mild Respiratory Illness Among Young Children Caused by Highly Pathogenic Avian Influenza A \(H5N1\) Virus Infection in Dhaka, Bangladesh, 2011](#)' Journal of Infectious Diseases 2017: volume 216, pages S520 to S528
6. Chotpitayasunondh T and others. '[Human disease from influenza A \(H5N1\), Thailand, 2004](#)' Emerging Infectious Diseases 2005: volume 11, issue 2, pages 201 to 209
7. Hien TT and others. '[Avian Influenza A \(H5N1\) in 10 Patients in Vietnam](#)' New England Journal of Medicine 2004: volume 350, pages 1,179 to 1,188
8. Oner AF and others. '[Avian influenza A \(H5N1\) infection in eastern Turkey in 2006](#)'. New England Journal of Medicine 2006: volume 355, issue 21, pages 2,179 to 2,185
9. Ungchusak K and others. '[Probable person-to-person transmission of avian influenza A \(H5N1\)](#)' New England Journal of Medicine 2005: volume 352, issue 4, pages 333 to 340
10. Wang H and others. '[Probable limited person-to-person transmission of highly pathogenic avian influenza A \(H5N1\) virus in China](#)' Lancet 2008: volume 371, issue 9622, pages 1,427 to 1,434
11. Zhang R and others. '[Clinical, epidemiological and virological characteristics of the first detected human case of avian influenza A\(H5N6\) virus](#)' Infection, Genetics and Evolution 2016: volume 40, pages 236 to 242
12. Tricco AC and others. 'Rapid reviews to strengthen health policy and systems: a practical guide' World Health Organization 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 humans?

Only studies where participants in the study have the H5 sub-type of influenza A will be included.

This evidence summary will summarise evidence (search up to 26 April 2024) on the infectious and incubation periods of influenza A (H5).

For this review, the definitions used are:

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

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

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	All humans	All animals, non-humans species
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 • time to viral clearance • viral load over time 	
Language	English	
Date of publication	Up to 26 April 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 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 • guidelines • opinion pieces • modelling studies • laboratory studies • ecological studies
Publication type	Published and preprint	<ul style="list-style-type: none"> • 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 26 April 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, objective, outcomes measures, participants, study period, results and any relevant contextual data (such as timing or level of community 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 participants in each study, effect size and variance and a summary of the risk of bias 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.

Variations across populations and subgroups, for example cultural variations or differences between ethnic or social groups will be considered, where evidence is available.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 25 April 2024)

1. Influenza in Birds/ 8749
2. influenza a virus, h5n1 subtype/ 6722
3. influenza a virus, h5n2 subtype/ 469
4. influenza a virus, h5n6 subtype/ 3
5. influenza a virus, h5n8 subtype/ 300
6. exp Birds/ and (Influenza A virus/ or Influenza, Human/) 6365
7. "h5n*".kf,tw. 8565
8. ((flu or influenza) adj5 (H5 or bird or avian or chicken or duck or fowl)).kf,tw. 15185
9. (HPAIV or AIV).kf,tw. 3257
10. (H5* adj3 (bird or avian or chicken or duck or fowl)).kf,tw. 4889
11. or/1-10 20534
12. ((Transmis* or transmit* or infectious* or isolation or shed or case or isolation) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. 60875
13. ((PCR positiv* or Viral proliferat*) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. 489
14. cycl* threshold*.tw,kw,kf. 2907
15. CT value*.tw,kw,kf. 5540
16. (peak* adj1 (vir* load* or vir* concentrat*)).tw,kw,kf. 430
17. (Viral Load/ or exp Disease Transmission, Infectious/) and exp Time/ 9458
18. "serial interval".kf,tw. 451
19. chain of transmission.tw,kf. 409
20. ((clearance* or "viral load*" or (virus adj2 amount) or (virus adj2 level)) adj5 (duration* or time* or length* or period*)).tw,kw,kf. 10513
21. incubat*.tw,kf. 349000
22. Infectious Disease Incubation Period/ 409
23. Time Factors/ 1231778
24. (latent or latency).tw,kf. 197965
25. Latent Infection/ 212
26. (time adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. 66636
27. (period adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. 17032
28. (asymptom* adj5 (duration or period or length*)).tw,kf. 2211
29. (generation adj3 time).tw,kf. 5880
30. or/12-29 1887818
31. 11 and 30 1107

