UK Health Security Agency

Zoonotic tuberculosis transmission from animals to humans

A rapid systematic review

Contents

Main messages

1. This rapid systematic review (search up to 12 November 2024) identified and summarised evidence on the risk of zoonotic (animal to human) transmission of *Mycobacterium (M.) tuberculosis* (TB) species (specifically, *M. bovis*, *M. caprae*, *M. microti*, *M. orygis*, and *M. TB*).

2. Sixteen studies were included (1 to 16). Of these, 2 were cohort studies (1, 15), 7 were cross-sectional (2 to 7, 16), and 7 were case-control studies (8 to 14). Eight studies were conducted in Africa (2 to 4, 6, 11 to 13, 16), 3 in Asia (1, 9, 10), one in Europe (8), 3 in North America (5, 7, 15) and one in South America (14).

3. The potential sources of TB infection identified in this review included consuming raw dairy products or raw animal meat, living with animals, and working with animals.

4. Fourteen studies assessed the risk of TB infection from eating or drinking raw dairy products (raw milk or raw-milk cheese) (1 to 14). Most studies reported an association between drinking raw milk and increased risk of TB infection (2, 4, 8 to 14), but some studies (all cross-sectional) found no evidence of an association (3, 6, 7). One cohort study reported an association with increased risk of TB infection in farmers, dairy workers, or livestock keepers who drank raw milk, but not in zookeepers or veterinarians who drank raw milk (1). However, only 2 zookeepers or veterinarians reported drinking raw milk, which is too few to provide a reliable estimate of the association.

5. Two studies (one case-control and one cross-sectional) looked at the association between risk of TB infection and eating raw animal meat (6, 13). The case-control study suggested that there may be an association between eating raw animal meat and increased risk of TB infection in children, but the association was weak, and the study did not adjust for other factors that have could have affected the outcome (13). The cross-sectional study reported no evidence of an association between TB infection and eating raw meat (6). Overall, the evidence doesn't show a clear association, but this was limited by risk of bias and small sample sizes which impacts the reliability of the results.

6. The evidence for the risk of TB infection in people who lived (4 studies) (6, 9, 12, 13) or had contact with animals through work environments (10 studies (1, 3 to 5, 7, 9, 11, 14 to 16)) was conflicting. The certainty of evidence (all rated very low) and risk of biases identified were similar for studies which showed both an association or no association with risk of TB infection from living with or having contact with animals through work environments. Therefore, it was not possible to determine the risk of TB from these animal exposures.

7. Several studies reported overlapping risk factors for TB infection, such as living with animals, or eating or drinking raw dairy products by people who also worked with animals

(such as farmers or veterinarians). Some studies adjusted for this, and other factors, in their analysis, but many used unadjusted analysis only and therefore other factors may have affected the risk of TB infection. Therefore, it was not possible to determine the relative contribution of each type of animal exposure to the overall risk of TB infection in these studies.

8. The evidence in these studies was mostly rated as very low certainty using a modified Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach (17) due to risk of bias in the studies, small sample sizes, and inconsistencies in the results. Selection bias was a key limitation because as participants already diagnosed with TB were included, making it unclear if they were infected before or after animal exposure. This limited the evidence to showing only an association between the studied factors and TB infection. Additionally, many studies did not account for other possible influencing factors (confounding variables). Some studies provided too little information to be assessed using GRADE, but they also had similar biases and small sample sizes.

9. In conclusion, the findings of this evidence review suggest that there may be an association between eating or drinking raw dairy products and risk of TB infection. However, there was some conflicting evidence, and evidence for other exposures assessed by the studies was less clear. The evidence was mostly rated as very low certainty and was subject to risk of bias across all studies. The conclusions of this review should therefore be interpreted with caution. No evidence was found on the risk of transmission of *M. orygis* and *M. microti*.

Purpose

The purpose of this rapid systematic review was to identify and summarise the available evidence that described the risk of transmission of specific zoonotic species of the *Mycobacterium (M.) tuberculosis (TB)* complex from animals to humans.

The review question was:

1. What is the risk of transmission of *M. bovis*, *M. caprae*, *M. microti*, *M. orygis*, and *M. TB* from animals to 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 12 November 2024. Backwards and forwards citation searching of primary studies included during full text screening was also conducted.

Studies investigating TB transmission to humans from any type of animal contact, regardless of context, were included. The following transmission routes were considered:

- oral (such as from unpasteurised (raw) dairy products, or contaminated meat)
- respiratory (inhalation of airborne bacterial particle droplets)
- direct contact (handling infected animal species or touching contaminated surfaces)

The specific tuberculosis species (*M. bovis*, *M. caprae*, *M. microti*, *M. orygis*, and *M. TB*) included in this review were agreed by subject matter experts within the UK Health Security Agency (UKHSA) Tuberculosis, Acute Respiratory Infections, Zoonoses, Emerging Infections and Travel Health (TARZET) Division, as those with greatest potential for transmission from animals to humans. 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.

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.

Screening title and abstract was undertaken in duplicate by 3 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening full text 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 for specific outcomes where appropriate, using a modified version of the GRADE approach (17). This process is described in detail in Annexe A. In brief, the certainty of evidence was assessed 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 (assessed using the appropriate JBI checklist (18).
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)

GRADE was not applied where there was no measure of variance reported with the outcome for a single study (for example, confidence intervals), as inconsistency and imprecision could not be assessed (risk of bias and indirectness alone are insufficient to effectively use GRADE).

Additionally, GRADE was not applied to outcomes assessed by univariate analysis when a multivariate analysis for the same outcome was available. Outcomes from different study designs were not combined. Studies that were not similar enough to combine were assessed individually, and therefore, the domain of ‘inconsistency’ was not assessed in these studies.

Glossary of terms

This review includes specific terminology relating to measures of risk and statistical methods. These terms are defined below, with specific reference to risk of TB after exposure to animals, to help with interpretation of the review’s findings.

Term	Meaning
95% confidence intervals (CI)	the range of possible values surrounding a result, indicating the precision of the study's findings (95% refers to the expectation that, if the study were repeated many times, 95% of the time the result would fall within this range)
confounding variable	a factor that influences both the likelihood of animal exposure and the risk of TB infection (for example, type of work or living conditions)
multivariate or adjusted analysis:	analysis which considers more than one factor at a time (for example, looking at how TB is affected by drinking raw milk and living with animals)
odds ratio (OR)	the ratio of the probability of TB infection to the probability of no infection
prevalence	the proportion of a population with TB at a given time
prevalence ratio (PR)	the ratio of the prevalence of TB in an exposed group to the prevalence of TB in an unexposed group
risk ratio (RR)	the likelihood of TB infection occurring out of the total population exposed
univariate or unadjusted analysis	analysis which considers one factor at a time (for example, how risk of TB in people who drank raw milk), but does not consider any potential confounding variables

Evidence

In total, 5,055 studies were screened at title and abstract and 114 studies were screened at full text. Of these, 16 studies met the inclusion criteria (1 to 16). No additional studies were identified through 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, risk of bias assessments are available in Annexe E, and GRADE assessments are available in Annexe F.

Of the included studies, 2 were cohort studies (1, 15), 7 were cross-sectional studies (2 to 7, 16), and 7 were case-control studies (8 to 14).

Eight studies were conducted in Africa (2 to 4, 6, 11 to 13, 16), 3 in Asia (1, 9, 10), one in Europe (8), 3 in North America (5, 7, 15), and one in South America (14).
The exposures identified were:

- eating or drinking raw dairy products
- eating of raw meat products
- living with animals
- working with animals

The studies included in this review diagnosed TB in humans using tuberculin skin tests (TST), interferon gamma release assays (IGRA), the polymerase chain reaction (PCR), chest x-rays (CXR), assessment of clinical symptoms, smear tests and culture. People who tested positive for TST and/or IGRA, but who tested negative in additional tests, were diagnosed with latent TB infection (LTBI). A person with LTBI has TB bacteria present in their body but does not have TB symptoms and cannot spread the disease. People who tested positive for TST and/or IGRA, and then tested positive in additional tests, were diagnosed with active TB. A person with active TB can spread TB to others and is usually (but not always) symptomatic for TB.

The evidence in this review has been summarised by exposure (defined as having been exposed and infected to the source of infection). Where outcomes could be assessed across studies using GRADE, the evidence from these studies has been synthesised narratively. Where outcomes could not be assessed using GRADE or could not be grouped for GRADE assessment, these have been reported separately.

Eating or drinking raw dairy products

Fourteen studies looked TB infection in people who ate or drank raw dairy products (raw milk or raw-milk cheese) (1 to 14). Detailed study characteristics are available in Table D.1.

Cohort studies

One prospective cohort study calculated the odds of TB infection in people who drank raw milk compared to those who did not drink raw milk, in 2 separate populations: (1) farmers, dairy workers, and livestock keepers, and (2) zookeepers and veterinarians, Table 1a (1). The evidence for outcomes from these population groups were assessed together using GRADE.

Table 1a. Cohort study of TB transmission in people who drank raw milk

Study	TB species	Participants	Outcome	Results
Bapat and others (1), prospective cohort, March 2014 to June 2015, India	*M. bovis* *M. TB*	105 farmers, dairy workers, or livestock keepers (23 people with TB, 23.8%): 51 people drank raw milk, 54 people did not	Odds of TB in people who drank raw milk compared to people who did not drink raw milk	Unadjusted OR: 6.34 (95% CI: 1.32 to 30.56) p=0.02
		45 zookeepers or veterinarians (11 people with TB, 24.4%): 2 people drank raw milk, 43 people did not	Odds of TB in people who drank raw milk compared to people who did not report drinking raw milk	Unadjusted OR: 1.76 (95% CI: 0.07 to 42.60) p=0.73

The results were different for each population. Farmers, dairy workers and livestock keepers who drank raw milk had higher odds of TB infection compared those who did not, whereas no difference in TB risk was observed among zookeepers or veterinarians who drank raw milk compared to those who did not. However, there were only 2 people who drank raw milk in the zookeeper and veterinarian group which means this result is unlikely to be reliable.

The certainty of evidence was rated as very low. The study relied on self-reported information about drinking raw milk, which could introduce bias if this information was not accurate. Not all participants were free of TB at the start of the study, therefore it is difficult to determine if transmission was associated with drinking raw milk or if TB infection occurred due to other exposures prior to the study. The study population was people who worked in environments where they had contact with animals. The effect this exposure to animals may have had on the association was not adjusted for in the analysis. There was also no discussion of participant withdrawal, and the study did not consider other factors that could have had an impacted transmission (confounding variables). The result was uncertain with wide confidence intervals (imprecision), likely due to the relatively small sample sizes of the subgroups compared.

Cross-sectional studies

Six cross-sectional studies looked at TB infection in people who drank raw milk, Table 1b (2 to 7).

Table 1b. Cross-sectional studies of TB infection related to consuming raw dairy products

Study	TB species	Participants	Outcomes	Results
Gebre and others, (2), February 2010, Ethiopia	*M. bovis* or *M. TB*	160 people with suspected pulmonary TB (PTB), of which 17 (10.6%) had PTB Number who drank raw milk not reported	Association between drinking raw milk and TB smear positivity	Chi-squared test (X^2): 8.99, p=0.003
Meisner and others, (3), 2014 to 2016, Uganda.	*M. TB*	493 cattle owners Number who drank raw milk not reported	Prevalence ratio of TB in people who drank raw (22.8% people with TB) milk compared to TB in people who did not (32.1% people with TB)	Adjusted PR: 0.94, (95% CI: 0.64 to 1.39)
Monde and others (4), April 2020 to December 2021, Zambia	*M. TB*	255 people recruited from TB outpatient clinics: 46 drank raw milk on a daily or weekly basis (13 people with TB, 28.3%) 209 drank raw milk when needed (13 people with TB, 6.2%)	Odds of TB in people who drank raw milk on a daily or weekly basis compared to people who drank raw milk when needed	Adjusted OR: 2.72 (95% CI: 1.73 to 4.28)
Torres-Gonzalez and others (5), Mexico, from 2009 to 2011	*M. bovis*	63 people with confirmed presence or absence of LTBI (subgroup of a larger cohort of 311 dairy farm workers) 45 people with LTBI and 18 people without LTBI drank raw milk	Odds of drinking raw milk in people with confirmed presence or absence of LTBI	Adjusted OR: 0.4 (95% CI: 0.17 to 0.91) $p < 0.05$

Study	TB species	Participants	Outcomes	Results
Tschopp and others (6), November 2006 to May 2007, Ethiopia	*M. bovis* or *M. TB*	449 cattle owners, of which 86 households contained people with TB (19%): 307 drank raw milk, 141 did not, 1 unknown	Odds of TB in people who drank raw milk compared to people who did not drink raw milk	Unadjusted OR: 0.3 (95% CI: 0.5 to 1.8) p=0.70
Winthrop and others (7), May 2002, USA	*M. bovis*	88 people exposed to cattle during an *M. bovis* outbreak at a dairy farm: 41 drank raw milk (51% people with TB), 47 did not (all TB negative)	Risk of TB in people who drank raw milk compared people who did not drink raw milk	Unadjusted RR: 1.5, (95% CI: 0.8 to 3.0), p=0.13

Five of these cross-sectional studies reported different outcomes or used different analysis methods, and therefore certainty of evidence was assessed individually per study.

