UK Health Security Agency

Zoonotic tuberculosis transmission between humans

A rapid systematic review

Contents

Main messages

1. This rapid systematic review (search up to 11 November 2024) identified and summarised evidence on the risk of transmission of *Mycobacterium (M.) bovis*, *M. orygis* and *M. caprae* between humans.

2. Three studies were included (1 to 3). Of these, one was a retrospective cohort study (1), one a prospective cohort study (2), and the third was a case-control study (3). Studies were conducted in Canada (1), India (2), and Spain (3).

3. One study retrospectively investigated TB transmission among people who had contact with someone with *M. bovis*, *M. orgyis* or *M. caprae*. This study reported that in 20 people with *M. bovis* who had 37 contacts, 21 people with *M. orygis* who had 119 contacts, and 1 person with *M. caprae* who had 4 contacts, no onward transmission of TB was identified (1).

4. One prospective cohort study found that farmers, dairy workers, and livestock keepers who reported having had previous contacts with a TB case, had higher odds of being infected with TB (odds ratio: OR 23.5; 95% confidence intervals: 3.0568 to 180.7912, p=0.0024). However, the study found that in zookeepers and veterinarians who reported having had previous contacts with TB cases, and people living in high prevalence TB areas who reported having had previous contacts with TB cases, neither group had higher odds of being infected with TB (2). This study did not separate the analysis by type of TB (*M. bovis* or *M. TB*).

5. A case-control study found that people who had previously stayed in a hospital and people who had shared the same ward as someone with *M. bovis* were themselves at greater risk of developing TB. In this study, all cases with *M. bovis* were also living with HIV and had an impaired immune function, which may have increased their risk of *M. bovis* transmission. Therefore, the findings may not be applicable to populations with normal immune function (3).

6. The certainty of evidence was very low across all studies due to risk or bias and imprecision. Risk of bias concerns included lack of reporting of demographic information and limited and unclear reporting of the method for measuring how people came into contact with a person with TB. Studies also had small sample sizes and few people with TB which resulted in imprecision in the results. Some studies did not consider other factors that could have influenced the results (confounding variables) or did not clearly report which factors they had considered. One study did not separate their analysis by TB type, and therefore it was not possible to ascertain if the TB transmitted was *M. bovis* or *M. TB*. The certainty of evidence from one study could not be assessed using Grading of Recommendations, Assessment, Development and Evaluations (GRADE) (4) but had similar issues with bias, small sample sizes, and low precision.

7. In conclusion, the available evidence was very limited and is rated as very low certainty evidence, meaning that it is not possible to determine from this evidence what the risk of transmission of *M. bovis*, *M. orygis*, *M. microti* and *M. caprae* between humans is.

Purpose

The purpose of this rapid systematic review was to identify and summarise the available evidence that discussed the risk of transmission of *Mycobacterium (M.) bovis*, *M. orygis*, *M. microti* and *M. caprae* between humans.

The review question was:

1. What is the risk of transmission of *Mycobacterium (M.) bovis*, *M. orygis*, *M. microti* and *M. caprae* between humans?

Methods

A rapid systematic review was conducted, following streamlined systematic methods to accelerate the review process. A literature search was undertaken to look for relevant observational studies, published or available as preprint, up to 11 November 2024. Backwards and forwards citation searching of primary studies included during full text screening was also conducted.

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.

Studies investigating zoonotic TB species (*Mycobacterium (M.) bovis*, *M. orygis*, *M. microti* and *M. caprae*) transmission between humans, regardless of context, were included. The following transmission routes were considered:

- oral (such as from ingesting contaminated food or drink)
- respiratory (inhalation of airborne bacterial particle droplets)
- direct contact (physical touch or touching contaminated surfaces)

The specific tuberculosis species (*M. bovis*, *M. caprae*, *M. microti*, *M. orygis*) included in this review were agreed by subject matter experts within the UKHSA ‘Tuberculosis, Acute Respiratory Infections, Zoonoses, Emerging Infections and Travel Health’ (TARZET) Division, as those with greatest potential for transmission between humans after transmission of TB from an animal. Other members of the *M. TB* complex were not included as they are particularly rare or have not been reported in the UK to date.

Screening of title and abstracts was undertaken in duplicate by 3 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening of full texts was undertaken by one reviewer and checked by a second. Data extraction was performed by one reviewer and checked by a second.

The certainty of evidence identified within this review was assessed by outcome where appropriate, using a modified version of the GRADE approach (4). This process is described in detail in Annexe A. In brief, the certainty of evidence at the outcome level was assessed across 4 domains:

1. Risk of bias: where results may not represent the true effect because of limitations in the design or conduct of the study (assessed using the JBI checklists) (5)
2. Inconsistency: where studies show different effects for the same outcome.
3. Indirectness: where elements of the study differ from the review question.
4. Imprecision: a measure of how uncertain the result is.

Outcomes were given one of 4 ratings for certainty of evidence:

- very low (the true effect is probably different from the estimated effect)
- low (the true effect might be different from the estimated effect)
- moderate (the true effect is probably close to the estimated effect)
- high (the authors are confident that the true effect is similar to the estimated effect)

Evidence

In total, 5,055 studies were screened at title and abstract and 114 studies were screened at full text. Of these, 3 studies met the inclusion criteria. No additional studies were identified from citation searching. A PRISMA diagram showing the flow of studies through the review is shown in Annexe B, and studies excluded on full text screening are available with the reasons why in Annexe C. Study characteristics are available in Annexe D, and risk of bias assessments are available in Annexe E.

The evidence included one retrospective cohort study (1), one prospective cohort study (2), and one case-control study (3). Details of the methods studies used to diagnose TB can be found in Annexe D.

Prospective cohort study

Bapat and others conducted a prospective cohort study from March 2014 to June 2015 in India (2). Additional details of this study are presented in Annexe D. The study calculated the odds of having TB (*M. bovis* or *M. TB*) in 3 groups who reported previous contact with a person with TB (type unspecified). These groups were:

- 105 farmers, dairy workers, livestock keepers (12 with *M. bovis* and 13 with *M. TB*)
- 45 zookeepers and veterinarians (4 *M. bovis* and 7 *M. TB*)
- 151 people who lived in an area with a high rate of TB (19 *M. bovis* and 41 *M. TB*)

This study found that farmers, dairy workers, livestock keepers were the only group of people to have higher odds of having TB due to contact with someone with TB with an odds ratio of 23.5 (95% confidence intervals |CI|: 3.0568 to 180.7912, p=0.0024).

However, the certainty of evidence for this outcome was rated as very low. This was due to serious risks of bias, such as not all participants being free of TB at the start of the study making it difficult to determine if transmission occurred from contact with other people infected with TB or from other sources which occurred prior to the study. The study did not separate the analysis by type of TB (*M. bovis* or *M. TB*). There was also no discussion of whether participants dropped out of the study, and the study did not consider other factors that could have had an impacted transmission. The findings were imprecise for all groups as shown by wide confidence intervals indicating these results were likely unreliable. This uncertainty may have been due to small numbers of people in each group, and because all the studies used self-reporting to measure previous contact with someone with TB, which relied on people's memory and may have been inaccurate. The small number of participants in each group also means this may not accurately represent the odds of TB in a wider population, limiting the generalisability of these findings.

Retrospective cohort study

Riopel and others conducted a retrospective study of the prevalence of secondary cases of TB in contacts of people with *M. bovis*, *M. orgyis* and *M. caprae* in Canada, between January 1995 and 2021 (1). There were 37 contacts of 20 people with *M. bovis*, 119 contacts of 21 people with *M. orygis*, and 4 contacts of one person with *M. caprae*. Additional details of this study are presented in Annexe D.

This study did not identify any secondary cases of TB in any contacts of people with *M. bovis*, *M. orygis* or *M. caprae*.

Case-control study

Guerrero and others conducted a case-control study which included 19 people with *M. bovis* (cases) and 33 randomly selected controls during an outbreak of drug-resistant TB in a hospital in Spain in 1997 (3). All participants were people living with HIV who had impaired immune function. Additional details of this study are presented in Annexe D.

The study reported evidence suggesting transmission occurred within people who had previously stayed in any hospital and between people who had shared the same ward as an index case infected with *M. bovis*. The study reported the odds of being infected with *M. bovis* in

people who reported having previously stayed in a hospital with an outbreak were 47.6 (95% CI: 6.8 to 440.9). Similarly, the odds of being infected with *M. bovis* in patients who shared the same ward as an index case were 82.7 (95% CI: 9.9 to 1008.1). The certainty of evidence was rated as very low using GRADE(4) due to high risk of bias and uncertainty in the results.

Risk of bias was difficult to assess in this study because the reporting of the methodology was mostly unclear and therefore it was not possible to know what biases might have had an impact of the results. However, the unclear reporting of the study methodology raised doubts and indicated that the results may be at high risk of bias and findings may be unreliable. This study only included a small number of people which likely resulted in the uncertainty in the findings.

Furthermore, as all participants of this study were living with HIV and had low immune function which could increase risk of transmission, the findings of this study may not be generalisable to populations with normal immune function. While the study stated that they had considered factors that could have had an impact on the results in their analyses, the authors did not specify which factors were controlled for. However, it is possible this study had adjusted for HIV status and therefore may have accounted for the influence of HIV on the risk of TB transmission.

Health inequalities

Studies did not routinely report sufficient demographic details necessary to assess health inequalities in groups at increased risk of infection or transmission of zoonotic TB.