Embase (1974 to 24 April 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)"/ 11579
2. exp bird/ and (influenza/ or influenza a virus/) 2103

3. "h5n*".kf,tw. 9537
4. ((flu or influenza) adj5 (H5 or bird or avian or chicken or duck or fowl)).kf,tw. 16573
5. (HPAIV or AIV).kf,tw. 3578
6. (H5* adj3 (bird or avian or chicken or duck or fowl)).kf,tw. 5303
7. or/1-6 23143
8. ((Transmis* or transmit* or infectious* or isolation or shed or case or isolation) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. 82184
9. ((PCR positiv* or Viral proliferat*) adj5 (duration* or time* or length* or period* or peak*)).tw,kw,kf. 649
10. cycl* threshold*.tw,kw,kf. 3809
11. CT value*.tw,kw,kf. 8777
12. (peak* adj1 (vir* load* or vir* concentrat*)).tw,kw,kf. 678
13. (virus load/ or exp disease transmission/) and exp time/ 6631
14. "serial interval*".kf,tw. 501
15. chain of transmission.tw,kf. 507
16. ((clearance* or "viral load*" or (virus adj2 amount) or (virus adj2 level)) adj5 (duration* or time* or length* or period*)).tw,kw,kf. 15156
17. incubat*.tw,kf. 429496
18. incubation time/ or time factor/ or exp latent infection/ 119947
19. (latent or latency).tw,kf. 246347
20. (time adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. 108188
21. (period adj5 (asymptom* or symptom* or onset or clinical presentation)).tw,kf. 25374
22. (asymptom* adj5 (duration or period or length*)).tw,kf. 3190
23. (generation adj3 time).tw,kf. 6420
24. or/8-23 978945
25. 7 and 24 776

Global Health (1973 to Week 16 2024)