One study reported that people who drank raw milk on a daily or weekly basis were more likely to be infected with TB, compared to people who only drank raw milk when needed (4). This was rated as very low certainty of evidence. The study relied on self-reported information about raw milk drinking. A large proportion of the participants were farmers (45.8%), but the study did not adjust for this in their analysis. Therefore, it is possible that exposure to animals through work may also have affected the risk of TB infection. Furthermore, the authors did not report the methods used to diagnose TB, therefore the validity of the diagnostic methods used could not be assessed. The outcome was also downgraded for indirectness to the review question, because the comparator group included people who drank raw milk less frequently rather than not at all. This may have had an impact on the result as both groups drank some raw milk.

Three studies reported no association between TB infection and drinking raw milk compared to those who didn't (3, 6, 7). All outcomes were rated as very low certainty evidence. The studies relied on self-reported information about raw milk consumption. Two studies used TST to diagnose TB, which may not have correctly identified all cases of TB (3, 7). One study did not report the number of participants who did or did not drink raw milk (3). The studies either did not adjust for any confounding variables in their analyses, or the confounding variables adjusted for did not cover all factors that might have affected the outcome. None of these studies adjusted for type of work as an overlapping risk factor for TB, despite including participants who may have had contact with animals through their place of work. All results were very uncertain with wide confidence intervals (imprecision), likely due to the small numbers of people included who consumed raw milk compared to people who did not consume raw milk.

Gebre and others reported that drinking raw milk was associated with TB infection in people with suspected PTB (2). This outcome could not be assessed using GRADE as the study did not report a measure of variance of the result and does not show how much uncertainty there was in the result. Several potential risks of bias were identified in the study which were similar to the risks of bias described for other studies for this exposure. These included that the study relied on self-reported information about drinking raw milk. Many of the participants were farmers (42%), but the study did not adjust for this as another risk factor for TB infection. The study also used smear tests to identify active TB, which may have missed cases with low bacterial loads, due to early-stage infection or immunosuppression (immune status of participants not reported). The number of people who did or did not drink raw milk was also not reported.

One cross-sectional study looked at the prevalence of TB in dairy farm workers exposed to cattle (5). The study reported a negative association with eating or drinking raw dairy products in people with confirmed LTBI (both TST and IGRA positive) compared to people confirmed to not have LTBI (both TST and IGRA negative). This evidence was rated as low certainty evidence. The study relied on self-reported information about raw dairy product consumption, no other risks of bias were identified. The study was also downgraded for indirectness to the review question, as instead of looking at the risk of transmission of TB from raw dairy products, the study looked at association of potential risk factors, one of which was eating or drinking raw dairy products, in people with LTBI compared to those who did not have LTBI.

Case-control studies

Seven case-control studies looked TB infection in people who ate or drank raw dairy products (8 to 14), Table 1c.

Table 1c. Case-control studies of TB infection related to eating or drinking raw dairy products

Study	Participants	TB species	Outcomes	Results
Coker and others (8), 1 January to 31 December 2003, Russia	334 cases with PTB, 334 controls without TB Number who drank raw milk not reported	*M. TB* complex	Odds of TB in people who drank raw milk compared to those who did not drink raw milk (TB positivity not reported in this subgroup)	Adjusted OR: 2.75 (95% CI: 1.80 to 4.20)
Fetene and others (11), December 2007 to May 2008, Ethiopia	51 cases and 21 controls who owned cattle infected with TB	*M. bovis* and *M. TB*	Odds of TB in people who drank raw milk compared to those who did not drink raw milk (TB	Unadjusted OR: 3.23 p=0.001

Study	Participants	TB species	Outcomes	Results
	Number who drank raw milk not reported		positivity not reported in this subgroup)	
Gompo and others (10), January 2018 to December 2019, Nepal	145 cases with TB (93 reported contact with sick cattle, or ate or drank unspecified raw dairy products, 52 did not report such exposure) 145 controls without TB, relatives of cases, matched by area of residence, (63 reported contact with sick cattle, or ate or drank unspecified raw dairy products, 82 who did not report such exposure)	*M. bovis* or *M. TB*	Odds of TB in people who reported contact with sick cattle, or ate or drank raw dairy products, compared to people who did not report exposures	Adjusted OR: 3.9 (95% CI: 2.1 to 7.4) p<0.001
Gebremichael and others (13), case-control, August to December 2016, Ethiopia	142 child cases with active TB (105 fed raw milk, 37 not fed raw milk) 284 child controls without TB (86 fed raw milk, 196 not fed raw milk, 2 unknown)	*M. TB* complex	Odds of TB in children who drank raw milk compared to children who did not drink raw milk	Adjusted OR: 4.23 (95% CI: 2.26 to 7.88)
Getachew and others (pre-print) (12), case-control, March 2019 to	31 cases with PTB, (13 who drank raw milk, 7 drank boiled milk,	*M. TB* complex	Odds of TB in people who drank raw milk compared to people who drank boiled milk	Adjusted OR: 9.97 (95% CI: 1.67 to 59.35) p < 0.05

Study	Participants	TB species	Outcomes	Results
January 2020, Ethiopia	11 drank sour milk) 61 controls without PTB (8 drank raw milk, 21 drank boiled milk, 32 drank sour milk)			
Jabeen and others (9), study period not reported, Pakistan	85 cases with TB, (26 who drank raw milk, 38 who did not drink raw milk, 21 who drank raw and boiled milk) 85 controls without TB (7 who drank raw milk, 71 who did not drink raw milk, 7 who drank raw and boiled milk)	*M. bovis* or *M. TB*	Odds of TB in people who drank raw milk compared to people who did not drink raw milk	Adjusted OR: 7.7 (95% CI: 1.95 to 30.68) p=0.003
Silva and others (14), March 2008 to February 2010, Brazil	3 cases, defined as co-infected with *M. bovis* and *M. TB*, (all ate above lifetime median levels of raw-milk cheese) 42 controls, defined as infected with *M. TB* only, (19 ate above lifetime median levels of raw-milk cheese, 23 did not)	*M. bovis* and *M. TB*	Odds of TB in people who ate above lifetime median levels of raw-milk cheese compared to people who did not	OR: 3.58 (95% CI: 2.02 to 24.13) p=0.055

Four case-control studies reported odds of TB in populations similar enough to combine and were assessed jointly for certainty of evidence (8, 9, 12, 13). These all showed an association between drinking raw milk and risk of TB infection, but this was rated as very low certainty evidence. All studies relied on self-reported information about drinking raw milk, and controls were not tested for TB (assumed to be negative for TB because they did not have any TB symptoms). This could have resulted in people incorrectly classified as controls, as people can be infected with TB but not display symptoms. One study did not clearly report participant demographics (8). Another study did not adjust for participants type of work as another risk factor for TB infection or specify adjustment of any confounding variables beyond age and sex (12). Similarly, the study conducted in children did not adjust for parental work, which may have impacted a child's risk of TB infection (13). There was inconsistency in the results between studies, with some reporting a larger association between raw milk consumption and TB infection than others. There was also a lot of uncertainty in the estimates of risk of TB infection with very wide confidence intervals across the range of the effect (likely due to relatively small sample sizes).

Silva and others reported more people with TB infection in people who ate above median levels of raw-milk cheese (median level of lifetime raw-milk cheese consumption defined as 21,840 days), compared to people who did not consume above median levels of raw-milk cheese (14). This evidence was rated as very low certainty. This study also relied on self-reported information about eating raw-milk cheese which may not have been accurate, did not test controls for TB and did not adjust for participants type of work (employment not reported in this study). Furthermore, all the people who reported eating below median levels of raw milk-cheese were in the control group, which skews the results towards a positive association between eating raw-milk cheese and TB infection. The results were also uncertain with wide confidence intervals (likely due to the small sample size as there were only 3 cases included).

Gompo and others concluded that people who had contact with sick cattle or consumed raw dairy products had greater odds of TB than those not exposed in this way (10). This was rated as low certainty evidence. The study did not report what diagnostic tests were used to diagnose TB, relied on the accuracy of self-reported information about eating or drinking raw milk or contact with animals, and the controls were not tested for TB. The study also did not separate the data for contact with sick cattle or consumption of raw dairy products. Therefore, it was not possible to determine if TB infection was because of drinking raw milk consumption or contact with sick cattle.

Fetene and others reported that the odds of TB infection in people who owned cattle infected with TB and drank raw milk was greater than those who did not drink raw milk (11). The certainty of evidence could not be assessed for this study as it did not report any measure of variance in the results. However, several risks of bias were identified. People in the control group were not tested for TB, the study relied on the accuracy of self-reported information about exposure to animals and eating or drinking raw dairy products, and the analysis was not adjusted for confounding variables. The reporting was poor, as the study did not clearly state what data were used to calculate odds of TB (11). While the study results indicated an

increased likelihood of TB infection from drinking raw milk, this result did not align with the milk drinking habits reported for the overall cohort (60 cases consumed raw milk, compared to 87 controls). Therefore, it was assumed that the OR was calculated from the milk drinking habits of the subgroup of 51 cases and 21 controls who owned infected cattle, as more cases than controls reported drinking raw milk in this subgroup. There were further discrepancies in the reporting of figures in the text and tables of the study, which raises doubts about the reliability of the findings.

Summary of risk of TB from eating or drinking raw dairy products

Overall, the majority of studies suggested an association between TB infection and consumption of raw dairy products. However, some studies did not demonstrate any significant association, and all of the evidence was subject to risk of bias and considered low of very low certainty evidence. One of the studies which did not report an association between drinking raw dairy products and TB infection only included 2 people who consumed raw milk, which is unlikely to provide a reliable estimate of risk of transmission. One study reported a negative association with eating or drinking raw dairy products in people with LTBI compared to people confirmed to not have LTBI (5).

Eating raw meat

Two studies looked at TB infection in people who ate raw meat, Table 2 (6, 13). Detailed study characteristics are available in Table D.2.

Table 2. Studies of risk of TB in people who ate raw meat

Study	TB species	Participants	Outcomes	Results
Cross-sectional evidence				
Tschopp and others (6), November 2006 to May 2007, Ethiopia	*M. bovis* or *M. TB*	449 cattle owners, of which 86 households were People with TB (19%): 334 people ate raw meat, 115 did not	Odds of TB in people who ate raw meat compared to people who did not (TB positivity not reported in this subgroup)	Unadjusted OR: 1.10 (95% CI: 0.6 to 2.0) p=0.60
Case-control evidence				
Gebremichael and others (13), August to December 2016, Ethiopia	*M. TB* complex.	142 children with TB (cases), 115 fed raw meat, 27 not fed raw meat	Odds of TB children who ate raw meat compared to children who did not	Unadjusted OR: 1.67 (95% CI: 1.01 to 2.73)

Study	TB species	Participants	Outcomes	Results
		284 children without TB (controls). 204 controls fed raw meat, 90 not fed raw meat		

The cross-sectional study reported that there was no difference in odds of TB infection in people who ate raw meat compared to people who did not (6). This outcome was rated as very low certainty evidence. The study reported very limited information about participants demographics, relied on the accuracy of self-reported information about raw meat consumption, and did not adjust for confounding variables which could have impacted the results (such as type of work, which was not reported for this study, although all participants were livestock owners, which may or may not be their type of work). The result was also uncertain, with confidence intervals crossing the line of no effect.
The case-control study reported that there was no clear association between TB infection and feeding children raw meat (13). This outcome was also rated as very low certainty evidence. The study relied on the accuracy of parental reporting about their child's consumption of raw meat, did not test controls for TB, and did not adjust for confounding variables (such as parental type of work which could impact a child's risk of TB infection).

Summary of risk of TB from eating raw meat

The available evidence relating to eating raw meat was very limited in both quantity and quality, and was assessed as very low certainty evidence, therefore it is not possible to draw conclusions about the risk of TB infection from eating raw meat. Furthermore, none of the studies specified if the raw meat was likely to be contaminated.

Living with animals

Four studies reported looked at TB infection in people who lived with animals, Table 3 (6, 9, 12, 13). Detailed study characteristics are available in Table D.3.

Table 3. Studies of risk of TB from living with animals.