One study reported that all participants were people living with HIV who had impaired immune function, which may have increased the risk of transmission of *M. bovis* between people, but no comparison was made to people not living with HIV (3). Another study reported that some participants had HIV, but the HIV status of other participants was not reported, and the study did not compare transmission in people living with HIV compared to people not living with HIV (1). It's therefore not possible from this evidence to determine whether people living with HIV were at increased risk.

The studies in this review did not report outcomes for other groups at risk of health inequalities (such as people experiencing homelessness), or for groups specified in the protocol of this review

There was evidence to suggest that people living in rural areas such as farmers and livestock keepers who had come into contact someone with TB may themselves be at a higher risk of *M. bovis*. This increased risk may be due to factors such as deprivation, poorer housing. conditions and limited access to healthcare that may mean these groups are at greater risk of TB than groups such as zookeepers or veterinarians. But as limited evidence was identified overall, this does not mean that health inequalities do not exist in these groups or other unspecified population groups.

Limitations

This rapid systematic review used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted and most article screening was completed without duplication, so it is possible relevant evidence may have been missed.

The methodology of the studies was not always clear which made it difficult to assess risk of bias. However, studies either relied on self-reporting to measure the exposure or it did not clearly describe how the authors of the study assessed whether contacts had TB or not. This made it difficult to accurately assess the true risk of transmission between people because it was unclear whether TB infection occurred before or after the study had started. Moreover, studies generally had small sample sizes which resulted in low precision in the results and limited the extent to which the findings could be generalised.

One study only included people who were living with HIV and had impaired immune function. As these people may be more likely to be infected with and/or transmit TB, the findings of this study may not be generalisable to people with normal immune function.

The evidence identified on the risk of transmission of *M. bovis*, *M. orygis* and *M. caprae* between humans was very limited with only 3 studies identified by this review. No evidence was identified on the risk of transmission of *M. microti* between humans.

Conclusion

In conclusion, very limited evidence was identified on the transmission of *M. bovis*, *M. orygis* and *M. caprae* between humans.

One study reported an increased risk of being infected with TB in farmers, dairy workers and livestock keepers who had a previous contact with a person with TB, but the analysis did not separate by type of TB (*M. bovis* or *M. TB*) (2). Another reported an increased risk of *M. bovis* in people who had shared the same hospital ward with a person infected with *M. bovis*, and in those who had previously stayed in any hospital (3). However, a third study reported that no secondary cases were detected in people who came into contact with other people who had been diagnosed with *M. bovis*, *M. orygis* or *M. caprae* (1).

The certainty of the evidence from all of the studies was assessed as very low due to risk of bias and imprecision in the results. The study sample sizes were generally small which contributed to the imprecision in the results and means it is not possible from this evidence to draw meaningful conclusions about human-to-human transmission of zoonotic TB that would be generalisable to be a larger group. Therefore, the evidence identified in this review did not

enable us to determine the risk of transmission of *M. bovis*, *M. orygis*, *M. microti* and M. *caprae* between humans.

Acknowledgments

We would like to thank colleagues within the All Hazards Public Health Response Division who either reviewed or input into aspects of the review.

Disclaimer

UKHSA's rapid systematic 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:

- 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. Riopel ND and others. 'Characterization of Mycobacterium orygis, Mycobacterium bovis, and Mycobacterium caprae Infections in Humans in Western Canada' Journal of Infectious Diseases 2024: volume 230, issue 4, pages e789 to e797
2. Bapat PR and others. 'Prevalence of zoonotic tuberculosis and associated risk factors in Central Indian populations' Journal of Epidemiology and Global Health 2017: volume 7, issue 4, pages 277 to 283
3. Guerrero A and others. 'Nosocomial transmission of Mycobacterium bovis resistant to 11 drugs in people with advanced HIV-1 infection' Lancet 1997: volume 350, issue 9093, pages 1,738 to 1,742
4. TGW G. 'GRADE handbook for grading quality of evidence and strength of recommendations' 2013
5. JBI. 'JBI Critical appraisal tools' 2020

Annexe A. Protocol

Review question

The review question is:

1. What is the risk of transmission of *Mycobacterium (M.) bovis*, *M. orygis*, *M. microti* and *M. caprae* between humans?

A search for primary evidence to answer these questions will be conducted up to 11 November 2024.

Eligibility criteria

Table A.1. Inclusion and exclusion criteria

	Included	Excluded
Population	Humans	Non-human animal species
Context	Any context in which humans are in contact with other people infected the below specified zoonotic TB strains.	
Settings	Any	
Intervention or exposure	Exposure to humans infected with active *M. bovis*, *M. orygis*, *M. microti* or *M. caprae*. Routes of transmission include: • oral (such as from ingesting contaminated food or drink) • respiratory (inhalation of airborne bacterial particle droplets) • direct contact (physical touch or touching contaminated surfaces |fomites|)	Exposure to other infected non-human animal species
Comparator	No comparator required	
Outcomes	Risk of transmission between humans of *M. bovis*, *M. orygis*, *M. microti* or *M. caprae*, such as: • incidence • risk ratios (relative risk) • hazard ratios	Human to animal transmission risk Animal to human transmission risk

	Included	Excluded
	• odds ratios	
Language	English	Any other language
Date of search	Up to 11 November 2024	
Study design	Observational studies including cross-sectional, case-control and cohort studies	Experimental studies including randomised-controlled trials, quasi-experimental studies, cross-over designs, before-and-after studies Reviews (all types) Case reports, case series Qualitative research Mixed methods Modelling studies
Publication type	Peer-reviewed published research Preprints	Conference abstracts Editorials Letters News articles Other grey literature

Background

The bacterial strains included in this review are members of the mycobacterium tuberculosis complex. These are mycobacteria related to *M. TB* that cause a tuberculosis-like illness in humans and animals.

The specific tuberculosis strains included in this review were selected by experts within the UKHSA 'Tuberculosis, Acute Respiratory Infections, Zoonoses, Emerging Infections and Travel Health' (TARZET) Division, as those with greater potential for transmission from animals to humans. This review aims to explore the potential for further onward transmission between humans. *M. TB* was excluded from this review as risk of human to human transmission in this strain is already well established. Other members of the *M. TB* complex were not included as they are particularly rare or have not been reported in the UK to date.

Identification of studies

The following databases will be searched for studies published up to 29 October 2024: Ovid Medline, Ovid Embase, Scopus and Web of Science Preprint Citation Index. The search strategy is presented below.

Backwards and forwards citation searching of primary studies included during full text screening will be carried out by searching Lens.org via CitationChaser. References that are included following full text screening will be used as seed references.

Screening

Title and abstract screening will be undertaken in duplicate by 2 reviewers for at least 20% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion or with involvement of a third reviewer where necessary.

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

References retrieved through citation searching will be cross checked against the results of the database search, and duplicates will be removed. The remaining references will be screened by one reviewer.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information to be extracted will include country, study period, study design, exposure, participants, results, and any relevant contextual data. This will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

Two reviewers will independently complete a risk of bias assessment for included studies, with disagreements resolved by discussion or with a third reviewer. Primary studies will be assessed using the JBI critical appraisal checklists (5).

Certainty of evidence

If appropriate, the certainty of evidence identified within this review will be assessed using a modified version of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework (4).

Certainty of evidence will be assessed at the outcome level, and be rated as one of 4 levels:

- very low (the true effect is probably different from the estimated effect)
- low (the true effect might be different from the estimated effect)
- moderate (the true effect is probably close to the estimated effect)
- high (the authors are confident that the true effect is similar to the estimated effect)

The certainty of evidence will be assessed by one reviewer (and checked by a second) for each outcome across 4 domains:

1. Risk of bias: where results may not represent the true effect because of limitations in the design or conduct of the study.
2. Inconsistency: where studies show different effects for the same outcome of interest (only assessed where there are 2 or more studies measuring the same outcome). Inconsistency will be rated down if the point estimates are not similar, or the confidence intervals do not overlap.
3. Indirectness: where elements of the study differ from the intended elements in the review question (for example, the outcome of interest has not been directly measured). This will be rated down if the population, intervention, comparator, or outcome of interest have not been directly measured.
4. Imprecision: a measure of how uncertain the estimate is. Imprecision will be rated down if the confidence intervals cross the line of no effect, or if the reviewer judges that the confidence intervals are overly wide and so the true effect is likely to be different at the upper versus the lower end of the confidence interval.

Publication bias will not be used to assess the quality of the evidence in this review.

Evidence may be downgraded one or two levels following the assessment of quality or upgraded if there is a large magnitude of effect or clear dose-response gradient.

Synthesis

Where studies are similar enough to combine and 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 reporting each outcome will be summarised and presented. The evidence will be presented for each route of transmission separately (oral, respiratory, and direct contact).

Alternatively, if studies present methodological differences that would make synthesis inappropriate, a narrative summary of each study will be provided.