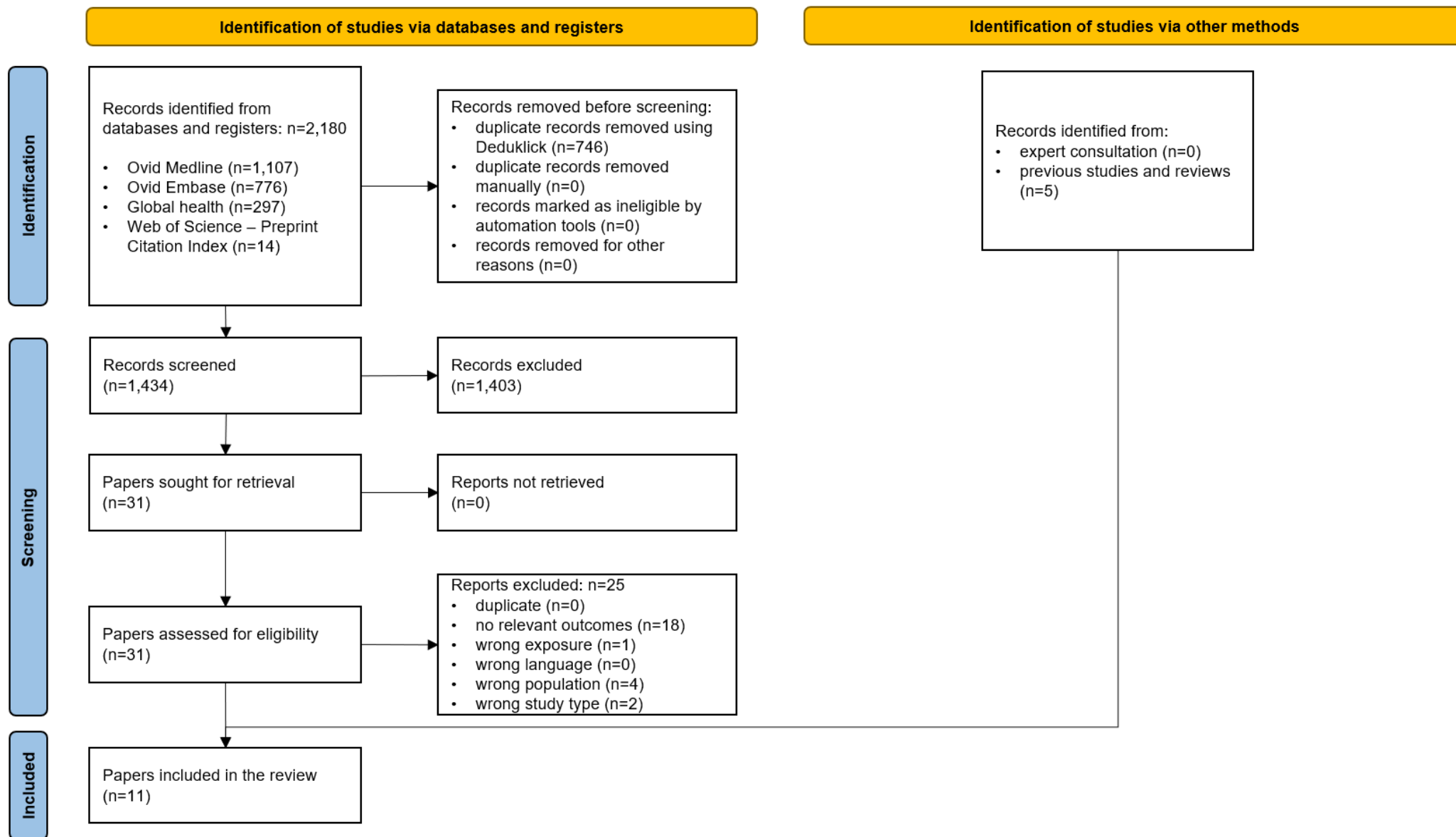
1. avian influenza a viruses/ or avian influenza viruses/ or avian influenza/ 6591
2. "h5n* ".ab,hw,ti. 4168
3. ((flu or influenza) adj5 (H5 or bird or avian or chicken or duck or fowl)).ab,hw,ti. 8431
4. (HPAIV or AIV).ab,hw,ti. 1027
5. (H5* adj3 (bird or avian or chicken or duck or fowl)).ab,hw,ti. 2453
6. (exp influenza a virus/ or influenza/) and exp birds/ 4511
7. or/1-6 9713
8. ((Transmis* or transmit* or infectious* or isolation or shed or case or isolation) adj5 (duration* or time* or length* or period* or peak*)).ab,hw,ti. 15296
9. ((PCR positiv* or Viral proliferat*) adj5 (duration* or time* or length* or period* or peak*)).ab,hw,ti. 345
10. (cycl* threshold* or CT Value*).ab,hw,ti. 3157
11. (peak* adj1 (vir* load* or vir* concentrat*)).ab,hw,ti. 209
12. (viral load/ or exp disease transmission/) and exp time/ 557
13. latent infections/ or incubation duration/ or time/ 8696

14. "serial interval*".ab,hw,ti. 280
15. chain of transmission.ab,hw,ti. 311
16. ((clearance* or "viral load*" or (virus adj2 amount) or (virus adj2 level)) adj5 (duration* or time* or length* or period*)).ab,hw,ti. 3514
17. incubat*.ab,hw,ti. 58247
18. (latent or latency).ab,hw,ti. 28896
19. ((time or period) adj5 (asymptom* or symptom* or onset or clinical presentation)).ab,hw,ti. 12439
20. (asymptom* adj5 (duration or period or length*)).ab,hw,ti. 461
21. (generation adj3 time).ab,hw,ti. 857
22. or/8-21 124166
23. 7 and 22 297

Web of Science Preprint Citation Index (search date: 26 April 2024)