Study	TB species	Participants	Outcomes	Results
Cross-sectional evidence				
Tschopp and others (6), November 2006 to May 2007, Ethiopia	Assumed *M. bovis* or *M. TB*	450 cattle owners, of which 86 households were people with TB (19%):	Odds of TB in people who housed cattle indoors compared to people who kept free-roaming cattle (TB positivity not	Unadjusted OR: 1.00 (95% CI: 0.40 to 2.60) p=0.20

Study	TB species	Participants	Outcomes	Results
		209 housed cattle indoors, 241 kept free-roaming cattle	reported in this subgroup)	
Case-control evidence				
Gebremichael and others (13), August to December 2016, Ethiopia	Assumed *M. TB* complex	142 children with TB (cases), 54 lived with animals and 88 did not 284 children without TB (controls), 34 lived with animals and 250 did not	Odds of TB in people who lived with animals compared to people who kept animals outdoors	Adjusted OR: 1.75 (95% CI: 0.86 to 3.56)
Getachew and others (pre-print) (12), March 2019 to January 2020, Ethiopia	Assumed *M. TB* complex	31 cases with PTB (12 shared a house with cattle, 19 did not) 61 controls without PTB (11 shared a house with cattle, 50 did not)	Odds of TB in people sharing a house with cattle compared to people not living with cattle	Adjusted OR: 8.11, (95% CI: 1.23 to 53.58), p<0.05
Jabeen (9), study period not reported, Pakistan	Assumed *M. bovis* or *M. TB*	85 cases with TB and 85 controls without TB (matched to same village) 45 lived with cattle at night (30 cases and 15 controls), 125 not did not (55 cases and 70 controls)	Odds of TB in people who lived with cattle at night compared to people who did not live with cattle at night	Unadjusted OR: 2.5, (95% CI: 1.20 to 5.20), p=0.0143

Evidence from cross-sectional studies

Tschopp and others reported no difference in odds of TB between people who kept cattle indoors at night and people who kept free-roaming cattle (6). This was rated as very low certainty evidence due to serious risks of bias and imprecision. The study did not specify the methods used to diagnose TB, or adjust for other factors that may have affected the outcome.

Evidence from case-control studies

Two studies reported the association between living with animals and active TB infection, and the outcomes were assessed together for certainty of evidence (12, 13). The results were conflicting, one study reported that there was an association between odds of TB infection and living with animals (12), whilst the second study found no association (13). This was rated as very low certainty of evidence. The studies did not test controls for TB and relied on self-reported information about living with animals. Furthermore, the study by Getachew and others also did not clearly specify which additional confounding factors were included in their analysis, beyond age and sex (in contrast, Gebremichael and others considered several variables including drinking raw milk, BCG vaccination status and family history of TB). Neither study adjusted for type of work (including parental type of work in the study conducted in children). The results were inconsistent across studies, as evidenced by the wide variation in the OR for each study, and imprecision across the results with a wide range of the possible effect, likely due to the small sample sizes of people who reported living with animals (33 to 88 people). Jabeen and others reported that living with cattle may be associated with active TB transmission (9). This outcome was assessed independently using GRADE and rated as very low certainty evidence. The study did not test controls for TB, relied on self-reported information about living with animals, and did not perform any adjustment for confounding variables that may have affected the results (including other risk factors such as drinking raw milk or type of work). There was also uncertainty in the results, which was may have been due to the small sample size of the subgroup of people who reported living with animals (45 people).

Summary of risk of TB from living with animals

The limited evidence identified on any association between living with animals and risk of TB infection was of very low certainty due to risks of bias identified and uncertain results. The sample sizes of the included studies were mostly small. It is therefore not possible from this evidence to determine a conclusive answer on the risk of TB infection in people living with animals.

Working with animals

Ten studies estimated the risk of active TB or LTBI transmission from working with animals (1, 3 to 5, 7, 9, 11, 14 to 16). Detailed study characteristics are available in Table D.4.

Evidence from cohort studies

Two cohort studies looked at TB infection in people who had contact with animals through their place of work, summarised in Table 4a (1, 15).

Table 4a. Cohort studies of risk of TB transmission from working with animals

Study	TB species	Participants	Outcome	Results
Bapat and others (1), prospective cohort, March 2014 to June 2015, India	*M. bovis* *M. TB*	105 farmers, dairy workers, or livestock keepers (23 people with TB, 23.8%) 82 had direct contact with animals, 23 did not	Odds of TB in people who direct contact with animals compared to people who did not	Unadjusted OR: 0.22 (95% CI: 0.06 to 0.78) p=0.02
		45 zookeepers or veterinarians (11 people with TB, 24.4%) 36 had direct contact with animals, 9 did not	Odds of TB in people who had direct contact with animals compared to people who did not	Unadjusted OR: 2.63 (95% CI: 0.13 to 53.37) p=0.53
Murphree and others (15), retrospective, 2006 to 2009, USA	*M. TB*	46 zoo employees 11 employees reported contact with elephants (2 people with TB), 35 did not (7 people with TB) 13 employees reported quarantine area exposure (8 people with TB), 33 did not (1 person with TB)	Risk of TB in zoo employees reporting any contact with elephants compared to employees who did not	Unadjusted RR: 0.91, (95% CI: 0.22 to 3.75)
			Risk of TB in zoo employees reporting exposure to the quarantine area compared to employees who did not	Unadjusted RR: 20.31, (95% CI: 2.81 to 146.69)

Bapat and others calculated the odds of TB in individuals who self-reported contact with animals through their place of work compared to those who did not in 2 separate populations, (1) farmers, dairy workers, and livestock keepers, and (2) zookeepers and veterinarians (1). These outcomes were assessed jointly for certainty of evidence. The study reported that farmers, dairy workers, and livestock keepers who had contact with animals may be less likely to have TB than those who did not. The study reported no association between contact with animals and risk of

TB infection in zookeepers or veterinarians, but there was a lot of uncertainty in this result with the confidence intervals ranging from lower odds to a greatly increased odds of TB infection. The certainty of evidence was rated as very low. Not all participants were free of TB at the start of the study, therefore it is difficult to determine if transmission was associated with contact with animals or if TB infection occurred due to other exposures prior to the study. The study relied on self-reported information about contact with animals. There was also no discussion of participant withdrawal, and the study did not consider other factors that could have affected risk of TB (including drinking raw milk which was another risk factor in this population). The uncertainty in the result and wide confidence intervals was likely due to the relatively small sample size.

Murphree and others looked at risk of TB infection in zookeepers during an outbreak of TB in elephants (15). The study found that, overall, there was no increased risk of TB for zoo employees who had contact with elephants compared to those who did not, regardless of whether any elephants were infected with TB. However, the study also showed that employees working inside the quarantine area with elephants infected with TB had higher odds of developing TB. This was rated as very low certainty evidence. The study used TST to diagnose TB which may not have correctly identified all TB cases, relied on self-reported information about contact with animals and did not adjust for confounding variables. The results were uncertain with wide confidence intervals likely due to the relatively small sample size, particularly in the analysis of risk of TB infections in employees with quarantine area exposure.

Evidence from cross-sectional studies

Five cross-sectional studies looked at TB infection in people who had contact with animals through place of work, summarised in Table 4b (3 to 5, 7, 16).

Table 4b. Cross-sectional studies of TB transmission in people who worked with or had direct contact with animals

Study	TB species	Participants	Outcomes	Results
Meisner and others, (3), 2014 to 2016, Uganda	Assumed *M. bovis* or *M. TB*	493 cattle owners: 88 owned *M. bovis*-positive cattle (29 people with TB, 15.8%), 405 did not (59 people with TB, 19.1%)	Prevalence ratio of TB in people who owned cattle with TB compared to people who owned cattle that did not have TB	Adjusted PR: 0.87 (95% CI: 0.62 to 1.22)

Study	TB species	Participants	Outcomes	Results
Monde and others (4), April 2020 to December 2021, Zambia	Assumed *M. TB*	255 people recruited from TB outpatient clinics: 71 had contact with animals, 184 did not	Odds of TB in people who had contact with animals (6 people with TB) compared to people who had no contact with animals (20 people with TB)	Unadjusted OR: 0.76 (95% CI: 0.29 to 1.97) p=0.567
Sichewo and others, (16), August to September 2017, South Africa	*M. TB*	150 cattle owners	Prevalence of TB: • in 42 households with *M. bovis*-positive cattle, 7 people were infected with TB, one was culture confirmed to be *M. TB* • in 41 households with *M. bovis*-negative cattle, 3 people were infected with TB, none were culture confirmed	
Torres-Gonzalez and others (5), Mexico, from 2009 to 2011	*M. bovis*	70 people with confirmed LTBI compared to people without LTBI (subgroup of a larger cohort of 311 dairy farm workers): 65 people with LTBI, 5 without LTBI	Odds of direct contact with livestock in closed spaces in people with confirmed presence or absence of LTBI	Adjusted OR 6.09 (95% CI: 2.04 to 18.23), p < 0.001)
Winthrop and others (7), May 2002, USA	Assumed *M. bovis*	88 people exposed to cattle during an *M. bovis* outbreak at a dairy farm 27 dairy workers (18 people with TB), 13 slaughterhouse workers (4 people with TB), and 48 family members of workers (11 people with TB)	Risk of TB in dairy staff workers compared to family members	Adjusted RR: 1.20 (95% CI: 0.60 to 2.10)
			Risk of TB in slaughterhouse workers compared to family members	Adjusted RR: 1.0, (95% CI: 0.40 to 2.50)

Four outcomes from cross-sectional studies were assessed independently using GRADE due to differences in the outcomes and analysis methods used by these studies.

One cross-sectional study looked at the prevalence of TB in dairy farm workers exposed to cattle (5). The study reported an association between direct contact with livestock in close spaces in people with confirmed LTBI, compared to people confirmed to not have LTBI. Participants had a median of 6 hours of daily exposure to cattle (interquartile range (IQR): 0 to 8 hours). This was assessed as very low certainty evidence due to risk of bias and imprecision. The study relied on self-reported information about contact with animals. The review was also downgraded due to indirectness to the review question, as instead of looking at risk of TB infection from contact with animals, the study looked at association of potential risk factors, one of which was close contact with animals in closed spaces, in people with LTBI compared to people with no LTBI. The results were also uncertain with wide confidence intervals.

Three studies reported no association between TB infection and contact with animals (3, 4, 7), These outcomes were not similar enough to combine for assessment of certainty of evidence as they all used different methods of analyses, but all were rated as very low certainty evidence due to risk of bias, imprecision, and indirectness in one study. All studies relied on self-reported information about contact with animals. Two studies used TST to diagnose TB, which may not have correctly identified all cases of TB (3), and another did not report the method used to diagnose TB (4). One study did not adjust for any confounding variables (4), and or did not adjust for other risk factors such as drinking raw milk (3, 7). Two of the results had very wide confidence intervals suggesting uncertainty in the true result (3, 7). Additionally, one outcome was downgraded for indirectness as the study compared TB infection in people owning *M. bovis* positive cattle compared to people who did not own *M. bovis* cattle, but it was not possible to tell whether direct contact with infected animals had occurred (3).

Sichewo and others reported a higher prevalence of TB in households with *M. bovis*-positive cattle (16.7% PCR positive, one culture positive) compared to those without (7.3%, no culture-positive cases) (16). However, since no statistical analysis was performed to find out whether households with *M. bovis*-positive cattle had statistically higher rates of TB than households M. bovis-positive cattle, it was not possible to draw conclusions from this study or assess the outcomes using GRADE.

Evidence from case-control studies

Three case-control studies reported the risk of TB from self-reported contact with animals through place of work, Table 4c (9, 11, 14).

Table 4c. Case-control studies of TB transmission in people who had contact with animals (other than living with them)

Study	TB species	Participants	Outcomes	Results
Fetene and others (11), December 2007 to May 2008, Ethiopia	*M. bovis* and *M. TB*	105 cases with active TB (94 reported contact with cattle, 11 did not) 105 controls without TB (96 reported contact with cattle, 9 did not)	Difference in prevalence of TB in people who reported contact with cattle and people who did not report contact with cattle	p=0.647
Jabeen and others (9), study period not reported, Pakistan	Assumed *M. bovis* or *M. TB*	85 cases with TB (53 worked at a cattle farm, 32 did not) 85 controls without TB (26 worked at a cattle farm, 59 did not)	Odds of TB in people who worked at a cattle farm compared to people who did not work in cattle farms	Adjusted OR: 4.2, 95% CI: 1.08 to 16.56, p=0.038
Silva and others (14), March 2008 to February 2010, Brazil	*M. bovis* and *M. TB*	3 cases co-infected with *M. bovis* and *M. TB*, and 42 *M. TB* controls 17 had animal exposure through place of work (3 cases, 14 controls) and 28 (all controls) did not	Odds of TB in people who reported direct contact with cattle compared to people who did not (all TB negative)	Unadjusted OR: 5.71, 95% CI: 2.827 to 40.99, p=0.024

Two outcomes relating to the risk of TB from contact with animals through their place of work were assessed independently using GRADE. One of these studies reported an association between people who worked on a cattle farm and TB infection (9), while the other reported an association of risk of TB infection in people who reported direct contact with cattle through agricultural work (14). The evidence from both studies were rated as very low certainty evidence due to serious risks of bias identified and the imprecision of the results (likely due to small

sample sizes). In one of the studies, all the controls were people who did not report animal exposure through their work environment (14), this skews the results towards a positive association between exposure to animals through their work and TB infection. Neither study tested controls for TB and the study by Silva and others did not adjust for any confounding variables (including eating raw milk-cheese, which was an overlapping risk factor in this population).