Health inequalities

Variations across the following populations and subgroups will be considered, where evidence is available, as these groups may be more likely to be infected with and/or to transmit TB such as immunocompromised individuals, people experiencing homelessness, and people who live in rural areas.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 12 November 2024)

1. Mycobacterium bovis/ (14,169)
2. Tuberculosis, Bovine/ (3,879)
3. (Tuberculosis/ or Latent Tuberculosis/) and exp Ruminants/ (1,784)
4. calmette-guerin bacillus.tw,kf. (121)
5. mycobacterium bovis.tw,kf. (8,203)
6. M Bovis.tw,kf. (5,386)
7. "M.Bovis".tw,kf. (80)
8. ((Bovine or cow or cattle) adj3 (TB or tuberculo*)).tw,kf. (4,130)
9. Mycobacterium orygis.tw,kf. (34)
10. M orygis.tw,kf. (28)
11. "M.orygis".tw,kf. (0)
12. Mycobacterium microti.tw,kf. (168)
13. M microti.tw,kf. (172)
14. "M.microti".tw,kf. (2)
15. Mycobacterium tuberculosis variation muris.tw,kf. (0)
16. vole bacillus.tw,kf. (61)
17. Mycobacterium caprae.tw,kf. (132)
18. M caprae.tw,kf. (145)
19. "M.caprae".tw,kf. (4)
20. Mycobacterium bovis subsp* caprae.tw,kf. (8)
21. Mycobacterium tuberculosis subsp* caprae.tw,kf. (3)
22. or/1-21 (22,178)
23. transmi*.tw,kf. (684,971)
24. exp Disease Transmission, Infectious/ (83,708)
25. ((Communit* or disease* or infection* or population* or human* or people* or group*) adj3 spread*).tw,kf. (39,042)
26. ((Communit* or disease* or infection* or population* or human* or people* or group*) adj3 contagio*).tw,kf. (6,901)
27. transmission.fs. (162,891)
28. inter-human.tw,kf. (143)
29. human-human.tw,kf. (726)
30. between human*.tw,kf. (22,959)
31. "human to human".tw,kf. (7,176)
32. inter-person*.tw,kf. (819)
33. person-person.tw,kf. (63)
34. (between adj2 (person* or people or population*)).tw,kf. (51,913)
35. "person to person".tw,kf. (4,462)
36. (within adj2 population*).tw,kf. (30,854)
37. ((human* or person* or people*) adj2 outbreak*).tw,kf. (2,622)
38. ((human* or person* or people*) adj2 disease*).tw,kf. (107,635)

39. ((human* or person* or people*) adj2 infect*).tw,kf. (92,875)
40. ((human* or person* or people*) adj2 illness*).tw,kf. (4,759)
41. recrudescen*.tw,kf. (3,904)
42. reactivat*.tw,kf. (52,101)
43. (reinfect* or re-infect*).tw,kf. (16,092)
44. Recurrence/ or Reinfection/ (205,275)
45. human*.ti. (1,202,029)
46. ((Community or disease* or infection*) adj3 spread*).tw,kf. (32,772)
47. (inhalation or inhale* or inhaling).tw,kf. (121,456)
48. aerosol*.tw,kf. (60,289)
49. ((air flow* or airflow* or aerodynamic* or air condition* or cough* or sneez* or breath* or sing or singing or shout* or (air adj2 circulat*) or (air adj2 recirculation) or (air adj2 re-circulation)) and (transmission* or transmit* or distanc* or dispers*)).tw,kf. (12,138)
50. ((ventilation or ventilated) and (transmission* or distanc* or dispers*)).tw,kf. (5,126)
51. ((route or routes or mode or modes) adj2 (transmission* or transmit*)).tw,kf. (16,579)
52. (far field and (exposure* or transmission* or transmit*)).tw,kf. (827)
53. (long* distance* adj2 (transmission* or transmit*)).tw,kf. (422)
54. bioaerosol*.tw,kf. (2,469)
55. droplet*.tw,kf. (69,721)
56. exp *Body Fluids/ (175,714)
57. body fluid*.tw,kf. (28,691)
58. (infect* adj (hide* or tissue*)).tw,kf. (5,754)
59. (exhalation or exhale* or exhaling).tw,kf. (17,984)
60. Inhalation Exposure/ (10,621)
61. Inhalation/ (5,973)
62. Exhalation/ (5,158)
63. Aerosols/ (35,724)
64. direct contact*.tw,kf. (18,669)
65. Skin Absorption/ (13,104)
66. ((cutaneous or skin or dermal*) adj1 contact*).tw,kf. (4,428)
67. ((cutaneous or skin or dermal*) adj3 absorb*).tw,kf. (1,040)
68. Fomites/ (669)
69. fomite*.tw,kf. (1,590)
70. indirect transmission.tw,kf. (460)
71. (contaminat* adj3 (surface* or environment* or touch*)).tw,kf. (21,547)
72. transmission.fs. (162,891)
73. or/23-72 (2,934,219)
74. 22 and 73 (3,988)
75. limit 74 to (comment or editorial or letter or news) (251)
76. 74 not 75 (3,737)

Embase (1974 to 12 November 2024)

1. exp Mycobacterium bovis/ (14,004)
2. bovine tuberculosis/ (2,832)
3. (tuberculosis/ or latent tuberculosis/) and exp ruminant/ (800)
4. calmette-guerin bacillus.tw,kf. (122)
5. mycobacterium bovis.tw,kf. (8,674)
6. M Bovis.tw,kf. (5,804)
7. "M.Bovis".tw,kf. (121)
8. ((Bovine or cow or cattle) adj3 (TB or tuberculo*)).tw,kf. (3,645)
9. Mycobacterium orygis.tw,kf. (30)
10. M orygis.tw,kf. (27)
11. "M.orygis".tw,kf. (0)
12. mycobacterium microti/ (263)
13. Mycobacterium microti.tw,kf. (172)
14. M microti.tw,kf. (181)
15. "M.microti".tw,kf. (4)
16. Mycobacterium tuberculosis variation muris.tw,kf. (0)
17. vole bacillus.tw,kf. (10)
18. mycobacterium caprae/ (187)
19. Mycobacterium caprae.tw,kf. (134)
20. M caprae.tw,kf. (139)
21. "M.caprae".tw,kf. (5)
22. Mycobacterium bovis subsp* caprae.tw,kf. (9)
23. Mycobacterium tuberculosis subsp* caprae.tw,kf. (3)
24. or/1-23 (20,325)
25. transmi*.tw,kf. (773,614)
26. exp disease transmission/ (258,631)
27. ((Communit* or disease* or infection* or population* or human* or people* or group*) adj3 spread*).tw,kf. (44,993)
28. ((Communit* or disease* or infection* or population* or human* or people* or group*) adj3 contagio*).tw,kf. (7,850)
29. transmission.fs. (0)
30. inter-human.tw,kf. (189)
31. human-human.tw,kf. (786)
32. between human*.tw,kf. (26,831)
33. "human to human".tw,kf. (8,620)
34. inter-person*.tw,kf. (1,122)
35. person-person.tw,kf. (94)
36. (between adj2 (person* or people or population*)).tw,kf. (62,839)
37. "person to person".tw,kf. (5,494)
38. (within adj2 population*).tw,kf. (37,425)
39. ((human* or person* or people*) adj2 outbreak*).tw,kf. (2,817)
40. ((human* or person* or people*) adj2 disease*).tw,kf. (131,139)

41. ((human* or person* or people*) adj2 infect*).tw,kf. (109,632)
42. ((human* or person* or people*) adj2 illness*).tw,kf. (5,774)
43. recrudescen*.tw,kf. (4,879)
44. reactivat*.tw,kf. (72,656)
45. (reinfect* or re-infect*).tw,kf. (20,148)
46. recurrent disease/ or reinfection/ (245,244)
47. human*.ti. (1342,265)
48. ((Community or disease* or infection*) adj3 spread*).tw,kf. (37,799)
49. (inhalation or inhale* or inhaling).tw,kf. (170,388)
50. aerosol*.tw,kf. (80,877)
51. ((air flow* or airflow* or aerodynamic* or air condition* or cough* or sneez* or breath* or sing or singing or shout* or (air adj2 circulat*) or (air adj2 recirculation) or (air adj2 re-circulation)) and (transmission* or transmit* or distanc* or dispers*)).tw,kf. (17,601)
52. ((ventilation or ventilated) and (transmission* or distanc* or dispers*)).tw,kf. (7,188)
53. ((route or routes or mode or modes) adj2 (transmission* or transmit*)).tw,kf. (19,486)
54. (far field and (exposure* or transmission* or transmit*)).tw,kf. (694)
55. (long* distance* adj2 (transmission* or transmit*)).tw,kf. (396)
56. bioaerosol*.tw,kf. (3,427)
57. droplet*.tw,kf. (79,557)
58. exp *body fluid/ (919,386)
59. body fluid*.tw,kf. (31,816)
60. (infect* adj (hide* or tissue*)).tw,kf. (6,314)
61. (exhalation or exhale* or exhaling).tw,kf. (27,087)
62. inhalational exposure/ (314)
63. inhalation/ (30,955)
64. exhalation/ (6,339)
65. aerosol/ (67,842)
66. direct contact*.tw,kf. (22,678)
67. skin absorption/ (8,463)
68. ((cutaneous or skin or dermal*) adj1 contact*).tw,kf. (5,643)
69. ((cutaneous or skin or dermal*) adj3 absorb*).tw,kf. (1,442)
70. fomite/ (906)
71. fomite transmission/ (129)
72. fomite*.tw,kf. (1,820)
73. indirect transmission.tw,kf. (478)
74. (contaminat* adj3 (surface* or environment* or touch*)).tw,kf. (24,809)
75. or/25-74 (3,975,704)
76. 24 and 75 (5,148)
77. limit 76 to (conference abstract or conference paper or editorial or letter) (719)
78. 76 not 77 (4,429)

Web of Science Preprint Citation Index (1990 to the present)