1. TS=(H5N*) 105
2. TS=((flu or influenza) NEAR/5 (H5 or bird or avian or chicken or duck or fowl)) 187
3. TS=((HPAIV or AIV)) 62
4. TS=(H5 NEAR/3 (bird or avian or chicken or duck or fowl)) 9
5. #4 OR #3 OR #2 OR #1 230
6. TS=((Transmis* or transmit*) NEAR/4 (duration* or time* or length* or period* or peak*)) OR TS=((Infectious* NEAR/4 (duration* or time* or length* or period* or peak*)) OR TS=(Contagio* NEAR/4 (duration* or time* or length* or period* OR peak*)) OR TS=((Isolation NEAR/2 (duration* or time or length* or period*)) OR TS=((shed* NEAR/4 (duration* or time* or length* or period* or peak*)) OR TS=((case* NEAR/4 (duration* or time* or length* or period* or peak*)) OR TS=((Isolation* NEAR/4 (duration* or time* or length* or period* or peak*)) OR TS=((PCR positiv* NEAR/4 (duration* or time* or length* or period* or peak*)) OR TS=((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* concent*)) OR TS=(serial interval*) OR TS=(chain of transmission) OR TS=((clearance* NEAR/4 (duration* or time* or length* or period*)) OR TS=((viral load* NEAR/4 (duration* or time* or length* or period*)) OR TS=((virus load* NEAR/4 (duration* or time* or length* or period*)) OR TS=((virus NEAR/1 amount* NEAR/4 (duration* or time* or length* or period*)) OR TS=((virus NEAR/1 level* NEAR/4 (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)) 43441
7. #6 AND #5 14

Figure A.1. PRISMA diagram



Text version of Figure A.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=2,180 records identified from databases and registers:

- Ovid Medline (n=1,107)
- Ovid Embase (n=776)
- Global health (n=297)
- Web of Science – Preprint Citation Index (n=14)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=746)
- duplicate records removed manually (n=0)
- records marked as ineligible by automation tools (n=0)
- records removed for other reasons (n=0)

n=1,434 records screened, of which n=1,403 were excluded, leaving n=31 papers sought for retrieval, all of which were retrieved.

Of the n=31 papers assessed for eligibility, n=25 reports were excluded:

- duplicate (n=0)
- no relevant outcomes (n=18)
- wrong exposure (n=1)
- wrong language (n=0)
- wrong population (n=4)
- wrong study type (n=2)

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

- expert consultation (n=0)
- previous studies and reviews (n=5)

Overall, n=11 papers were included in the review.

Annexe B. Excluded full texts

No relevant outcomes (18 studies)

Adisasmito W and others. ['Effectiveness of antiviral treatment in human influenza A\(H5N1\) infections: analysis of a Global Patient Registry'](#) Journal of Infectious Diseases 2010: volume 202, issue 8, pages 1,154 to 1,160

Adisasmito W. ['Epidemiology of human avian influenza in Indonesia, 2005-2009: A descriptive analysis'](#) Medical Journal of Indonesia 2010: volume 19, pages 64 to 70

Adisasmito W and others. ['Human influenza A H5N1 in Indonesia: health care service-associated delays in treatment initiation'](#) BMC Public Health 2013: volume 13, page 571

Brooks WA and others. ['Avian influenza virus A \(H5N1\), detected through routine surveillance, in child, Bangladesh'](#) Emerging Infectious Diseases 2009: volume 15, issue 8, pages 1,311 to 1,313

Castillo A and others. ['The first case of human infection with H5N1 avian influenza A virus in Chile'](#) Journal of Travel Medicine 2023: volume 30, issue 5

Centers for Disease Control and Prevention. ['Isolation of avian influenza A\(H5N1\) viruses from humans--Hong Kong, May to December 1997'](#) Morbidity and Mortality Weekly Report 1997: volume 46, issue 50, pages 1,204 to 1,207

Dur and others. ['Timing of influenza A\(H5N1\) in poultry and humans and seasonal influenza activity worldwide, 2004 to 2013'](#) Emerging Infectious Diseases 2015: volume 21, issue 2, pages 202 to 208

Fiebig L and others. ['Avian influenza A\(H5N1\) in humans: new insights from a line list of World Health Organization confirmed cases, September 2006 to August 2010'](#) Euro Surveillance: Bulletin Européen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2011: volume 16, issue 32, page 11

Kandeel A and others. ['Zoonotic transmission of avian influenza virus \(H5N1\), Egypt, 2006 to 2009'](#) Emerging Infectious Diseases 2010: volume 16, issue 7, pages 1,101 to 1,107

Kandun IN and others. ['Factors associated with case fatality of human H5N1 virus infections in Indonesia: a case series'](#) Lancet 2008: volume 372, issue 9,640, pages 744 to 749