Fetene and others reported no difference in prevalence of TB in people who reported contact with cattle compared to people who did not, but the study only reported the p value showing this was not significant and certainty of evidence could not be assessed using GRADE (11). However, this study also had serious risks of bias identified, as controls were not tested for TB and no confounding variables were considered in the analysis (including drinking raw milk, which was another risk factor in this population).

Summary of risk of TB from working with animals

Overall, the evidence for risk of TB transmission from contact with animals at work was mixed between studies with some showing no association, and others indicating an association with increased risk of TB infection. There was a lot of uncertainty in the direction and extent of any possible association and all the evidence was rated as being very low certainty. It is therefore not possible to draw a clear conclusion from this evidence base.

Health inequalities

Many of the studies in this review were conducted in countries such as Ethiopia, Pakistan, Nepal, Uganda, Zambia, and India, that have high rates of TB and will likely have under ascertainment of cases. Some populations within these countries experience high levels of poverty and associated food insecurity, overcrowded or inadequate housing, and limited access to healthcare, which are all factors that may increase the risk of TB transmission.

Two studies estimated zoonotic TB transmission in people residing in rural areas, finding no significant difference between people living in rural and town locations. However, as only 2 studies were identified, it is not possible to know if living in a rural location impacts the risk of being infected with or transmitting TB through animal related exposures (2, 11).

Limited evidence on the relationship between HIV status, being immunocompromised, and the likelihood of acquiring or transmitting zoonotic TB was provided by 2 studies. One study reported that 8 out of 37 cases were HIV positive with an impaired immune system, but the study did not compare likelihood of TB positivity in people who had HIV to people who did not have HIV (19). One study found no association between HIV status and *M. bovis* infection (14). However, since people living with HIV who take anti-HIV medication can maintain a functioning immune system and this study did not report the status of their immune system, it was not possible to determine whether HIV status influenced the risk of zoonotic TB infection or transmission. Another study reported no significant difference in the number of individuals who

were suspected but not confirmed to have HIV (from the detection of HIV antibodies in blood samples) and TB-positive compared to those who did not have HIV but tested TB-positive. However, HIV positivity was not confirmed by further testing, and this study also did not indicate whether individuals had impaired immune function or had well controlled HIV.

This review did not identify evidence of increased risk of infection or transmission of zoonotic TB in other population groups (such as people experiencing homelessness). But again, 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 reporting of exposure information (living with animals, contact with animals other than living with them, and eating or drinking of raw dairy products or meat) was always self reported. This means studies relied on people remembering their raw dairy products and animal meat consumption habits, as well as whether and how much contact they had with animals, which may not always be accurate.

Several studies reported overlapping risk factors for TB infection, should as living with animals, or eating or drinking raw dairy products by people who also worked in places which involve contact with animals (such as farmers or veterinarians), which may increase their risk of TB infection. Some studies adjusted for this, and other factors, in their analysis, but many used unadjusted analysis only and therefore these and other factors may have affected the risk of TB infection.

Across all study designs, including the prospective cohort study (which typically provides stronger evidence than other designs), there was a risk of selection bias because participants were already diagnosed with TB at the time of inclusion in the study. It's therefore unclear whether TB infection occurred before or after animal exposure and this evidence can only inform association between these factors and TB infection rather than reliably indicating risk.

Several limitations were noted in the TB diagnostic methods used in the included studies. Two studies reported that TST alone was used to identify TB (3, 15). The use of TST is not sufficient to confirm either LTBI or active TB, due to the potential for false positives, particularly where people have previously received BCG vaccination. One study only used smear positivity to detect TB, which may miss cases of TB with low bacterial loads due to early-stage infection or immunosuppression (2). Furthermore, 2 studies did not explicitly report the method used to

diagnose TB (4, 6). One study reported that PCR testing was followed by symptom assessment and CXR but did not report how many active cases were identified, therefore it is not possible to know if PCR positivity reflected active TB or LTBI (1).

Studies did not routinely report tests of specific TB species, but all were at least assumed to be of the *M. TB* complex. This could have resulted in the inclusion of TB species beyond the species specified in this review's eligibility criteria, but given that these species are rare, this is unlikely.

No studies of zoonotic TB risk from animals were identified in the United Kingdom, therefore the findings of this review may have limited generalisability to this country.

Evidence gaps

Limited evidence was identified on risk of zoonotic TB transmission from eating or drinking raw dairy products, eating raw meat (but studies did not specify if meat was likely to be contaminated), living with animals and contact with animals through work environments. No evidence was identified on the risk of transmission of the TB species *M. microti* and *M. orygis*, and only one study was identified which estimated the risk of transmission of *M. caprae*.

Conclusion

This rapid systematic review examined the risk of zoonotic TB transmission from animals to humans, including *M. bovis*, *M. tuberculosis*, *M. orygis*, *M. microti*, and *M. caprae*. A total of 24 studies were included, comprising cohort, cross-sectional and case-control studies. The evidence looked at potential risk of TB infection from living with animals, contact with animals other than living with them, eating or drinking raw dairy products and raw animal meat, and living in a rural location.

Most studies reported an association between TB infection and eating or drinking raw dairy products, but this evidence was all subject to risk of bias and rated low or very low certainty. Some studies reported no association or even a negative association of TB.

Only 2 studies examined the risk of TB from raw animal meat consumption, but did not specify if the meat was likely to be contaminated. The evidence was too limited in quality and quantity to draw conclusions on the potential association between this exposure and TB infection.

Thirteen studies looked at the association between living or working with animals and TB infection. Some studies suggested an association between these risk factors and TB infection, others did not. This evidence was again considered low or very low certainty where that could be assessed, and subject to risk of bias. Therefore, it was unclear from this body of evidence whether there was a clear association.

Differences in results between studies may be explained by small sample sizes leading to uncertain and unreliable results and differences in populations between studies, who may have also been exposed to other risk factors. There was an overlap of risk factors between studies. For example, many of the studies looking at association with eating or drinking raw dairy products were in people who lived or worked with animals. Some studies adjusted for this, and other factors, in their analysis, but many used unadjusted analysis only and therefore other factors may have affected the risk of TB infection.

The overall certainty of the evidence was assessed as very low, with one exception rated as low. Serious risks of bias were identified, including potential misclassification of controls, reliance on self-reported exposure data, and limited adjustment for confounding factors. Additionally, some studies lacked clear diagnostic methods or relied on less reliable tests, such as TST alone. Small samples were another common limitation, which created uncertainty in the results.

Overall, the evidence-base was mostly very low certainty due to risk of bias and imprecision and so the conclusions of this review should be interpreted with caution. Whilst there was evidence that suggested an association between eating or drinking raw milk products and increased risk of TB infection, the association was less clear between other risk factors assessed within the studies and the risk of TB infection. No evidence was found on the risk of transmission of *M. orygis* and *M. microti*.

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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

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References

1. 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
2. Gebre D, Mimano LN. '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
3. Meisner 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
4. 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
5. 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
6. Tschopp R and others. 'Risk factors of bovine tuberculosis in cattle in rural livestock production systems of Ethiopia' Preventive Veterinary Medicine 2009: volume 89, issue 3 to 4, pages 205 to 211
7. 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
8. Coker R and others. 'Risk factors for pulmonary tuberculosis in Russia: case-control study' BMJ 2006: volume 332, issue 7533, pages 85 to 87
9. 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
10. 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
11. 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
12. Getachew A and others 'Risk factors of pulmonary tuberculosis among cattle owner tuberculosis patients attending governmental health facilities in Gondar town, north-west Amhara, Ethiopia' Research Square 2023
13. 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

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
15. Murphree R and others. 'Elephant-to-human transmission of tuberculosis, 2009' Emerging Infectious Diseases 2011: volume 17, issue 3, pages 366 to 371
16. 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
17. TGW G. 'GRADE handbook for grading quality of evidence and strength of recommendations' 2013
18. JBI. 'JBI Critical appraisal tools' 2020
19. 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

Annexe A. Protocol

Review question

The review question is:

1. What is the risk of transmission of *Mycobacterium (M.) bovis*, *M. tuberculosis* (TB), *M. orygis*, *M. microti*, and *M. caprae*, from animals to humans?

A search for primary evidence to answer this question will be conducted up to 12 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 animals infected with the below specified zoonotic TB strains, whether domestic or agricultural or other.	
Settings	Any	
Intervention or exposure	Exposure to non-human animal species (such as domestic pets and agricultural animals) infected with active *M. bovis*, *M. caprae*, *M. microti*, *M. orygis* and *M. TB*. The following routes of transmission will be included: • oral (such as from unpasteurised dairy products, or contaminated meat) • respiratory (inhalation of airborne bacterial particle droplets) • direct contact (handling infected animal species or touching contaminated surfaces [fomites])	Exposure to other infected humans
Comparator	No comparator required	

	Included	Excluded
Outcomes	Risk of transmission from animals to humans of *M. bovis*, *M. TB*, *M. orygis*, *M. microti* or *M. caprae*, such as: • incidence • risk ratios (relative risk) • hazard ratios • odds ratios	Human to human transmission risk Human to animal transmission risk
Language	English	Any other language
Date of search	Up to 12 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. 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 4 November 2024: Ovid Medline, Ovid Embase 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, participant demographics, 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 (18).

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 (17).

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 2 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). Evidence relating to transmission risk modifiers (variables which may increase or decrease risk of transmission) will also be extracted separately where available, within each route of transmission. For example:

- evidence relating to transmission risk from consumption of unpasteurised dairy products will be presented separately to consumption of pasteurised dairy products
- evidence of transmission risk in people more likely to handle infected animals, such as agricultural, abattoir or veterinary workers, will be presented separately to evidence of transmission risk in people unlikely to handle infected animals

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 tuberculosis 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/ (344)
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 tuberculosis subsp* caprae.tw,kf. (3)
21. or/1-20 (21,900)
22. Mycobacterium tuberculosis/ (59,854)
23. exp *Tuberculosis/ (188,634)

24. Mycobacterium tuberculosis.tw,kf. (59,794)
25. "M.tuberculosis".tw,kf. (299)
26. M tuberculosis.tw,kf. (21,552)
27. tuberculosis.tw,kf. (246,837)
28. or/22-27 (277,181)
29. (transmi* adj3 (non-human* or nonhuman* or animal* or livestock* or cattle* or cow* or bovine or wildlife or wild life)).tw,kf. (5,902)
30. exp Disease Transmission, Infectious/ and ((non-human* or animal* or livestock* or cattle* or cow* or wildlife).tw,kf. or (exp Ruminants/ or exp Animals, Domestic/)) (10,146)
31. ((Community or disease* or infection*) adj3 spread*).tw,kf. (32,772)
32. Tuberculosis, Bovine/tm (635)
33. ((non-human* or animal* or livestock* or cattle* or cow* or wildlife*) adj3 (vector* or reservoir*)).tw,kf. (5,275)
34. Disease Reservoirs/ (16,231)
35. Zoonoses/ or Bacterial Zoonoses/ (19,688)
36. (zoonotic* or zoonos#s).tw,kf. (48,164)
37. animal* to human*.tw,kf. (37,027)
38. (animal adj1 human adj1 interface*).tw,kf. (388)
39. (livestock adj1 human adj1 interface*).tw,kf. (67)
40. (wildlife adj1 human adj1 interface*).tw,kf. (96)
41. ((livestock or animal* or wildlife) adj1 spillover).tw,kf. (17)
42. ((livestock or animal* or wildlife) adj1 spill over).tw,kf. (0)
43. (interspecies or inter species).tw,kf. (16,249)
44. between species.tw,kf. (17,298)
45. cross species.tw,kf. (9,505)
46. (infect* adj (animal* or livestock* or cattle* or cow* or wildlife)).tw,kf. (18,071)
47. exp *Animals/ and Humans/ and (transmi*.tw,kf. or transmission.fs.) (25,522)
48. or/29-47 (220,954)
49. (pasteuris* or pasteuriz*).tw,kf. (7,420)
50. (unpasteuris* or unpasteuriz* or un-pasteuris* or un-pasteuriz*).tw,kf. (1,365)
51. raw milk.tw,kf. (4,670)
52. raw meat.tw,kf. (1,760)
53. raw animal produc*.tw,kf. (24)
54. exp Pasteurization/ (3,233)
55. exp Dairy Products/ (113,116)
56. (dairy adj3 (eat* or drink* or consum*)).tw,kf. (3,308)
57. (dairy adj (produc* or food* or farm*)).tw,kf. (24,051)
58. (milk* or cheese* or yoghurt* or yogurt*).tw,kf. (176,165)
59. ((meats or meat) adj3 (eat* or consum* or produc*)).tw,kf. (22,292)
60. ((pork or beef or bacon or chicken or turkey or poultry) adj3 (eat* or consum* or produc*)).tw,kf. (15,889)
61. (contamina* adj3 (food* or drink* or beverage* or meat* or dairy or milk* or cheese* or yoghurt*)).tw,kf. (23,969)