Date of search: 12 November 2024

TS=("calmette-guerin bacillus") OR TS=("mycobacterium bovis") OR TS=("M Bovis") OR TS=("M.Bovis") OR TS=(((Bovine or cow or cattle) NEAR/2 (TB or tuberculo*))) OR TS=("Mycobacterium orygis") OR TS=("M orygis") OR TS=("M.orygis") OR TS=("Mycobacterium microti") OR TS=("M microti") OR TS=("M.microti") OR TS=("Mycobacterium tuberculosis variation muris") OR TS=("vole bacillus") OR TS=("Mycobacterium caprae") OR TS=("M caprae") OR TS=("M.caprae") OR TS=("Mycobacterium bovis subsp* caprae") OR TS=("Mycobacterium tuberculosis subsp* caprae")

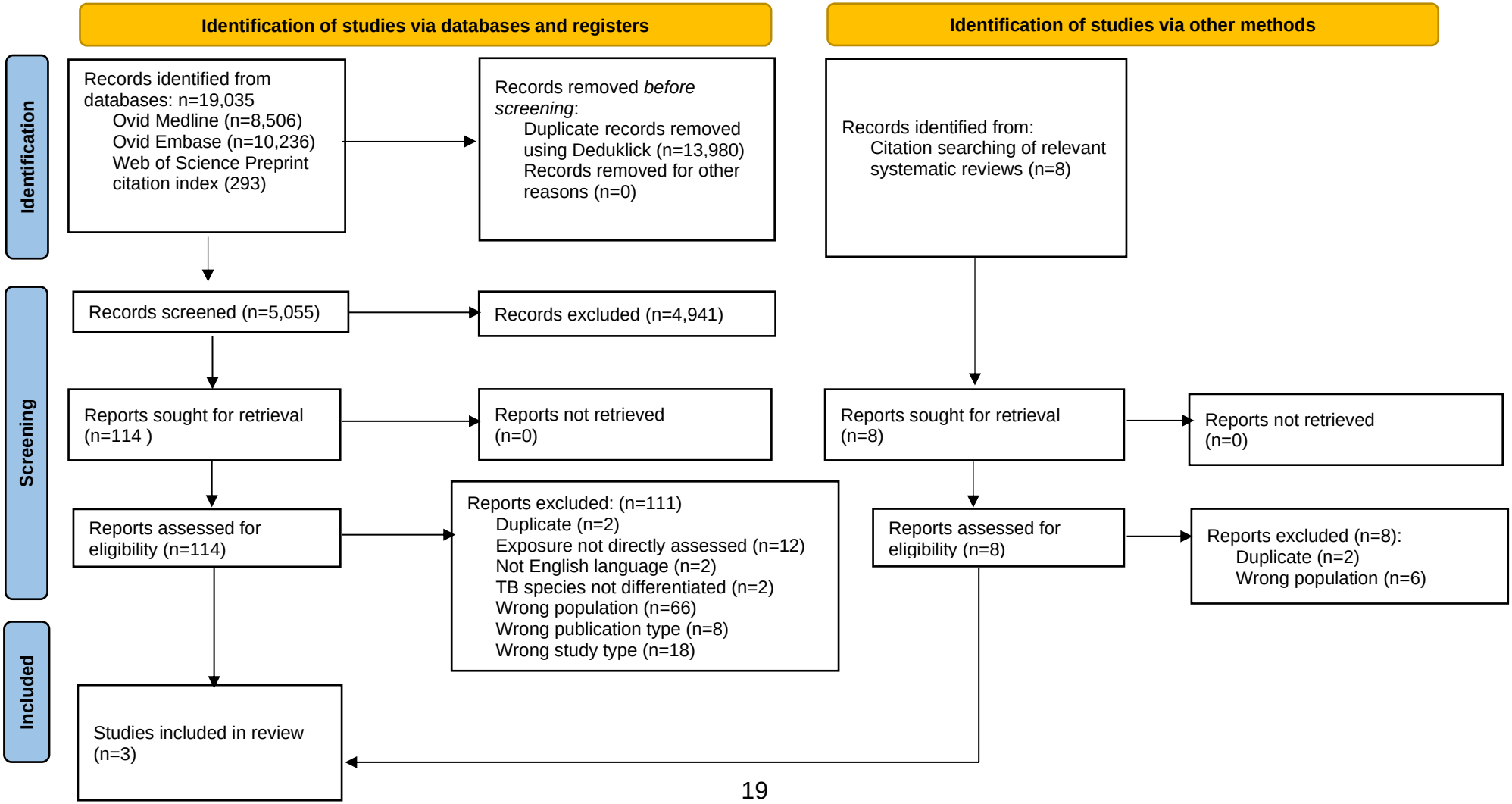
AND

TS=(transmi*) OR TS=(((Communit* or disease* or infection* or population* or human* or people* or group*) NEAR/2 spread*)) OR TS=(((Communit* or disease* or infection* or population* or human* or people* or group*) NEAR/2 contagio*))
OR TS=(inter-human) OR TS=(human-human) OR TS=("between human*") OR TS=("human to human") OR TS=(inter-person*) OR TS=(person-person) OR TS=((between NEAR/1 (person* or people or population*))) OR TS=("person to person") OR TS=((within NEAR/1 population*)) OR TS=(((human* or person* or people*) NEAR/1 outbreak*)) OR TS=(((human* or person* or people*) NEAR/1 disease*)) OR TS=(((human* or person* or people*) NEAR/1 infect*)) OR TS=(((human* or person* or people*) NEAR/1 illness*)) OR TS=(recrudescen*) OR TS=(reactivat*) OR TS=((reinfect* or re-infect*)) OR TI=(human*) OR TS=(((Community or disease* or infection*) NEAR/2 spread*)) OR TS=((inhalation or inhale* or inhaling)) OR TS=(aerosol*) OR TS=((("air flow*" or airflow* or aerodynamic* or "air condition*" or cough* or sneez* or breath* or sing or singing or shout* or (air NEAR/1 circulat*) or (air NEAR/1 recirculation) or (air NEAR/1 re-circulation)) and (transmission* or transmit* or distanc* or dispers*))) OR TS=(((ventilation or ventilated) and (transmission* or distanc* or dispers*))) OR TS=(((route or routes or mode or modes) NEAR/1 (transmission* or transmit*))) OR TS=(("far field" and (exposure* or transmission* or transmit*))) OR TS=(("long* distance*" NEAR/1 (transmission* or transmit*))) OR TS=(bioaerosol*) OR TS=(droplet*) OR TS=("body fluid*") OR TS=((infect* NEAR/0 (hide* or tissue*))) OR TS=((exhalation or exhale* or exhaling)) OR TS=("direct contact*") OR TS=(((cutaneous or skin or dermal*) NEAR/0 contact*)) OR TS=(((cutaneous or skin or dermal*) NEAR/2 absorb*)) OR TS=(fomite*) OR TS=("indirect transmission") OR TS=((contaminat* NEAR/2 (surface* or environment* or touch*)))

37 results.

Annexe B. Study selection flowchart

Figure B.1. PRISMA diagram



Text version of Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 3 studies.

From identification of studies via databases and registers, 19,035 records identified from databases:

- Ovid Medline (n=8,506)
- Ovid Embase (n=10,236)
- Web of Science Preprint citation index (n=293)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=13,980)
- records removed for other reasons (n=0)

5,055 records screened, of which 4,941 were excluded, leaving 114 papers sought for retrieval, of which 0 were not retrieved.

8 studies were identified from citation searching of relevant systematic reviews.

Of the 122 papers assessed for eligibility, 119 reports were excluded:

- duplicate (n=4)
- exposure not directly assessed (n=12)
- not English language (n=2)
- TB species not differentiated (n=2)
- wrong population (n=72)
- wrong publication type (n=8)
- wrong study type (n=18)

3 papers were included in the review.

Annexe C. Excluded full texts

Duplicate (4 studies)

Amemor EA and others. 'The prevalence of tuberculosis in cattle and their handlers in north Tongu, Volta region, Ghana' African Journal of Infectious Diseases 2017: volume 11, issue 1, pages 12 to 17

Buss BF and others. 'Possible Airborne Person-to-Person Transmission of Mycobacterium bovis Nebraska 2014-2015' MMWR - Morbidity and Mortality Weekly Report 2016: volume 65, issue 8, pages 197 to 201

Enquselassie F and others. 'Tuberculosis Infection in Cattle and Cattle Owners in North Eastern Parts' 2015

Sichewo PR and others. 'Risk practices for bovine tuberculosis transmission to cattle and livestock farming communities living at wildlife-livestock-human interface in northern KwaZulu Natal, South Africa' bioRxiv 2019

Exposure not directly assessed (12 studies)

Azami HY and others. 'Phylogenetic analysis of Mycobacterium bovis Reveals Evidence Of Animal And Zoonotic Tuberculosis Transmission Between Morocco And European Countries' bioRxiv. 2024: volume 10

Cotter TP and others. 'Tuberculosis due to Mycobacterium bovis in humans in the south-west region of Ireland: is there a relationship with infection prevalence in cattle?' Tubercle and Lung Disease 1996: volume 77, issue 6, pages 545 to 548

Dabade G and others. 'A study on zoonotic tuberculosis in selected rural areas of Bagalkot and Belgaum districts of Karnataka state' Journal of Clinical Tuberculosis and Other Mycobacterial Diseases 2017: volume 9, pages 30 to 35