Kitphati R and others. ['Kinetics and longevity of antibody response to influenza A H5N1 virus infection in humans'](#) Clinical and Vaccine Immunology: CVI 2009: volume 16, issue 7, pages 978 to 981

Lu P and others. ['Radiological features of lung changes caused by avian influenza subtype A H5N1 virus: report of 2 severe adult cases with regular follow-up'](#) Chinese Medical Journal (Beijing) 2010: volume 123, issue 5, pages 100 to 104

Manabe T and others. ['Chronological, geographical, and seasonal trends of human cases of avian influenza A \(H5N1\) in Vietnam, 2003-2014: a spatial analysis'](#) BMC Infectious Diseases 2016: volume 16, page 64

World Health Organization (WHO). ['Epidemiology of WHO-confirmed human cases of avian influenza A\(H5N1\) infection'](#) Weekly Epidemiological Record 2006: volume 81, issue 26, pages 249 to 257

WHO. ['Update: WHO-confirmed human cases of avian influenza A\(H5N1\) infection, November 2003-May 2008'](#) Weekly Epidemiological Record 2008: volume 83, issue 46, pages 415 to 420

WHO. ['Summary of human infection with highly pathogenic avian influenza A \(H5N1\) virus reported to WHO, January 2003 to March 2009: cluster-associated cases'](#) Weekly Epidemiological Record 2010: volume 85, issue 3, pages 13 to 20

WHO. ['Update on human cases of highly pathogenic avian influenza A\(H5N1\) virus infection, 2011'](#) Weekly Epidemiological Record 2012: volume 87, issue 13, pages 117 to 123

Yuen KY and others. ['Clinical features and rapid viral diagnosis of human disease associated with avian influenza A H5N1 virus'](#) Lancet 1998: volume 351, issue 9,101, pages 467 to 471

Wrong exposure (one study)

Apisarnthanarak A and others. ['Influenza outbreak among health care workers in an avian influenza \(H5N1\)-endemic setting'](#) Clinical Infectious Diseases 2006: volume 43, issue 11, pages 1,493 to 1,494

Wrong population (4 studies)

Bett B and others. ['Transmission rate and reproductive number of the H5N1 highly pathogenic avian influenza virus during the December 2005 to July 2008 epidemic in Nigeria'](#) Transboundary and Emerging Diseases 2014: volume 61, issue 1, pages 60 to 68

Kim WH and others. ['Spatiotemporal dynamics of highly pathogenic avian influenza subtype H5N8 in poultry farms, South Korea'](#) Viruses 2021: volume 13, issue 2, page 10

Marquetoux N and others. ['Estimating spatial and temporal variations of the reproduction number for highly pathogenic avian influenza H5N1 epidemic in Thailand'](#) Preventive Veterinary Medicine 2012: volume 106, issue 2, pages 143 to 151

Oyana TJ and others. ['Spatiotemporal distributions of reported cases of the avian influenza H5N1 \(bird flu\) in Southern China in early 2004'](#) Avian Diseases 2006: volume 50, issue 4, pages 508 to 515

Wrong study type (2 studies)

Balkhy H and others. ['Avian influenza: Are our feathers ruffled?'](#) Annals of Saudi Medicine 2006: volume 26, pages 175 to 182

Beigel JH and others. ['Avian influenza A \(H5N1\) infection in humans'](#) New England Journal of Medicine 2005: volume 353, pages 1,374 to 1,385

Annexe C. Data extraction table

Table C1. Study characteristics of included studies

Acronyms: CI: confidence interval, IQR: interquartile range, SD: standard deviation

Table C1a. Study characteristics of retrospective cohort studies reporting on infectious period

Study	Country Time period	Study type	Population	Outcomes
Aditama (1)	Indonesia 2005 to 2009	Retrospective cohort	11 secondary cases in infection clusters with inconclusive exposure to a zoonotic source of virus (confirmed or probable H5N1 [index case was confirmed])	Median interval between illness onset of serial cases: 8 days (range: 2 to 11 days)
Yang (2)	Indonesia 2005 to 2006	Retrospective cohort	8 cases, one index case likely exposed to dead poultry, 7 secondary cases with likely human-to-human transmission (age range: 18 months to 37 years) (all confirmed H5N1, except the index case)	Infectious period probable range: 5 to 13 days