62. abbattoir*.tw,kf. (7)
63. abbatoir*.tw,kf. (72)
64. abattoir*.tw,kf. (4,867)
65. slaughterhous*.tw,kf. (5,632)
66. slaughter hous*.tw,kf. (497)
67. exp *Meat-Packing Industry/ (3,337)
68. ((meats or meat) adj3 (packing or handling or processing)).tw,kf. (2,021)
69. farmer*.tw,kf. (33,388)
70. (agricultural adj (worker* or labo?rer*)).tw,kf. (2,832)
71. (farm adj (worker* or labo?rer*)).tw,kf. (1,795)
72. Farmers/ (4,671)
73. Farms/ (6,777)
74. exp *Animal Husbandry/ (12,435)
75. animal husbandry.tw,kf. (3,456)
76. animal handler*.tw,kf. (186)
77. ((domestic or companion) adj animal*).tw,kf. (16,221)
78. exp *Animals, Domestic/ (20,152)
79. ((livestock* or cattle* or cow or cows) adj2 human*).tw,kf. (6,869)
80. (pet or pets).tw,kf. (148,104)
81. (cat or cats).tw,kf. (172,544)
82. (dog or dogs).tw,kf. (244,834)
83. Cats/ or Dogs/ (466,311)
84. exp Camelidae/ (7,541)
85. llama*.tw,kf. (2,550)
86. alpaca*.tw,kf. (1,703)
87. Veterinarians/ (5,862)
88. (veterinarian or vet or veterinary nurse*).tw,kf. (7,083)
89. (occupational* expos* and (non-human* or animal* or livestock* or cattle* or cow* or wildlife)).tw,kf. (2,060)
90. Occupational Exposure/ and (non-human* or animal* or livestock* or cattle* or cow* or wildlife).tw,kf. (2,601)
91. or/49-90 (1,077,741)
92. (inhalation or inhale* or inhaling).tw,kf. (121,456)
93. aerosol*.tw,kf. (60,289)
94. ((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)
95. ((ventilation or ventilated) and (transmission* or distanc* or dispers*)).tw,kf. (5,126)
96. ((route or routes or mode or modes) adj2 (transmission* or transmit*)).tw,kf. (16,579)
97. (far field and (exposure* or transmission* or transmit*)).tw,kf. (827)
98. (long* distance* adj2 (transmission* or transmit*)).tw,kf. (422)
99. bioaerosol*.tw,kf. (2,469)
100. droplet*.tw,kf. (69,721)
101. exp *Body Fluids/ (175,714)

102. body fluid*.tw,kf. (28,691)
103. (infect* adj (hide* or tissue*)).tw,kf. (5,754)
104. (exhalation or exhale* or exhaling).tw,kf. (17,984)
105. Inhalation Exposure/ (10,621)
106. Inhalation/ (5,973)
107. Exhalation/ (5,158)
108. Aerosols/ (35,724)
109. direct contact*.tw,kf. (18,669)
110. Skin Absorption/ (13,104)
111. ((cutaneous or skin or dermal*) adj1 contact*).tw,kf. (4,428)
112. ((cutaneous or skin or dermal*) adj3 absorb*).tw,kf. (1,040)
113. Fomites/ (669)
114. fomite*.tw,kf. (1,590)
115. indirect transmission.tw,kf. (460)
116. (contaminat* adj3 (surface* or environment* or touch*)).tw,kf. (21,547)
117. transmi*.ti,kf. (143,568)
118. transmission.fs. (162,891)
119. or/92-118 (803,949)
120. 28 and 48 (4,579)
121. 28 and 91 (4,173)
122. 120 or 121 (7,729)
123. 48 or 91 or 119 (1,981,723)
124. 21 and 123 (4,546)
125. 122 or 124 (8,997)
126. limit 125 to (comment or editorial or letter or news) (491)
127. 125 not 126 (8,506)

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 tuberculosis subsp* caprae.tw,kf. (3)
23. or/1-22 (20,325)
24. Mycobacterium tuberculosis/ (80,138)
25. tuberculosis/ or latent tuberculosis/ (145,167)
26. Mycobacterium tuberculosis.tw,kf. (65,399)
27. "M.tuberculosis".tw,kf. (681)
28. M tuberculosis.tw,kf. (25,547)
29. tuberculosis.tw,kf. (227,492)
30. or/24-29 (277,237)
31. (transmi* adj3 (non-human* or nonhuman* or animal* or livestock* or cattle* or cow* or bovine or wildlife or wild life)).tw,kf. (6,331)
32. exp disease transmission/ and ((non-human* or animal* or livestock* or cattle* or cow* or wildlife).tw,kf. or (exp ruminant/ or domestic animal/)) (30,230)
33. ((Community or disease* or infection*) adj3 spread*).tw,kf. (37,799)
34. ((non-human* or animal* or livestock* or cattle* or cow* or wildlife*) adj3 (vector* or reservoir*)).tw,kf. (5,961)
35. exp disease reservoir/ (1,354)
36. zoonosis/ or bacterial zoonosis/ (22,032)
37. (zoonotic* or zoonos#s).tw,kf. (53,137)
38. animal* to human*.tw,kf. (43,908)
39. (animal adj1 human adj1 interface*).tw,kf. (435)
40. (livestock adj1 human adj1 interface*).tw,kf. (68)
41. (wildlife adj1 human adj1 interface*).tw,kf. (100)
42. ((livestock or animal* or wildlife) adj1 spillover).tw,kf. (23)
43. ((livestock or animal* or wildlife) adj1 spill over).tw,kf. (0)
44. (interspecies or inter species).tw,kf. (17,834)
45. between species.tw,kf. (17,730)
46. cross species.tw,kf. (10,892)
47. (infect* adj (animal* or livestock* or cattle* or cow* or wildlife)).tw,kf. (19,957)
48. exp *animal/ and human/ and transmi*.tw,kf. (23,458)
49. or/31-48 (243,487)
50. (pasteuris* or pasteuriz*).tw,kf. (7,377)
51. (unpasteuris* or unpasteuriz* or un-pasteuris* or un-pasteuriz*).tw,kf. (1,651)
52. raw milk.tw,kf. (4,887)
53. raw meat.tw,kf. (1,790)
54. raw meat/ (1,235)
55. raw animal produc*.tw,kf. (32)
56. pasteurization/ (3,780)

57. pasteurized milk/ or raw milk/ (1,516)
58. exp dairy product/ (133,278)
59. (dairy adj3 (eat* or drink* or consum*)).tw,kf. (4,317)
60. (dairy adj (produc* or food* or farm*)).tw,kf. (27,757)
61. (milk* or cheese* or yoghurt* or yogurt*).tw,kf. (196,576)
62. ((meats or meat) adj3 (eat* or consum* or produc*)).tw,kf. (24,117)
63. ((pork or beef or bacon or chicken or turkey or poultry) adj3 (eat* or consum* or produc*)).tw,kf. (16,741)
64. (contamina* adj3 (food* or drink* or beverage* or meat* or dairy or milk* or cheese* or yoghurt*)).tw,kf. (26,274)
65. abbattoir*.tw,kf. (7)
66. abbatoir*.tw,kf. (65)
67. abattoir*.tw,kf. (5,670)
68. slaughterhous*.tw,kf. (6,767)
69. slaughter hous*.tw,kf. (704)
70. slaughterhouse/ (11,474)
71. ((meats or meat) adj3 (packing or handling or processing)).tw,kf. (1,901)
72. farmer*.tw,kf. (37,032)
73. (agricultural adj (worker* or labo?rer*)).tw,kf. (2,754)
74. (farm adj (worker* or labo?rer*)).tw,kf. (2,101)
75. agricultural worker/ (30,290)
76. exp agricultural land/ (25,715)
77. animal husbandry/ (20,976)
78. animal husbandry.tw,kf. (3,933)
79. animal handler*.tw,kf. (227)
80. ((domestic or companion) adj animal*).tw,kf. (17,552)
81. domestic animal/ (16,105)
82. ((livestock* or cattle* or cow or cows) adj2 human*).tw,kf. (7,446)
83. wild animal/ (13,909)
84. (pet or pets).tw,kf. (256,709)
85. (cat or cats).tw,kf. (186,395)
86. (dog or dogs).tw,kf. (251,004)
87. exp cat/ or exp dog/ (397,962)
88. exp camelid/ (8,498)
89. llama*.tw,kf. (2,442)
90. alpaca*.tw,kf. (2,013)
91. exp veterinarian/ (9,243)
92. (veterinarian or vet or veterinary nurse*).tw,kf. (9,716)
93. (occupational* expos* and (non-human* or animal* or livestock* or cattle* or cow* or wildlife)).tw,kf. (2,682)
94. occupational exposure/ and (non-human* or animal* or livestock* or cattle* or cow* or wildlife).tw,kf. (4,387)
95. or/50-94 (1,213,881)
96. (inhalation or inhale* or inhaling).tw,kf. (170,388)

97. aerosol*.tw,kf. (80,877)
98. ((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)
99. ((ventilation or ventilated) and (transmission* or distanc* or dispers*)).tw,kf. (7,188)
100. ((route or routes or mode or modes) adj2 (transmission* or transmit*)).tw,kf. (19,486)
101. (far field and (exposure* or transmission* or transmit*)).tw,kf. (694)
102. (long* distance* adj2 (transmission* or transmit*)).tw,kf. (396)
103. bioaerosol*.tw,kf. (3,427)
104. droplet*.tw,kf. (79,557)
105. exp body fluid/ (3,003,264)
106. body fluid*.tw,kf. (31,816)
107. (infect* adj (hide* or tissue*)).tw,kf. (6,314)
108. (exhalation or exhale* or exhaling).tw,kf. (27,087)
109. inhalational exposure/ (314)
110. inhalation/ (30,955)
111. exhalation/ (6,339)
112. aerosol/ (67,842)
113. direct contact*.tw,kf. (22,678)
114. skin absorption/ (8,463)
115. ((cutaneous or skin or dermal*) adj1 contact*).tw,kf. (5,643)
116. ((cutaneous or skin or dermal*) adj3 absorb*).tw,kf. (1,442)
117. fomite/ (906)
118. fomite transmission/ (129)
119. fomite*.tw,kf. (1,820)
120. indirect transmission.tw,kf. (478)
121. (contaminat* adj3 (surface* or environment* or touch*)).tw,kf. (24,809)
122. transmi*.ti,kf. (161,147)
123. or/96-122 (3,574,778)
124. 30 and 49 (5,360)
125. 30 and 95 (6,527)
126. 49 or 95 or 123 (4,814,725)
127. 23 and 126 (8,253)
128. 125 or 127 (12,926)
129. limit 128 to (conference abstract or conference paper or editorial or letter) (2,690)
130. 128 not 129 (10,236)

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

Date of search: 13 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 tuberculosis subsp* caprae") OR TS=("Mycobacterium tuberculosis") OR TS=("M.tuberculosis") OR TS=("M tuberculosis") OR TS=(tuberculosis)