Dankner WM and others. 'Mycobacterium bovis as a significant cause of tuberculosis in children residing along the United States-Mexico border in the Baja California region' Pediatrics 2000: volume 105, issue 6, page E79

Foddai A and others. 'Assessment of the probability of introducing Mycobacterium tuberculosis into Danish cattle herds' Preventive Veterinary Medicine 2015: volume 122, issue 1 to 2, pages 92 to 98

Genewein A and others. 'Molecular approach to identifying route of transmission of tuberculosis in the community' Lancet 1993: volume 342, issue 8875, pages 841 to 844

Gibson AL and others. 'Molecular epidemiology of disease due to Mycobacterium bovis in humans in the United Kingdom' Journal of Clinical Microbiology 2004: volume 42, issue 1, pages 431 to 434

Koro K and others. 'The genetic population structure of Mycobacterium bovis strains isolated from cattle slaughtered at the Yaounde and Douala abattoirs in Cameroon' Revue Scientifique et Technique 2015: volume 34, issue 3, pages 1,001 to 1,010

Oloya J and others. 'Mycobacteria causing human cervical lymphadenitis in pastoral communities in the Karamoja region of Uganda' Epidemiology and Infection 2008: volume 136, issue 5, pages 636 to 643

Prasad HK and others. 'Bovine tuberculosis in India: potential basis for zoonosis' Tuberculosis 2005: volume 85, issue 5 to 6, pages 421 to 428

Sarkar S and others. 'Occurrence of tuberculosis among people exposed to cattle in Bangladesh' Veterinary Medicine and Science 2023: volume 9, issue 4, pages 1,923 to 1,933

Wanzala SI and others. 'Retrospective Analysis of Archived Pyrazinamide Resistant Mycobacterium tuberculosis Complex Isolates from Uganda-Evidence of Interspecies Transmission' Microorganisms 2019: volume 7, issue 8, page 29

Not English language (2 studies)

Schliesser T and others. '|The role of tuberculosis in carnivorous animals in infection histories of human tuberculosis|' Beitrage zur Klinik und Erforschung der Tuberkulose und der Lungenkrankheiten 1967: volume 136, issue 1, pages 262 to 264

Szungyi Z and others. '|The role of tuberculin-positive cattle in human extrapulmonary tuberculosis|' Orvosi Hetilap 1963: volume 104, pages 832 to 834

TB species not specified (2 studies)

Buss BF and others. 'Possible Airborne Person-to-Person Transmission of Mycobacterium bovis - Nebraska 2014-2015' MMWR - Morbidity and Mortality Weekly Report 2016: volume 65, issue 8, pages 197 to 201

Meisheri DT and others. 'Assessment of Risk Factors for Human Mycobacterium Bovis Infections in Rural Communities in Central Gujarat, India' Journal of Population Therapeutics and Clinical Pharmacology 2024: volume 31(7), pages 1,191 to 1,199

Wrong exposure (1 study)

Brassard P and others. 'Evaluation of Mycobacterium tuberculosis transmission from a pediatrician and initial compliance to prophylaxis of contacts in an outpatient pediatric clinic' Pediatric Infectious Disease Journal 2000: volume 19, issue 10, pages 968 to 972

Wrong population (72 studies)

Abdel-Moein K and others. 'Molecular detection of Mycobacterium tuberculosis in cattle and buffaloes: a cause for public health concern' Tropical Animal Health and Production 2016: volume 48, issue 8, pages 1,541 to 1,545

Adesokan HK and others. 'Reverse zoonotic tuberculosis transmission from an emerging Uganda I strain between pastoralists and cattle in South-Eastern Nigeria' BMC Veterinary Research [Electronic Resource] 2019: volume 15, issue 1, page 437

Alelign A and others. 'Tuberculosis at Farmer-Cattle Interface in the Rural Villages of South Gondar Zone of Northwest Ethiopia' Tuberculosis Research and Treatment Print 2019: volume 2019

Alemayehu R and others. 'Bovine tuberculosis is more prevalent in cattle owned by farmers with active tuberculosis in central Ethiopia' Veterinary Journal 2008: volume 178, issue 1, pages 119 to 125

Amemor EA and others. 'The Prevalence of Tuberculosis in Cattle and Their Handlers in North Tongu, Volta Region, Ghana' African Journal of Infectious Diseases 2017: volume 11, issue 1, pages 12 to 17

Anonymous. 'Human tuberculosis caused by Mycobacterium bovis--New York City, 2001 to 2004' MMWR - Morbidity and Mortality Weekly Report 2005: volume 54, issue 24, pages 605 to 608

Badalik L and others. 'Surveillance of tuberculosis caused by Mycobacterium bovis in Slovakia' Journal of the Royal Society of Health 1995: volume 115, issue 5, pages 310 to 313

Bashe WJ and others. 'Relationship between human and bovine tuberculosis in Ohio. An epidemiologic study' Ohio State Medical Journal 1962: volume 58, pages 46 to 48

Bates MN and others. 'Bovine ownership and reduced pulmonary tuberculosis risk in Nepal: A case-control study' Zoonoses and Public Health 2021: volume 68, issue 6, pages 650 to 657

Berg S and others. 'Investigation of the high rates of extrapulmonary tuberculosis in Ethiopia reveals no single driving factor and minimal evidence for zoonotic transmission of Mycobacterium bovis infection' BMC Infectious Diseases 2015: volume 15, page 112

Bolanos CAD and others. 'Nontuberculous mycobacteria in milk from positive cows in the intradermal comparative cervical tuberculin test: implications for human tuberculosis infections' Revista do Instituto de Medicina Tropical de Sao Paulo 2018: volume 60, page e6

Boukary AR and others. 'Risk factors associated with bovine tuberculosis and molecular characterization of Mycobacterium bovis strains in urban settings in Niger' Transboundary and Emerging Diseases 2012: volume 59, issue 6, pages 490 to 502

Ciambrone L and others. 'Presence of Mycobacterium bovis in slaughterhouses and risks for workers' Preventive Veterinary Medicine 2020: volume 181, 105072

Coker R and others. 'Risk factors for pulmonary tuberculosis in Russia: case-control study' BMJ 2006: volume 332, issue 7533, pages 85 to 87

Cook AJ and others. 'Human and bovine tuberculosis in the Monze District of Zambia--a cross-sectional study' British Veterinary Journal 1996: volume 152, issue 1, pages 37 to 46

Cordova E and others. 'Human Mycobacterium bovis infection in Buenos Aires: epidemiology, microbiology and clinical presentation' International Journal of Tuberculosis and Lung Disease 2012: volume 16, issue 3, pages 415 to 417

Cvetnic Z and others. 'Mycobacterium caprae in cattle and humans in Croatia' International Journal of Tuberculosis and Lung Disease 2007: volume 11, issue 6, pages 652 to 658

Dalovisio JR and others. 'Rhinoceros' rhinorrhea: cause of an outbreak of infection due to airborne Mycobacterium bovis in zookeepers' Clinical Infectious Diseases 1992: volume 15, issue 4, pages 598 to 600

Davidson JA and others. 'Epidemiology of Mycobacterium bovis Disease in Humans in England, Wales, and Northern Ireland, 2002 to 2014' Emerging Infectious Diseases 2017: volume 23, issue 3, pages 377 to 386

Doran P and others. 'An outbreak of tuberculosis affecting cattle and people on an Irish dairy farm, following the consumption of raw milk' Irish Veterinary Journal 2009: volume 62, issue 6, pages 390 to 397

Duguma A and others. 'Status of bovine tuberculosis and its zoonotic implications in Borana zone, Southern Ethiopia' Tropical Animal Health and Production 2017: volume 49, issue 3, pages 445 to 450

Fanning A and others. 'Mycobacterium bovis infection in human beings in contact with elk (Cervus elaphus) in Alberta, Canada' Lancet 1991: volume 338, issue 8,777, pages 1,253 to 1,255

Fetene T and others. 'Tuberculosis infection in animal and human populations in three districts of Western Gojam, Ethiopia' Zoonoses and Public Health 2011: volume 58, issue 1, pages 47 to 53

Gebre D and others. 'Prevalence of smear positive pulmonary tuberculosis among patients attending Seka Health Center, Jimma, Oromia Region, Ethiopia' East African Journal of Public Health 2010: volume 7, issue 3, pages 268 to 273

Gebremichael B and others. 'Predictors of pediatric tuberculosis in public health facilities of Bale zone, Oromia region, Ethiopia: a case control study' BMC Infectious Diseases 2018: volume 18, issue 1, page 252

Gompo TR and others. 'Risk factors of tuberculosis in human and its association with cattle TB in Nepal: A one health approach' One Health 2020: volume 10, 100156

Habitu T and others. 'Prevalence and risk factors analysis of bovine tuberculosis in cattle raised in mixed crop-livestock farming system in Tigray region, Ethiopia' Transboundary and Emerging Diseases 2019: volume 66, issue 1, pages 488 to 496

Ibrahim S and others. 'Tuberculosis in humans and cattle in jigawa state, Nigeria: risk factors analysis' Veterinary medicine international 2012: volume 2012, page 865924

Jabeen C and others. 'A retrospective analysis of tuberculosis in livestock farmers in Lahore district, Pakistan' Journal of Infection in Developing Countries 2024: volume 18, issue 8, pages 1,249 to 1,257

Jalava K and others. 'No increase in human cases of Mycobacterium bovis disease despite resurgence of infections in cattle in the United Kingdom' Epidemiology and Infection 2007: volume 135, issue 1, pages 40 to 45