Table C1b. Study characteristics of retrospective cohort studies reporting on incubation period

Study	Country Time period	Study type	Population	Outcomes
Cowling (3)	China, 2003 to 2013	Retrospective cohort	27 cases with information about dates of recent exposure to live poultry (51% male, median age: 26 years, IQR: 19 to 35 years) (confirmed H5N1)	Mean incubation period: 3.3 days (95% CI: 2.7 to 3.9 days, SD: 1.5 days, 95th percentile: 6.0 days)

Study	Country Time period	Study type	Population	Outcomes
Huai (4)	China, Not stated	Retrospective cohort	24 cases exposed to sick or dead poultry, or to wet poultry market (H5N1)	Median incubation period: 5 days (range: 2 to 9.5 days)
			18 cases exposed to sick or dead poultry, or to wet poultry market, with exposure on multiple days (H5N1)	Median incubation period: 5 days (range: 2 to 9.5 days)
			6 cases exposed to sick or dead poultry, or to wet poultry market, with a single known exposure (H5N1)	Median incubation period: 5 days (range: 2 to 9 days)
			16 cases exposed to sick or dead poultry only (25% male, median age: 25 years, age range: 6 to 44 years) (H5N1)	Median incubation period: 4.3 days (range: 2 to 9 days)
			8 cases exposed to wet poultry market only (63% male, median age: 30 years, age range: 16 to 41 years) (H5N1)	Median incubation period: 7 days (range: 3.5 to 9 days)
Yang (2)	Indonesia, 2005 to 2006	Retrospective cohort	8 cases, one index case likely exposed to dead poultry, 7 secondary cases with likely human-to-human transmission (age range: 18 months to 37 years) (all confirmed H5N1, except the index case)	Incubation period probable range: 3 to 7 days

Table C1c. Study characteristics of case series and case reports

Study	Country, time period	Study type	Population	Outcomes
Chakraborty (5)	Bangladesh, 2011	Case series	Case A: 13 month old girl exposed to chickens (confirmed H5N1)	Incubation period: 7 days
			Case B: 31 month old boy exposed to poultry (confirmed H5)	Incubation period: 9 to 10 days
Chotpitayasunondh (6)	Thailand, 2004	Case series	8 cases that had direct contact with dead chickens (at least 6 cases were less than 14 years old) (confirmed H5N1)	Incubation period: 4 days (range: 2 to 8 days)
Hien (7)	Vietnam, 2003 to 2004	Case series	6 hospitalised cases, all exposed to poultry (67% male, age range: 8 to 24 years) (confirmed H5N1)	Median incubation period: 3 days (range and IQR: 2 to 4 days)
Oner (8)	Turkey, 2005 to 2006	Case series	8 hospitalised cases exposed to poultry (37.5% male, median age: 10 years, age range: 5 to 15 years) (confirmed H5N1)	Mean incubation period (time from last known exposure to sick or dead poultry to onset of illness): 5.0 days (SD: 1.3 days, range: 4 to 7 days)
Ungchusak (9)	Thailand, 2004	Case series	Case one: 11 year old hospitalised girl, exposed to dying chickens (confirmed H5N1)	Incubation period: 3 to 4 days
			Case 2: 26 year old hospitalised woman, suspected human-to-human transmission (confirmed H5N1)	Incubation period: 3 days

Study	Country, time period	Study type	Population	Outcomes
			Case 3: 32 year old hospitalised woman, suspected human-to-human transmission (confirmed H5N1)	Incubation period: likely 7 to 9 days, given case history
Wang (10)	China, 2007	Case series	Case one: 24 year old man, exposure at poultry market (confirmed H5N1)	Incubation period: 6 days
			Case 2: 52 year old man, suspected human-to-human transmission from case one after multiple exposures (confirmed H5N1)	The study reported most likely incubation period was 4 to 5 days (possible range: 3 to 6 days)
Zhang (11)	China, 2014	Case report	5 year old girl, exposed to poultry (confirmed H5N6)	Incubation period: 2 to 5 days

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