AND

TS=((transmi* NEAR/2 (non-human* or nonhuman* or animal* or livestock* or cattle* or cow* or bovine or wildlife or "wild life"))) OR TS=(((Community or disease* or infection*) NEAR/2 spread*)) OR TS=(((non-human* or animal* or livestock* or cattle* or cow* or wildlife*) NEAR/2 (vector* or reservoir*))) OR TS=((zoonotic* or zoonos?s)) OR TS=("animal* to human*") OR TS=((animal NEAR/0 human NEAR/0 interface*)) OR TS=((livestock NEAR/0 human NEAR/0 interface*)) OR TS=((wildlife NEAR/0 human NEAR/0 interface*)) OR TS=(((livestock or animal* or wildlife) NEAR/0 spillover)) OR TS=(((livestock or animal* or wildlife) NEAR/0 "spill over")) OR TS=((interspecies or "inter species")) OR TS=("between species") OR TS=((infect* NEAR/0 (animal* or livestock* or cattle* or cow* or wildlife))) OR TS=(human and transmi*) OR TS=((pasteuris* or pasteuriz*)) OR TS=((unpasteuris* or unpasteuriz* or un-pasteuris* or un-pasteuriz*)) OR TS=("raw milk") OR TS=("raw meat") OR TS=("raw animal produc*") OR TS=((dairy NEAR/2 (eat* or drink* or consum*))) OR TS=((dairy NEAR/0 (produc* or food* or farm*))) OR TS=((milk* or cheese* or yoghurt* or yogurt*)) OR TS=(((meats or meat) NEAR/2 (eat* or consum* or produc*))) OR TS=(((pork or beef or bacon or chicken or turkey or poultry) NEAR/2 (eat* or consum* or produc*))) OR TS=((contamina* NEAR/2 (food* or drink* or beverage* or meat* or dairy or milk* or cheese* or yoghurt*))) OR TS=(abbattoir*) OR TS=(abbatoir*) OR TS=(abattoir*) OR TS=(slaughterhous*) OR TS=("slaughter hous*") OR TS=(((meats or meat) NEAR/2 (packing or handling or processing))) OR TS=(farmer*) OR TS=((agricultural NEAR/0 (worker* or labo$rer*))) OR TS=((farm NEAR/0 (worker* or labo$rer*))) OR TS=("animal husbandry") OR TS=("animal handler*") OR TS=(((domestic or companion) NEAR/0 animal*)) OR TS=(((livestock* or cattle* or cow or cows) NEAR/1 human*)) OR TS=((pet or pets)) OR TS=((cat or cats)) OR TS=((dog or dogs)) OR TS=(llama*) OR TS=(alpaca*) OR TS=((veterinarian or vet or "veterinary nurse*")) OR TS=(("occupational* expos*" and (non-human* or animal* or livestock* or cattle* or cow* or wildlife))) 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*))) OR TS=(transmi*)

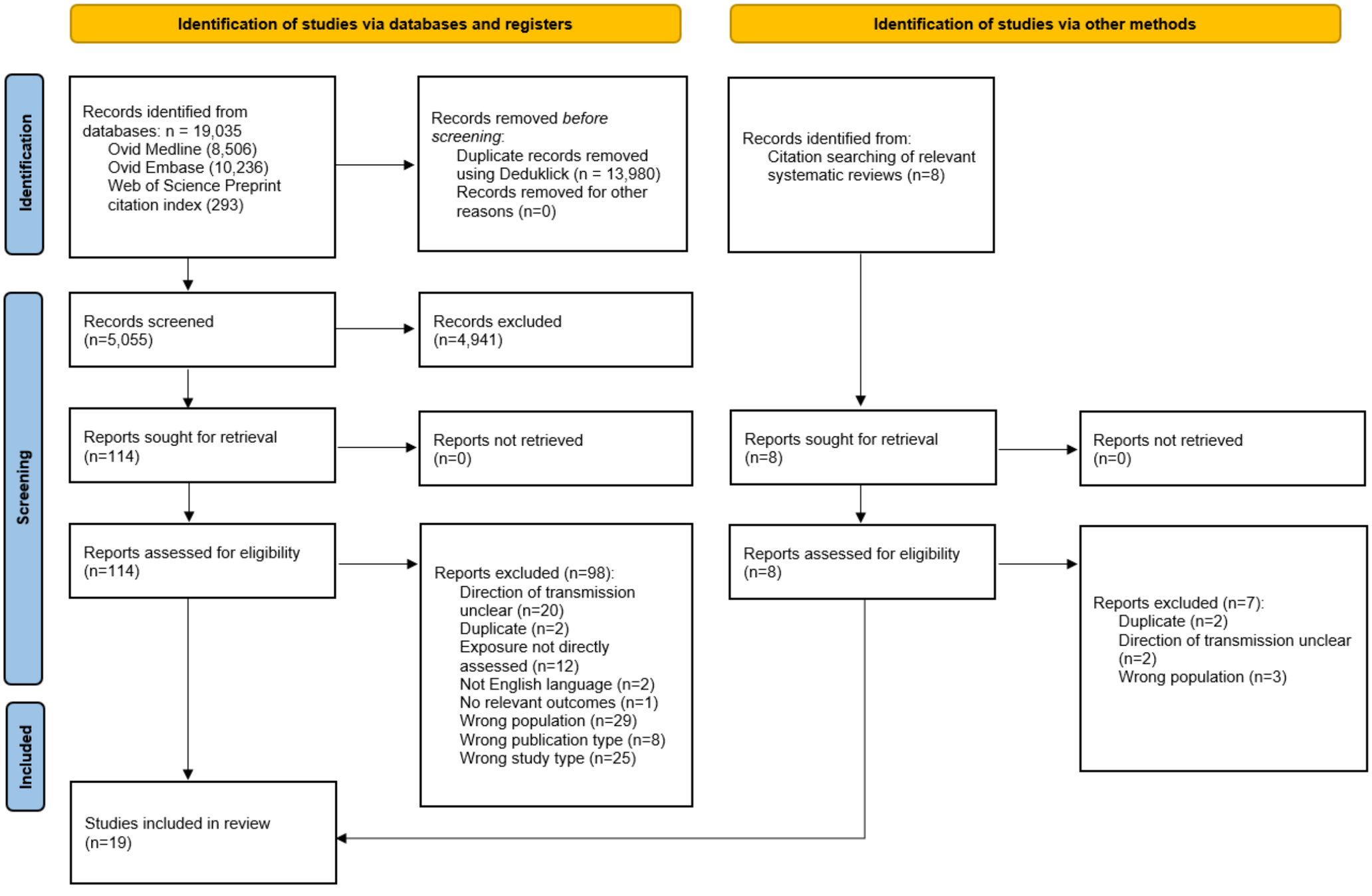
293 results.

Deviations

There were no deviations from the review protocol.

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 17 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, 105 reports were excluded:

- direction of transmission unclear (n=22)
- duplicate (n=4)
- exposure not directly assessed (n=12)
- not English language (n=2)
- no relevant outcomes (n=1)
- wrong population (n=32)
- wrong publication type (n=8)
- wrong study type (n=25)

16 papers were included in the review.

Annexe C. Excluded full texts

Direction of transmission unclear (22 studies)

Abdel-Moein KA 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, 2106981

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

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

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

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

Kassa GM 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

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

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

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, page 45,444

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

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

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. '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 SD 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 SD 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

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 Bryan 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' Volume 4 Issue 4 2015

Sichewo EA 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 8,875, 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. '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. 'The role of tuberculin-positive cattle in human extrapulmonary tuberculosis' Orvosi Hetilap 1963: volume 104, pages 832 to 834

No relevant outcomes (1 study)

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

Wrong population (32 studies)

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

Anonymous. 'Human tuberculosis caused by *Mycobacterium bovis*--New York City, 2001-2004' 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

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

Brassard P. '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

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

Ciambrone L and others. 'Presence of *Mycobacterium bovis* in slaughterhouses and risks for workers' Preventive Veterinary Medicine 2020: volume 181, page 105,072

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

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

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

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, 865924

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. '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

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, issue Supplement 1, pages S35 to S37

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

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, issue 7, pages 1,191 to 1,199

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

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

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

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 and others. '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 1,536 to 1,541

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

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

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

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

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

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

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 Suppl 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 JIT. '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 (25 studies)

Akkerman OW and others. 'Infection of great apes and a zoo keeper 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

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. '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

de la Rua-Domenech. '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

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

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 human beings in contact with elk (Cervus elaphus) in Alberta, Canada' Lancet 1991: volume 338, issue 8,777, pages 1,253 to 1,255

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 LAJ 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

Lee JY 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

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 Supplement 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 MH and others. '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, volume 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 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

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

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

Annexe D. Data extraction tables

Abbreviations: AIDS: acquired immunodeficiency syndrome, BCG: bacillus calmette-guérin, CI: confidence interval, CXR: chest x-ray, EPTB: extrapulmonary tuberculosis, HIV: human immunodeficiency virus, IGRA: interferon-gamma release assay, LTBI: latent TB infection, *M. bovis*: *Mycobacterium bovis*, *M. TB*: *Mycobacterium tuberculosis*, OR: odds ratio, PCR: polymerase chain reaction, PPD: purified protein derivative, PR: prevalence ratio, PTB: pulmonary tuberculosis, RR: risk ratio, SD: standard deviation, TST: tuberculin skin test, X^2: chi-squared

Table D.1. Studies of TB transmission in people who ate or drank raw dairy products

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
Bapat 2017 (1)	India, March 2014 to June 2015	Prospective cohort	Group A: - 105 farmers, dairy workers and livestock keepers - 25 samples PCR positive (23.8%) - age: less than 18 years. = 2 (1.9%), 18 to 40 years= 62 (59.1%), more than 40 years = 41 (39%) - sex: 72 male (68.6%), 33 female (31.4%) Group B: - 45 zoo-keepers and animal handlers - 11 samples PCR positive (24.4%) - age: less than 18 years= 0 (0%), 18 to 40 years= 11 (24.4%), more than 40 years= 34 (75.6%) - sex: 41 male (91.1%), 4 female (8.9%) One sample corresponded to one individual	Measurement of exposure: questionnaire Drank raw milk: - group A: 51 (48.6%) - group B: 2 (4.4%)	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)	Differential tests performed: yes (genotyping) *M. bovis*: Group A: 12 (11.4%) Group B: 4 (8.9%) *M.TB*: Group A: 13 (12.4%) Group B: 7 (15.6)	Odds of TB in people who drank raw milk (reference = people who did not drink raw milk)	Group A (farmers): OR: 6.3415 (95% CI: 1.3161 to 30.5553, p=0.0213) No adjustment for potential confounding variables
							Odds of TB in people who drank raw milk (reference = people who did not drink raw milk)	Group B (zookeepers): OR: 1.7556 (95% CI: 0.0723 to 42.6042, p=0.7294) No adjustment for potential confounding variables
Coker 2006 (8)	Russia, 1 January to 31 December 2003	Case-control	334 cases with PTB and 334 controls with no history of TB (matched to cases for year of birth and sex)	Measurement of exposure: questionnaire - drinking raw milk: raw data not reported	Cases were described as culture confirmed TB, unclear if controls were tested for TB	Differential tests performed: no (unspecified *M. TB* complex species)	Odds of TB in people who drank raw milk (univariate analysis, reference = people who did not drink raw milk)	OR: 3.58 (95% CI: 2.58 to 4.97)

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			No demographic information reported				Odds of TB in people who drank raw milk (multivariate analysis, reference = people who did not drink raw milk)	OR: 2.75 (95% CI: 1.80 to 4.20) Adjusted for diabetes, relative with TB, possession of household assets, living with others, employment, shortage of food, financial security, smoking habit, alcohol drinking habit, illicit drug use, history of imprisonment
Gebre 2010 (2)	Ethiopia, February 2010	Cross-sectional	Overall sample: - 160 people with suspected PTB at a health centre Sex: 105 males (65.6%), 55 females (34.4%) Occupation: - farmers: 68 cases (42.5%) - students: 38 cases (23.8%) - house wives: 29 cases (18.1%) - governmental employee: 10 cases (6.3%) - merchants: 8 cases (5%) - others: 7 cases (4.4%) Origin: - rural: 125 cases (78.1%) - urban: 35 cases (21.9%)	Measurement of exposure: questionnaire Drinking raw milk - raw data not reported	Smear positivity only 17 smear positive cases out of 160 (10.6%)	Differential test performed: no (unspecified *M. TB* complex species including *M. TB*, *M. bovis* and *M. africanum*)	Association between drinking raw milk and smear positivity	X^2: 8.99, p=0.003
Gebremichael 2018 (13)	Ethiopia, August to December 2016	Case-control	**Cases:** - 144 children, of which 142 participated, recruited from health clinics where they were receiving treatment for TB Sex:	Measurement of exposure: interview Drank raw milk: - cases: yes = 105 (73.9%), no = 37 (26.1%) - controls: yes = 86	Cases: diagnostic test not directly reported, but cases were receiving TB treatment (study states: TB diagnosis made based on National Comprehensive Tuberculosis, Leprosy,	Differential tests performed: no (unspecified *M. TB* complex species)	Odds of TB in children who drank raw milk (univariate analysis, reference = people who did not drink raw milk)	OR: 6.53 (95% CI: 4.16 to 10.27)
							Odds of TB in children who drank raw milk (multivariate	OR: 4.23 (95% CI: 2.26 to 7.88) Adjusted for: age, mother's educational status, number of