Kassa A and others. 'Bovine Tuberculosis (Btb) as a Risk Factor for Developing Tuberculosis in Humans in the Rural Community of Ethiopia: A Case-Control Study' Ethiopian Medical Journal 2015: volume 53, issue 1, pages 1 to 8

Kassa A and others. 'Tuberculosis in Goats and Sheep in Afar Pastoral Region of Ethiopia and Isolation of Mycobacterium tuberculosis from Goat' Veterinary medicine international 2012: volume 2012, 869146

Kouengoua APK and others. 'Prevalence and zoonotic risk factors of Mycobacterium bovis tuberculosis in cattle at the cattle-wildlife-human interface in South and East Cameroon' Veterinary World 2024: volume 17, issue 1, pages 8 to 16

Krajewska-Wedzina M and others. 'Human as a potential vector of bovine tuberculosis in cattle' Annals of Agricultural and Environmental Medicine 2019: volume 26, issue 3, pages 396 to 399

Krishnaswami KV and others. 'Mycobacterium tuberculosis humanis causing zoonotic tuberculosis among cattle' Indian Journal of Public Health 1983: volume 27, issue 2, pages 60 to 63

Kwaghe AV and others. 'Prevalence and molecular characterization of Mycobacterium tuberculosis complex in cattle and humans, Maiduguri, Borno state, Nigeria: a cross-sectional study' BMC Microbiology 2023: volume 23, issue 1, page 7

Lakra SB and others. 'Practices that are Potential Risks to an Increase in Zoonotic Tuberculosis: A Cross-sectional Study among Cattle Holders in Peri-Urban Area of Sonipat' Indian Journal of Community Medicine 2020: volume 45, supplement 1, pages S35 to S37

Lee HY and others 'A Mycobacterium bovis outbreak among exhibition animals at a zoo in the Republic of Korea: the first contact investigation of zoonotic tuberculosis' Osong Public Health and Research Perspectives 2024: volume 15, issue 3, pages 248 to 259

Malama S and others. 'Isolation and molecular characterization of Mycobacterium tuberculosis from humans and cattle in Namwala District, Zambia' Ecohealth 2014: volume 11, issue 4, pages 564 to 570

Mandal S and others. 'Investigating transmission of Mycobacterium bovis in the United Kingdom in 2005 to 2008' Journal of Clinical Microbiology 2011: volume 49, issue 5, pages 1,943 to 1,950

Marangon S and others. 'A case-control study on bovine tuberculosis in the Veneto Region (Italy)' Preventive Veterinary Medicine 1998: volume 34, issue 2 to 3, pages 87 to 95

Meisnern J and others. 'Cattle-associated risk factors for human tuberculosis in rural livestock-keeping communities, Uganda' Zoonoses and Public Health 2019: volume 66, issue 1, pages 73 to 82

Michalak K and others. 'Mycobacterium tuberculosis infection as a zoonotic disease: transmission between humans and elephants' Emerging Infectious Diseases 1998: volume 4, issue 2, pages 283 to 287

Monde N and others. 'Risk factors associated with zoonotic tuberculosis at the animal-human interface in a tuberculosis-endemic sub-Saharan country' Journal of Veterinary Medical Science 2023: volume 85, issue 10, pages 1,136 to 1,141

Moyo M and others. 'Tuberculosis patients at the human-animal interface: Potential zooanthroponotic and zoonotic transmission' One Health 2021: volume 13, 100319

Murphree R and others. 'Elephant-to-human transmission of tuberculosis, 2009' Emerging Infectious Diseases 2011: volume 17, issue 3, pages 366 to 371

Nation PN and others. 'Observations on animal and human health during the outbreak of Mycobacterium bovis in game farm wapiti in Alberta' Canadian Veterinary Journal 1999: volume 40, issue 2, pages 113 to 117

Nuru A and others. 'Preliminary investigation of the transmission of tuberculosis between farmers and their cattle in smallholder farms in northwestern Ethiopia: a cross-sectional study' BMC Research Notes 2017: volume 10, issue 1, page 31

O'Halloran C and o. 'Feline tuberculosis caused by Mycobacterium bovis infection of domestic UK cats associated with feeding a commercial raw food diet' Transboundary and Emerging Diseases 2021: volume 68, issue 4, pages 2,308 to 2,320

Palacios JJ and others. 'Molecular and epidemiological population-based integrative analysis of human and animal Mycobacterium bovis infections in a low-prevalence setting' Veterinary Microbiology 2016: volume 195, pages 30 to 36

Parsons SDC and others. 'Detection of Mycobacterium tuberculosis infection in dogs in a high-risk setting' Research in Veterinary Science 2012: volume 92, issue 3, pages 414 to 419

Portillo-Gomez L and others. 'Molecular identification of Mycobacterium bovis and the importance of zoonotic tuberculosis in Mexican patients' International Journal of Tuberculosis and Lung Disease 2011: volume 15, issue 10, pages 1,409 to 1,414

Prabhu SR and others. 'A retrospective analysis of 1019 cases of tuberculous cervical lymphadenitis in a rural setup in 20 years' Indian Journal of Tuberculosis 2023: volume 70, issue 2, pages 162 to 167

Robert J and others. 'A national survey of human Mycobacterium bovis infection in France. Network of Microbiology Laboratories in France' International Journal of Tuberculosis and Lung Disease 1999: volume 3, issue 8, pages 711 to 714

Rodriguez E. 'Human tuberculosis due to Mycobacterium bovis and M. caprae in Spain, 2004-2007' International Journal of Tuberculosis and Lung Disease 2009: volume 13, issue 12, pages 1536 to 1541

Saitanu K and others. 'An epizootic of Mycobacterium intracellulare, serotype 8 infection in swine' Nordisk Veterinaermedicin 1977: volume 29, issue 4 to 5, pages 221 to 226

Sichewo PR and others. 'Risk Factors for Zoonotic Tuberculosis at the Wildlife-Livestock-Human Interface in South Africa' Pathogens 2019: volume 8, issue 3, page 14

Silva MR and others. 'Risk factors for human Mycobacterium bovis infections in an urban area of Brazil' Memorias do Instituto Oswaldo Cruz 2018: volume 113, issue 8, e170445

Thomas A and others. 'High Mycobacterium bovis exposure but low IGRA positivity in UK farm workers' medRxiv. 2024: volume 28

Torres-Gonzalez P and others. 'Human tuberculosis caused by Mycobacterium bovis: a retrospective comparison with Mycobacterium tuberculosis in a Mexican tertiary care centre, 2000-2015' BMC Infectious Diseases 2016: volume 16, issue 1, page 657

Torres-Gonzalez P and others. 'Prevalence of latent and active tuberculosis among dairy farm workers exposed to cattle infected by Mycobacterium bovis' PLoS Neglected Tropical Diseases |electronic resource| 2013: volume 7, issue 4, e2177

Tschopp R and others. 'Risk factors of bovine tuberculosis in cattle in rural livestock production systems of Ethiopia' Preventive Veterinary Medicine 2009: volume 89, issues 3 to 4, pages 205 to 211

Wangmo K and others. 'Seroprevalence and risk factors associated with bovine tuberculosis in cattle in Eastern Bhutan' PLoS Neglected Tropical Diseases [electronic resource] 2024: volume 18, issue 5, e0012223

Wilkins MJ and others. 'Absence of Mycobacterium bovis infection in dogs and cats residing on infected cattle farms: Michigan, 2002' Epidemiology and Infection 2008: volume 136, issue 12, pages 1,617 to 1,623

Winthrop KL and others. 'Investigation of human contacts: a Mycobacterium bovis outbreak among cattle at a California dairy' International Journal of Tuberculosis and Lung Disease 2005: volume 9, issue 7, pages 809 to 813

Zlot A and others. 'Diagnosis of Tuberculosis in Three Zoo Elephants and a Human Contact - Oregon, 2013' MMWR - Morbidity and Mortality Weekly Report 2016: volume 64, issue 52, pages 1,398 to 1,402

Getachew A and others. 'Risk factors of pulmonary tuberculosis among cattle owner tuberculosis patients attending governmental health facilities in Gondar town, northwest Amhara, Ethiopia' 2023:

Hassanain Nawal NA and others. 'Bovine tuberculosis in a dairy cattle farm as a threat to public health' African Journal of Microbiology Research 2009: volume 3, issue 8, pages 446 to 450

Mengistu A and others. 'Tuberculosis Infection in Cattle and Cattle Owners in North Eastern Parts of Ethiopia' Biology and Medicine 2015: volume 7, issue 4, 45474

Mengistu A and others. 'Bovine Tuberculosis in Rural Ethiopia: A Comparative Cross-Sectional Study on Cattle Owned by Households with and without Tuberculosis' Mycobacterial Diseases 2014: volume 5, issue 4, 45444

Romha g and others. 'Assessment of Bovine Tuberculosis and Its Risk Factors in Cattle and Humans, at and around Dilla Town, Southern Ethiopia' Animal and Veterinary Sciences 2014: volume 2, issue 4, page 94

Tibebu M and others. 'A High Prevalence of Tuberculosis among Dairy Farm Workers in Addis Ababa and its Surroundings' Mycobacterial Diseases 2013: volume 4, issue 1, 45413

Wrong publication type (8 studies)

Al-Thwani AN and others. 'Tuberculosis in slaughtered cattle and workers in some abattoirs of Baghdad governorate' The International Journal of Mycobacteriology 2016: volume 5 supplement 1, pages S250 to S251