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			- 71 males (50%) and 71 females (50%) - mean age: 8.4 years (SD: 4.3 years) Family history of TB: - yes: 45 (31.7%) - no: 97 (68.3%) BCG vaccination status: - yes: 103 (72.5%) - no: 39 (27.5%) HIV status: - positive: 16 (11.3%) - negative or unknown: 126 (88.7%) **Controls:** - 288 children of which 284 participated attending health clinics for any reason other than TB - sex: 136 male (47.9%) and 148 females (52.1%) - mean age: 7.3 years (SD: 4.1 years) Family history of TB: - yes: 10 (3.5%) - no: 274 (96.5%) BCG vaccination status: - yes: 277 (97.5%) - no: 7 (2.5%) HIV status: - positive: 4 (1.4%) - negative or unknown: 280 (98.6%)	(30.3%), no = 196 (69.7%)	and TB or HIV Diagnosis and Treatment Manual) Controls: the study does not report that any tests were performed to confirm controls did not have TB (however any children with TB associated symptoms were excluded)		analysis, reference = people who did not drink raw milk)	people residing in the house, availability of windows and separate kitchen, presence of waste disposal, presence of animals living in the house, drank raw milk, BCG vaccination status and family history of TB
Getachew 2023 (Preprint) (12)	Ethiopia, March 2019	Case-control	**Cases:** 31 cattle owners (of 115	Measurement of exposure: structured	Cases: smears, culture (31 collected from 31	Differential tests performed: no	Odds of TB in 21 people who drank	OR = 4.27 (95% CI: 1.29 to 14.1, p value not reported)

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
	to January 2020		cattle) who were newly diagnosed as new smear positive PTB patients Age: - 18 to 24 years = 7 (22.6%) - 25 to 59 years = 21 (67.7%) - more than 59 years = 3 (9.7%) Sex: 19 males (61.3%), 12 females (38.7%) Contact history with human TB cases: yes = 10 (32.3%), no = 21 (67.7%) Type of work: employment = 3 (9.7%), farmer = 24 (77.4%), merchant = 4 (12.9%) **Controls:** 61 cattle owners (of 222 cattle) Age: - 18 to 24 years = 8 (13.1%) - 25 to 59 years = 45 (73.8%) - more than 59 years = 8 (13.1%) Sex: 37 males (60.7%), 24 females (39.3%) Contact history with human TB cases:	interview using a questionnaire Milk drinking habit - cases: boiled milk = 7 (22.6%), sour milk = 11 (35.5%), raw milk = 13 (41.9%) - controls: boiled milk = 21 (34.3%), sour milk = 32 (52.5%), raw milk = 8 (13.1%)	cases) Controls: no diagnostic test performed, living in same village as cases but with no productive cough for at least 2 weeks Cattle: intradermal tuberculin test, milk sample culture (8 from tuberculin positive cows)	(unspecified *M. TB* complex species)	raw milk (univariate analysis, reference = 28 people who drank boiled milk	
							Odds of 21TB in people who drank raw milk (multivariate analysis, reference = people who drank boiled milk)	OR: 9.97 (95% CI: 1.67 to 59.35, $p < 0.05$) Adjusted for potential confounders which included variables with $p < 0.05$ at univariate analysis. Specific confounders not fully reported, but paper mentions age and sex

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			yes = 7 (11.5%), no = 54 (88.5%) Type of work: employment = 8 (13.1%), farmer = 44 (72.1%), merchant = 9 (14.8%)					
Fetene 2011 (11)	Ethiopia, December 2007 to May 2008	Case-control	**Cases:** - 105 cattle owners with TB and 212 cattle - 80 cases with PTB and 25 cases with EPTB (combined demographics for both TB types) - age: less than 18 years: 19, 18 to 40 years: 60, more than 40 years: 26 - sex: 44 (42%) female, 61 male (58%) **Controls:** - 105 cattle owners with 212 cattle who visited the same hospital as cases for 'any reason other than TB' - age: less than 18 years: 22, 18 to 40 years: 58, more than 40 years: 25 - sex: 37 female (35%), 68 male (65%) Type of work: not reported	Measurement of exposure: questionnaire Contact with cattle: - cases: yes:94, no: 11 - controls: yes:96, no: 9 Milk consumption (raw, mixed, or boiled): - cases: raw: n=60, mixed: n=28, boiled: n=17 - controls: raw: n=87, mixed: n=8, boiled: n=10	Humans: CXR, sputum staining and culture, lymph node aspiration, ultrasound and other unspecified methods Animals: comparative intradermal tuberculin test	Differential tests performed: yes (colony morphology and nitrate reduction test) Humans: *M. TB* (35 cases), *M. bovis* (8 cases), other unspecified atypical mycobacteria (4 cases) Animals: not reported	Odds of TB in people who drank raw milk compared to those who did not drink raw milk	Unadjusted OR: 3.23 p=0.001
Gompo 2020 (10)	Nepal, January 2018 to December 2019	Case-control	**Cases:** - 145 TB cases from the National TB centre Age: - 1 to 15 years : 6 cases (4.1%) - 16 to 30 years: 70 cases (48.3%)	Measurement of exposure: interview using questionnaire Contact with sick cattle or unpasteurized dairy product consumption: Cases: 93 = yes, 52 =	Human: not reported Animals: intradermal comparative TB test	Differential tests performed: no Human: Not differentiated (likely *M. bovis* or *M. TB*) Animals: *M. bovis*	Odds of TB positivity in people who reported contact with sick cattle or consumed raw dairy products (multivariate analysis, reference = people who reported no contact with sick	OR: 3.9 (95% CI: 2.1 to 7.4, p < 0.001) Adjusted for smoking habit and previous TB history

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			- 31 to 45 years : 25 cases (17.2%) - 46 to 60 years : 21 cases (14.5%) - 61 to 75 years : 18 cases (12.4%) - over 75 years : 5 cases (3.4%) Sex: 84 males (42.1%), 61 females (57.9%) BCG vaccination: - yes: 59 cases (40.7%) - no: 37 cases (22.5%) - patient doesn't know: 49 cases (33.8%) Type of work: - housewives: 19 cases (13.1%) - farmers: 21 cases (14.5%) - businesses: 11 cases (7.6%) - students: 35 cases (24.1%) - others (drivers, labourers, service people): 59 cases (40.7% **Controls:** - 145 relatives of non-TB patients matched for areas of residence Age: - 1 to 15 years : 5 controls (3.4%) - 16 to 30 years: 57	no Controls: 63 = yes, 82 = no			cattle and never consumed raw dairy products)	

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			controls (39.3%) - 31 to 45 years : 39 controls (26.9%) - 46 to 60 years : 32 controls (22.1%) - 61 to 75 years : 8 controls (5.5%) - over 75 years : 4 controls (2.8%) Sex: 77 males (46.9%), 68 females (53.1%) BCG vaccination: - yes: 52 controls (35.9%) - no: 35 controls (24.1%) - patient doesn't know: 58 controls (40.0%) Type of work: - housewives: 46 controls (31.7%) - farmers: 22 controls (15.2%) - businesses: 11 controls (7.6%) - students: 19 controls (13.1%) - others (drivers, labourers, service people): 47 controls (32.4%)					
Jabeen 2024 (9)	Pakistan, not reported	Case-control	**Cases:** - 85 people with TB who owned livestock, recruited from hospitals Age: 15 to 24 years old: 20, 25 to 34 years old: 13, 35 to 44 years old: 16, 45 to 54 years old: 8, 55 years and	Measurement of exposure: interview using questionnaire Cases: - drank raw milk: yes: 26, no: 38 Controls: - drank raw milk: yes: 7, no: 71	Cases: symptoms, CXR Controls: "no clinical signs of TB like illness at the time of visit"	Differential tests performed: no (*M. bovis* or *M. TB*)	Odds of TB in people who drank raw milk (univariate analysis, reference = people who did not drink raw milk)	OR: 6.5 (95% CI: 2.75 to 15.35, p < 0.0001)
							Odds of TB in people who drank raw milk (multivariate analysis, reference = people	OR: 7.7 (95% CI: 1.95 to 30.68, p=0.003) Adjusted for gender, working at a cattle farm, and living in a large family

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			above: 28 Sex: male: 40, female: 45 BCG vaccination: yes: 48 (56.5%), no: 37 Type of work: not reported **Controls:** - 85 people without TB who owned livestock, matched to cases from the same village Age: 15 to 24 years old: 9, 25 to 34 years old: 45, 35 to 44 years old: 17, 45 to 54 years old: 8, 55 years and above: 6 Sex: male: 71, female: 14 BCG vaccination: yes: 76 (89.4%), no: 9 Type of work: not reported				who did not drink raw milk)	
Meisner 2019 (3)	Uganda, 2014 to 2016	Cross-sectional	493 livestock owners - sex: 250 males (50.7%) - age: mean = 40.8 (SD: 14.0) - 184 people with TB (37.3%) No TB reactors in cattle herd (n=405) - 200 (49.4%) - age: mean = 40.8 (SD: 14.2)	Measurement of exposure: questionnaire Frequency of milk drinking per week: Overall: mean = 2.46 (SD: 3.0) Sometimes consume raw milk: people with TB: 39 (22.8%)	Humans: TST only Animals: caudal fold test	Differential tests performed: no (reported as human TB, no species provided)	PR of TST positivity in people who drank raw milk (total effect)	PR: 0.94 (95% CI: 0.64 to 1.39) adjusted for self-reported knowledge of TB
							PR of TST positivity in people who drank raw milk (direct effect, reference = people who did not consume raw milk)	PR: 0.94 (95% CI: 0.64 to 1.39) adjusted for sex, religion, TST positivity in other household members and self-reported knowledge of TB *Cattle herd size was identified as a potential confounder of the raw milk-TST association but was not adjusted for due to the large amount of missing data

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			At least one TB reactor (n=88) - 50 (56.8%) - age: mean = 40.7 (SD: 13.3) Type of work: not reported (other than livestock keeping, which may or may not be their type of work)	people without TB: 86 (32.1%)				(169 out of 493 observations missing)
							PR of TST positivity when people sometimes drank raw milk, no TB reactor in herd combined (multivariate analysis, reference = no reactors in herd, never consume raw milk, n=258)	PR: 0.75 (95% CI: 0.55 to 1.03), n=100 (reference n=258) No confounder adjustment performed
							PR of TST positivity when people never drank raw milk, TB reactor in herd (multivariate analysis, reference = no reactors in herd, never consume raw milk, n=258)	PR: 0.92 (95% CI: 0.70 to 1.22), n=56 (reference n=258) No confounder adjustment performed
							PR of TST positivity when people sometimes drank raw milk, TB reactor in herd (multivariate analysis, reference = no reactors in herd, never consume raw milk, n=258)	PR: 0.66 (95% CI: 0.29 to 1.50), n=25 (reference n=258) No confounder adjustment performed
Monde 2023 (4)	Zambia, April 2020 to December 2021	Cross-sectional	Humans: - 255 people recruited from TB outpatient clinics, 26 of which (10.2%) were infected with *M. TB* Sex: 150 males, 105 females Age: - 0 to 24 years: 38 cases - 25 to 44 years: 132 cases	Measurement of exposure: questionnaire Drank milk regularly: - yes = 48, people with TB = 9 (18.8%) - no = 207, people with TB = 17 (8.2%) Frequency of milk drinking:	Humans: not reported Animals: PCR	Differential tests performed: for animals only (genotyping) Humans: *M. TB* (assumed) Animals: *M. bovis*	Odds of TB in people who drank raw milk on a daily or weekly basis (univariate analysis, reference = people who drank raw milk when needed)	OR: 2.50 (95% CI: 1.62 to 3.87), p<0.001
							Odds of TB in people who drank raw milk (univariate analysis, reference: people	OR: 0.42 (95% CI: 0.16 to 1.08), p=0.063

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			- more than 45 years: 85 cases HIV status: - reactive*: 100 (of which 11 were people with TB) - non-reactive: 149 (of which 19 were people with TB) - no difference (p=0.680) was identified in the number of people who were HIV reactive and people with TB Type of work: - farmer: 117 cases - trader: 47 cases - others: 91 cases Cattle: - 156 cattle carcasses tested, 62 of which (39.7%) were infected with *M. bovis* - 90 out 156 (57.7%) male - median age: 9.47 years	- daily or weekly = 46, people with TB = 13 (28.3%) - when needed = 209, people with TB = 13 (6.2%) Type of milk: - boiled = 153, people with TB = 20 (13.1%) - raw = 102, people with TB = 6 (5.9%)			who consumed boiled milk)	
							Odds of TB in people who drank raw milk on a daily or weekly basis (multivariate analysis, reference = people who drank raw milk when needed	OR: 2.72 (95% CI: 1.73 to 4.28) Adjusted for main source of meat, drank milk regularly, how milk is consumed, water treated, contact with TB patients
Silva 2018 (14)	Brazil, March 2008 to February 2010	Case-control (nested within previous cross-sectional study)	Cross-sectional study demographics 189 people recruited from 2 public referral centres for human TB treatment housing area: urban area = 185, rural = 4 Nested case-control study demographics 45 selected for inclusion in nested case-control study	Measurement of exposure: interview Eating of above median levels of raw-milk cheese: - cases = 3 out of 3 - controls = 19 out of 42	cases and controls: culture (details not reported)	Differential tests performed: yes (genotyping) Cases: *M. bovis* and *M. TB* (co-infected) Controls: *M. TB* only	Odds of *M. bovis* in people who reported eating of above median levels of raw-milk cheese (univariate analysis, reference = no to eating of above median levels of raw-milk cheese)	OR*: 3.58 (95% CI: 2.02 to 24.13), p=0.055 (two-tailed), likelihood ratio: 4.70 *Haldane's correction applied for variables with zero frequency
							Odds of *M. bovis* in people who reported eating of above median levels of raw milk (univariate analysis, reference =	OR: not reported, 0 cases exposed, p=0.110 (two-tailed), likelihood ratio: 3.49