Gutierrez Garcia JM. 'Milk as a vector of transmission of bovine tuberculosis to humans in Spain: a historical perspective' Veterinary Heritage: Bulletin of the American Veterinary History Society 2006: volume 29, issue 2, pages 41 to 44

Indra J. 'Bovine tubercle bacilli and human extra-pulmonary tuberculous lesions in the Punjab' Indian Medical Gazette 1946: volume 81, pages 67 to 70

Jones T. 'Uncertainty in bovine TB transmission routes' Veterinary Record 2024: volume 194, issue 2, pages 83 to 84

Mallick SM and others. 'An Investigation into the Incidence and Type of Tuberculous Infection in Cattle at Amritsar with Special Reference to Human Infections' Indian Medical Gazette 1942: volume 77, issue 11, pages 668 to 672

Raw N. 'Human and Bovine Tuberculosis: The Possibility of Human Infection from Cattle' British Medical Journal 1903: volume 1, issue 2202, pages 596 to 598

Vitale M. 'Zoonotic tuberculosis: a complex issue of the Mycobacterium tuberculosis complex' The Lancet. Microbe 2020: volume 1, issue 2, pages e45 to e46

Yakubu Y and others. 'Evidence and potential risk factors of tuberculosis among captive Asian elephants and wildlife staff in Peninsular Malaysia' Preventive Veterinary Medicine 2016: volume 125, pages 147 to 153

Wrong study type (18 studies)

Akkerman OW and others. 'Infection of great apes and a zookeeper with the same Mycobacterium tuberculosis spoligotype' Medical Microbiology and Immunology 2014: volume 203, issue 2, pages 141 to 144

Cosivi O and others. 'Epidemiology of Mycobacterium bovis infection in animals and humans, with particular reference to Africa' Revue Scientifique et Technique 1995: volume 14, issue 3, pages 733 to 746

De la Rua-Domenech R. 'Human Mycobacterium bovis infection in the United Kingdom: Incidence, risks, control measures and review of the zoonotic aspects of bovine tuberculosis' Tuberculosis 2006: volume 86, issue 2, pages 77 to 109

El-Sayed A and others. 'Molecular Epidemiology of Mycobacterium bovis in Humans and Cattle' Zoonoses and Public Health 2016: volume 63, issue 4, pages 251 to 264

Evans JT and others. 'Cluster of human tuberculosis caused by Mycobacterium bovis: evidence for person-to-person transmission in the UK' Lancet 2007: volume 369, issue 9569, pages 1,270 to 1,276

Fanning A and others. 'Mycobacterium bovis infection in humans exposed to elk in Alberta' Canada Diseases Weekly Report 1991: volume 17, issue 44, pages 239 to 240

Hassan AS and others. 'Dynamics of Mycobacterium and bovine tuberculosis in a human-buffalo population' Computational and Mathematical Methods in Medicine 2014: volume 2014, 912306

Haydock IAJ and others. 'Diagnostic and public health investigation of Mycobacterium tuberculosis infection in a dog in Ontario, Canada' Journal of Veterinary Diagnostic Investigation 2022: volume 34, issue 2, pages 292 to 297

Isaac J and others. 'An outbreak of Mycobacterium bovis infection in cats in an animal house' Australian Veterinary Journal 1983: volume 60, issue 8, pages 243 to 245

Jacob CMA and others. 'Mycobacterium bovis dissemination (BCG strain) among immunodeficient Brazilian infants' Journal of Investigational Allergology and Clinical Immunology 1996: volume 6(3), pages 202 to 206

Lindau A. 'On the value of tuberculin-negative herds in the detection of tuberculosis in human beings' Acta Pathologica et Microbiologica Scandinavica. Supplementum 1956: volume 39, issue Suppl 111, pages 179 to 183

Liu S and others. 'Canine tuberculosis' Journal of the American Veterinary Medical Association 1980: volume 177, issue 2, pages 164 to 167

Marfil MJ. 'Mycobacterium tuberculosis infection in a free-ranging urban dog from Argentina' Veterinary Research Communications 2022: volume 46, issue 3, pages 781 to 788

Pintado V and others. 'Microepidemic of Mycobacterium bovis tuberculosis: evidence of air-borne human-to-human transmission' European Journal of Internal Medicine 1990: volume 1(5), pages 347 to 350

Reilly LV. 'Human tuberculosis of bovine origin in Northern Ireland' Journal of Hygiene 1950: volume 48, issue 4, pages 464 to 471

Sedighi T and others. 'Evaluating the Bovine Tuberculosis Eradication Mechanism and Its Risk Factors in England's Cattle Farms' International Journal of Environmental Research and Public Health [Electronic Resource] 2021: volume 18, issue 7, page 26

Sichewo PR and others. 'Risk practices for bovine tuberculosis transmission to cattle and livestock farming communities living at wildlife-livestock-human interface in northern KwaZulu Natal, South Africa' PLoS Neglected Tropical Diseases |electronic resource| 2020: volume 14, issue 3, e0007618

Wilkins. 'Human Mycobacterium bovis infection and bovine tuberculosis outbreak, Michigan, 1994-2007' Emerging Infectious Diseases 2008: volume 14, issue 4, pages 657 to 660

Annexe D. Data extraction tables

Abbreviations

BCG: bacillus calmette-guérin, CD4: cluster of differentiation 4, CI: confidence interval, CXR: chest x-ray, HIV: human immunodeficiency virus, IGRA: interferon-gamma release assay, IQR: interquartile range, *M. bovis*: *Mycobacterium bovis*, MDR: multidrug-resistant TB, M. TB: *Mycobacterium tuberculosis*, OR: odds ratio, PCR: polymerase chain reaction, PTB: pulmonary tuberculosis, SD: standard deviation, TST: tuberculin skin test, uL: microlitre

Table D.1. Summary of included studies

Study	Country, time period	Study type	Population	Exposure	Outcome type	Result
Riopel 2024 (1)	Canada, January 1995 to July 2021	Retrospective cohort study	*M. bovis* cases - 20 cases Age: - median age: 35 years (IQR: 30 to 62 years) - 0 to 14 years: 0 - 15 to 24 years: 4 (20%) - 25 to 44 years: 10 (50%) - 45 to 64 years: 2 (10%) - 65 and over years: 4 (20%) Sex: 8 males (40%), 12 females (60%) Birth region: - Northern Africa: 2 (10%) - Sub-Saharan Africa: 5 (25%) - North America: 4 (20%) - Latin America and the Caribbean: 2 (10%) - Southern Asia: 1 (5%) - Western Asia: 3 (15%) - Eastern Europe: 1 (5%) - Western Europe: 2 (10%) HIV status: - positive: 2 (10%) - negative: 17 (85%) - unknown: 1 (5%) Medical immunosuppression: - Yes: 1 (5%) - No: 19 (95%) *M. orygis* cases - 21 cases Age: - median age: 77 years (IQR: 61 to 85 years) - 0 to 14 years: 0	TB species: - Differential tests performed: yes (genotyping) - *M. TB*, *M. bovis*, *M.orygis*, *M. caprae* Diagnostic tests: - index cases: culture - contacts: TST and IGRA Measurement of exposures: contact tracing of cases	Prevalence of *M. bovis* (in 37 close contacts to PTB cases)	No secondary cases identified, no new TST or IGRA conversions (incomplete testing: 9 cases (24%))
					Prevalence of *M. orgyis* (119 close contacts to PTB cases)	No secondary cases and 3 new TST and IGRA conversions (but genotype negative for *M. orgyis*), incomplete testing: 15 cases (13%)
					Prevalence of *M. caprae* (4 close contacts were identified)	"No evidence of transmission" reported (TST or IGRA results not reported), incomplete testing not reported

Study	Country, time period	Study type	Population	Exposure	Outcome type	Result
			- 15 to 24 years: 2 (10%) - 25 to 44 years: 1 (5%) - 45 to 64 years: 2 (10%) - 65 and over years: 16 (76%) Sex: - Male: 2 (10%) - Female: 19 (90%) Birth region: - Southern Asia: 21 (100%, India/Pakistan) HIV status: - Positive: 0 - Negative: 0 - Unknown: 1 Medical immunosuppression: - Yes: 3 (14%) - No: 18 (86%) *M. caprae* case - 1 case - age: 84 year - sex: male - birth region: Ukraine - HIV status: unknown - medical immunosuppression: unknown			
Bapat 2017 (2)	India, March 2014 to June 2015	Prospective cohort	Overall cohort - 301 people recruited from camps across the central India region, split into 3 groups (a/b/c) Sex: - 179 males (59.5%) - 122 females (40.5%) Ethnicity: not reported Group A: - 105 farmers, dairy workers and livestock keepers Age: - less than 18 years old: 2 (1.9%) - 18 to 40 years old: 62 (59.1%) - more than 40 years old: 41 (39%)	TB species: - Differential tests performed: yes (genotyping) Group A (105 blood samples collected, 25 tested positive): 12 cases of *M. bovis* (11.4%), 13 cases of *M. TB* (12.4%) Group B (45 blood samples collected, 11 tested positive): 4 cases of *M. bovis* (8.9%), 7 cases of *M. TB* (15.6%)	Odds of PCR positivity in farmers who had previous contact with a TB case (univariate)	OR = 23.5 (95% CI: 3.0568 to 180.7912, p=0.0024)
					Odds of PCR positivity in zookeepers who had previous contact with a TB case (univariate)	OR = 1.2 (95% CI: 0.0540 to 27.6783, p=0.8997)
					Odds of PCR positivity in residents of a highly endemic TB area who reported contact with a TB case (univariate)	OR = 3.7 (95% CI: 0.9612 to 14.4533, p=0.0571)

Study	Country, time period	Study type	Population	Exposure	Outcome type	Result
			Sex: - 72 male (68.6%) - 33 female (31.4%) Group B: - 45 zoo-keepers and animal handlers Age: - less than 18 years old: 0 (0%) - 18 to 40 years old: 11 (24.4%) - more than 40 years old: 34 (75.6%) Sex: 41 male (91.1%), 4 female (8.9%) Group C: - 151 residents of high TB endemic areas - high crowding index with a mean of 6 to 8 people living in a poorly ventilated room. - some (number not reported) also participated in cattle and goat rearing. - 60 samples PCR positive (39.7%) Age: - less than 18 years old: 12 (7.9%) - 18 to 40 years old: 83 (55%) - more than 40 years old: 56 (37.1%) Sex: 66 male (43.7%), 85 female (37.1%) One sample corresponded to one individual.	Group C (151 blood samples collected, 60 tested positive): 19 cases of *M. bovis* (12.6%), 41 cases of *M. TB* (27.2%) Diagnostic tests: Individuals with respiratory symptoms were investigated for active TB by culture and CXR (however, the study does not report how many were confirmed to have active TB) Measurement of exposure: questionnaire Previous contact with a TB case: - group A: 15 (14.3%) - group B: 3 (6.7%) - group C: 77 (51%) Living in a high endemic area: - group A: 20 (19%) - group B: 2 (4.4%) - group C: 151 (100%) Animal contact: - group A: 82 (78.1%) - group B: 36 (80%) - group C: 49 (32.5%) Raw milk consumption: - group A: 51 (48.6%) - group B: 2 (4.4%) - group C: 38 (25.2%)		
Guerrero 1997 (3)	Spain, December 1993 to February 1995	Case-control	Cases: - 19 in-patients diagnosed with multidrug-resistant *M. bovis* and HIV - mean age: 31 years (SD: 6.5 years) - sex: 16 males, 3 females - mean CD4 lymphocyte count: 43 per uL (range: 4 to	TB species: - differential tests performed: yes (genotyping) - *M. bovis* Diagnostic tests:	Prevalence of *M. bovis* in people who shared a room with *M. bovis* cases	5 out 38 (7.6%)
					Median incubation period of *M. bovis*	111 days (range 90 to 270 days, calculated for 10 cases with one exposure event)

Study	Country, time period	Study type	Population	Exposure	Outcome type	Result
			156 uL), median CD4 count: 54 lymphocytes per uL - stage of HIV: 3 were stage B, 16 were stage C - BCG vaccine status: not reported Controls: - 33 patients with drug susceptible M.TB and HIV treated at the same hospital - stage of HIV: 10 were stage A, 13 were stage B, 6 were stage C, 4 were unknown stage - median CD4 lymphocyte counts: 200 lymphocytes per uL	- cases: smear, culture, CXR (it is not clearly reported if all cases received all 3 tests, but the study does report that CXR was negative in 4 cases on admission and 5 cases were smear negative on admission to hospital) - controls: not reported Measurement of exposure: method of collecting exposure information unclear - close contact defined as sharing a hospital ward with a *M. bovis* case - the index case and 2 other cases were reported to have previously treated in another hospital with a multidrug resistant TB outbreak, before transfer to the study hospital - 38 patients shared a room with an *M. bovis* cases Note: this study compares MDR TB patients (cases) with drug-susceptible TB patients (controls), both of whom were exposed to *M. bovis*-infected individuals. The review solely reports outcomes related to the transmission of *M. bovis* between humans, irrespective of case or control status.	Incidence of *M. bovis* in ward A	One case per 625 patient-days of exposure in ward A
					Incidence of *M. bovis* in ward B	One case per 1,328 patient-days of exposure in ward B (note: the study reports that the 2 cases exposed in Ward B were also exposed in Ward A)
					Attack rate of *M. bovis* for ward A	16 out of 38 (42%)
					Attack rate of *M. bovis* for ward B	The study reports an attack rate of 1.1% for ward B but does not report the raw data.
					Odds of *M. bovis* transmission in people who reported a previous stay in a hospital (multivariable analysis)	OR = 47.6 (95% CI: 6.8 to 440.9)* This study did not report which variables were adjusted for
					Odds of *M. bovis* transmission in patients who shared the same ward as an index case (multivariable analysis)	OR = 82.7 (95% CI: 9.9 to 1008.1)* This study did not report which variables were adjusted for
					M. bovis transmission among healthcare workers	Four healthcare workers (3 from ward A, 1 from Ward B) tested TST positive but none developed *M. bovis* MDR TB (no demographic variables or information about BCG vaccination status was reported for these healthcare workers)
					Evidence of transmission between hospitals	The same strain that was isolated from the index cases above was identified in 2 other patients and a physician exposed at another hospital, suggesting evidence of transmission between hospitals

Annexe E. Risk of bias assessment

Table E.1 Risk of bias assessment for case-control studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Comments (including reason for no)
Guerrero 1997 (3)	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	No	Q1 and 2: study does not report demographic data for control group, or full demographic data for cases, and no reference to matching. Q4, 5 and 8: measurement of exposure and outcome not clearly reported. Q6 and 7: Study states they adjusted for confounding variables but does not report what these were. Q10: Reporting of statistical methods unclear, for example attack rate in wards.

Critical appraisal was done using the JBI checklist for case-control studies (5)

List of questions
Q1: Were the groups comparable other than presence of disease in cases or absence of disease in controls?
Q2: Were cases and controls matched appropriately?
Q3: Were the same criteria used for identification of cases and controls?
Q4: Was exposure measured in a standard, valid and reliable way?
Q5: Was exposure measured in the same way for cases and controls?
Q6: Were confounding factors identified?
Q7: Were strategies to deal with confounding factors stated?
Q8: Were outcomes assessed in a standard, valid and reliable way for cases and controls?
Q9: Was the exposure period of interest long enough to be meaningful?
Q10: Was appropriate statistical analysis used?

Table E.2 Risk of bias assessment for cohort studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Comments (including reason for no)
Bapat 2017 (2)	Yes	Yes	No	No	No	Unclear	Yes	Yes	No	No	Yes	Q3: potential for information bias in self-reported exposures Q4 and Q5: No adjustment for confounding variables Q6: unclear if free of bovine TB at the start of study Q9/10: no mention of loss to follow-up
Riopel 2024 (1)	Yes	Yes	No	NA	NA	NA	Yes	NA	NA	NA	Yes	Q3: potential for information bias in self-reported exposures Q4 and Q5: outcome was prevalence, confounding factors not applicable Q6: Retrospective study, participants not free of outcome at start of study Q8, 9 and 10: Retrospective study, participants not followed up over time

Critical appraisal was done using the JBI checklist for cohort studies (5).

List of questions

Q1: Were the 2 groups similar and recruited from the same population?
Q2: Were the exposures measured similarly to assign people to both exposed and unexposed groups?
Q3: Was the exposure measured in a valid and reliable way?
Q4: Were confounding factors identified?
Q5: Were strategies to deal with confounding factors stated?
Q6: Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
Q7: Were the outcomes measured in a valid and reliable way?
Q8: Was the follow up time reported and sufficient to be long enough for outcomes to occur?
Q9: Was follow up complete, and if not, were the reasons to loss to follow up described and explored?
Q10: Were strategies to address incomplete follow up utilized?
Q11: Was appropriate statistical analysis used?

Annexe F. GRADE assessment of certainty of evidence

Abbreviations: OR: odds ratio, 95% CI: 95% confidence interval.

Certainty assessment							Effect (95% CI)	Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Odds of PCR positivity in 1) farmers, dairy farm workers and livestock keepers, 2) zookeepers and veterinarian, 3) residents of highly endemic TB areas (univariate analyses)								
1	Prospective cohort	very serious [note 1]	Serious [note 2]	not serious	very serious [note 3]	none	OR range: 1.2 to 23.5 (0.05 to 180.79)	⊕◯◯◯ Very low
Odds of *M. bovis* transmission in people who reported a previous stay in a hospital (multivariable analysis)								
1	Case control	very serious [note 4]	not assessed [note 5]	Serious [note 6]	Serious [note 7]	none	OR 47.6 (9.9 to 1008.1)	⊕◯◯◯ Very low
Odds of *M. bovis* transmission in patients who shared the same hospital ward as an index case (multivariable analysis)								
1	Case control	very serious [note 4]	not assessed [note 5]	not serious	Serious [note 7]	none	OR 47.6 (6.8 to 440.9)	⊕◯◯◯ Very low

Explanations

Note 1: the study was at high risk of bias in one or more critical areas, such as the participants were not free of TB at baseline and no adjustment for confounding variables.
Note 2: there was a wide variance in point estimates.
Note 3: the confidence intervals were overly wide and crossed the line of no effect.
Note 4: the study was at high risk of bias in one or more critical areas, such as lack of reporting comprehensive information about demographic data for cases or controls, measurement of the exposure and outcome was not clearly reported, and not reporting which confounding variables were adjusted for in analyses.
Note 5: one outcome, could not assess inconsistency.
Note 6: outcome assessed previous stay in hospital, but did not directly assess contact with other human cases of TB.
Note 7: the confidence intervals were overly wide.

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