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			Cases: - 3 people (1.6%) co-infected with both *M. TB* and *M. bovis* - 2 EPTB, 1 PTB - sex: not reported (but matched to controls) - age: not reported (but matched to controls) - BCG vaccine: yes = 1, no = 2 - HIV or AIDs status: all negative **Controls** (14 controls matched for each case): - 42 people, infected with *M. TB* only - 5 EPTB, 37 PTB - sex: not reported, but matched to cases - age: not reported, but matched to cases (SD: 10 years) - BCG vaccine: yes = 9, no = 33 - HIV or AIDS status: 4 positive, 34 negative, 8 not reported Type of work: not reported				no to eating of above median levels of raw-milk cheese)	
Torres-Gonzalez 2013 (5)	Mexico, 2009 to 2011	Cross-sectional	Humans: - Overall cohort: 311 dairy farm workers - median age: 36 years (IQR: 27 to 45 years) - 78% male (244 out of 311) - Type of work: 268 dairy farm workers, 34 dairy farm	Measurement of exposure: questionnaire Milk consumption in 63 people with confirmed LTBI status: - 45 people with LTBI drank raw milk	Humans: LTBI confirmed by TST and IGRA, active TB confirmed by CXR and culture in participants with respiratory or systematic symptoms. Animals: post-mortem culture	Differential tests performed: yes (genotyping) M. bovis	Odds of raw milk consumption among individuals with concordant LTBI test results, comparing LTBI-positive individuals to LTBI-negative individuals (multivariable analysis, reference = people who had	OR: 0.40, 95% CI: 0.17 to 0.91, $p < 0.05$ Adjusted for age, sex, more than 4 hours of daily contact with cattle, more than 1 year of stay at the facility, high exposure activity reported, BCG scar and previous contact with TB cases

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			worker household contacts, 9 abattoir workers Subgroup of 190 people with confirmed LTBI status (both TST and IGRA positive or TST and IGRA negative): - LTBI positive: 149 - LTBI negative: 41 - mean age: 37.1 years (SD: 11.5 years) - 81% male (153 out of 190) - BCG scar: yes = 160, no = 23, unknown = 7 Cattle: - Of 1,561 routine necropsies performed during the study period on dead cattle, 154 had *M. bovis*	- 18 people without LTBI drank raw milk			exposure and tested negative)	
Tschopp 2009 (6)	Ethiopia, November 2006 to May 2007	Cross-sectional	450 cattle owners (demographic information not reported) - TB cases in the household (confirmed, TB or EPTB): 86 households Animals: 2,216 cattle	Diagnostic tests Measurement of exposure: interview Raw milk consumption: 68.5% (307 out of 448)	Humans: clinical diagnosis, testing regimen otherwise not reported Animals: skin test	Differential tests performed: no Humans: *M. bovis* or *M. TB* Animals: *M. bovis*	Odds of TB in people who drank raw milk (univariate analysis, reference = people who did not drink raw milk)	OR: 0.30 (95% CI: 0.50 to 1.80, p=0.70)
Winthrop 2005 (7)	USA, May 2002	Cross-sectional	Humans: - 88 people who potentially had contact with cattle during outbreak of *M. bovis* at a dairy farm Median age (range):	Measurement of exposure: questionnaire Drank raw milk: yes = 41, no = 47	Humans: TST, CXR if positive for TST and clinical evaluation Animals: screened with skin test and post-mortem culture	Differential tests performed: no (however no human contacts tested positive for TB and lesions in infected	Risk of positive TST result in people who drank raw milk (reference = people who did not drink raw milk, all TB negative)	Unadjusted RR: 1.5 (95% CI: 0.8 to 3.0, p=0.13)

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome	Result
			- overall: 22 years (0 to 45 years) - dairy staff: 22 years (17 to 42 years) - family of dairy staff: 13 years (0 to 42 years) - slaughterhouse staff: 35 years (20 to 45 years) Sex: 53 male, 26 female, 9 unknown Birth place: Mexico = 53, US = 25, unknown = 10 Received BCG vaccine: - yes: 49 - no: 28 - unknown: 11 Animals: - approximately 3,500 cattle screened, of which 38 cattle were positive for M. bovis			cattle were consistent with *M. bovis*)		

Table D.2. Studies of TB transmission in people who consumed raw meat

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome type	Result
Gebremichael 2018 (13)	Ethiopia, August to December 2016	Case-control	**Cases:** - 144 children, of which 142 participated, recruited from health clinics where they were receiving treatment for TB Sex: 71 males (50%) and 71 females (50%) - mean age: 8.4 years (SD:	Measurement of exposure: interview Ate raw meat: - cases: yes = 115 (81%), no = 27 (19%) - controls: yes = 204 (71.8%), no = 80 (28.2%)	Cases: diagnostic test not directly reported, but cases were receiving TB treatment (study states: TB diagnosis made based on National Comprehensive Tuberculosis, Leprosy, and TB or HIV Diagnosis and Treatment Manual Controls: the study does not	Differential tests performed: no (unspecified *M. TB* complex species)	Odds of TB in children who ate raw meat (univariate analysis, reference = no consumption of raw meat)	Unadjusted OR: 1.67 (95% CI: 1.01 to 2.73)

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome type	Result
			4.3 years) Family history of TB: - yes: 45 (31.7%) - no: 97 (68.3%) BCG vaccination status: - yes: 103 (72.5%) - no: 39 (27.5%) HIV status: - positive: 16 (11.3%) - negative or unknown: 126 (88.7%) **Controls:** - 288 children of which 284 participated attending health clinics for any reason other than TB - sex: 136 male (47.9%) and 148 females (52.1%) - mean age: 7.3 years (SD: 4.1 years) Family history of TB: - yes: 10 (3.5%) - no: 274 (96.5%) BCG vaccination status: - yes: 277 (97.5%) - no: 7 (2.5%) HIV status: - positive: 4 (1.4%) - negative or unknown: 280 (98.6%)		report that any tests were performed to confirm controls did not have TB (however, any children with TB associated symptoms were excluded)			
Tschopp 2009 (6)	Ethiopia, November	Cross-sectional	450 cattle owners (demographic information not reported)	Measurement of exposure: interview	Humans: clinical diagnosis, testing regimen otherwise	Differential tests performed: no	Odds of TB in people who ate raw meat	Unadjusted OR: 1.10 (95% CI: 0.60 to 2.00, p 0.60)

Study	Country, time period	Study type	Population	Exposure	Diagnostic method	TB species	Outcome type	Result
	2006 to May 2007		- TB case in the household (confirmed, TB or EPTB): 86 households Animals: 2,216 cattle	Raw meat consumption: 74.4% (334 out of 449)	not reported Animals: skin test	Humans: *M. bovis* or *M. TB* Animals: *M. bovis*	(univariate analysis, reference = no raw meat consumption)	

Table D.3. Studies of TB transmission in people living with animals

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
Gebremichael 2018 (13)	Ethiopia, August to December 2016	Case-control	**Cases:** - 144 children, of which 142 participated, recruited from health clinics where they were receiving treatment for TB - sex: 71 males (50%) and 71 females (50%) - mean age: 8.4 years (SD: 4.3 years) Family history of TB: - yes: 45 (31.7%) - no: 97 (68.3%) BCG vaccination status: - yes: 103 (72.5%) - no: 39 (27.5%) HIV status: - positive: 16 (11.3%) - negative or unknown: 126 (88.7%) **Controls:** - 288 children of which 284 participated attending health clinics for any	Measurement of exposure: interview Animals (unspecified) living in home: - cases: yes = 54 (38%), no = 88 (62%) - controls: yes = 34 (12%), no = 250 (88%)	Cases: diagnostic test not directly reported, but cases were receiving TB treatment (study states: TB diagnosis made based on National Comprehensive Tuberculosis, Leprosy, and TB or HIV Diagnosis and Treatment Manual Controls: the study does not report that any tests were performed to confirm controls did not have TB (however any children with TB associated symptoms were excluded)	Differential tests performed: no (unspecified *M. TB* complex species)	Odds of TB in children who lived with animals (univariate analysis, reference = not living with animals)	OR: 4.51 (95% CI: 2.76 to 7.39)
							Odds of TB in children who lived with animals (multivariate analysis, reference = not living with animals)	OR: 1.75 (95% CI: 0.86 to 3.56) Adjusted for: age, mother's educational status, number of people residing in the house, availability of windows and separate kitchen, presence of waste disposal, consumption of raw milk, BCG vaccination status and family history of TB

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			reason other than TB - sex: 136 male (47.9%) and 148 females (52.1%) - mean age: 7.3 years (SD: 4.1 years) Family history of TB: - yes: 10 (3.5%) - no: 274 (96.5%) BCG vaccination status: - yes: 277 (97.5%) - no: 7 (2.5%) HIV status: - positive: 4 (1.4%) - negative or unknown: 280 (98.6%)					
Getachew 2023 (Preprint) (12)	Ethiopia, March 2019 to January 2020	Case-control	**Cases:** 31 cattle owners (of 115 cattle) who were newly diagnosed as new smear positive PTB patients Age: - 18 to 24 years = 7 (22.6%) - 25 to 59 years = 21 (67.7%) - more than 59 years = 3 (9.7%) Sex: 19 males (61.3%), 12 females (38.7%) Contact history with human TB cases: yes = 10 (32.3%), no = 21 (67.7%)	Measurement of exposure: questionnaire 92 cases and controls were interviewed using a structured questionnaire about risk factors for TB transmission. House sharing with cattle - cases: yes = 12 (38.7%, no = 19 (61.3%) - controls: yes = 11 (18.0%), no = 50 (82.0%)	Cases: smears, culture (31 collected from 31 cases) Controls: no diagnostic test performed, living in same village as cases but with no productive cough for at least 2 weeks Cattle: intradermal tuberculin test, milk sample culture (8 from tuberculin positive cows)	Differential tests performed: no unspecified *M. TB* complex organism	Odds of TB in people living with cattle (univariate analysis, reference = not living with cattle)	OR: 2.87 (95% CI: 1.19 to 7.75, p value not reported)
							Odds of TB in people living with cattle (multivariate analysis, reference = not living with cattle)	OR: 8.11 (95% CI: 1.23 to 53.58, $p < 0.05$) Adjusted for potential confounders which included variables with $p < 0.05$ at univariate analysis. Specific confounders not fully reported, but paper mentions age and sex

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			Occupation: employment = 3 (9.7%), farmer = 24 (77.4%), merchant = 4 (12.9%) **Controls:** 61 cattle owners (of 222 cattle) Age: - 18 to 24 years = 8 (13.1%) - 25 to 59 years = 45 (73.8%) - more than 59 years = 8 (13.1%) Sex: 37 males (60.7%), 24 females (39.3%) Contact history with human TB cases: yes = 7 (11.5%), no = 54 (88.5%) Type of work: employment = 8 (13.1%), farmer = 44 (72.1%), merchant = 9 (14.8%)					
Jabeen 2024 (9)	Pakistan, not reported	Case-control	**Cases:** - 85 people with TB who owned livestock, recruited from hospitals Age: 15 to 24 years old: 20, 25 to 34 years old: 13, 35 to 44 years old: 16, 45 to 54 years old: 8, 55 years and	Measurement of exposure: interview using questionnaire Cases: - cohouse with cattle: yes: 30, no: 55 Controls: - cohouse with cattle: yes: 15, no: 70	Cases: symptoms, CXR Controls: "no clinical signs of TB like illness at the time of visit"	Differential tests performed: no *M. bovis* or *M.TB*	Odds of TB in people who co-house with cattle at night (univariate analysis, reference = no to co-housing with cattle at night)	OR: 2.5 (95% CI: 1.20 to 5.20, p=0.0143)

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			above: 28 Sex: male: 40, female: 45 - BCG vaccination: yes: 48 (56.5%), no: 37 Type of work: not reported **Controls:** - 85 people without TB who owned livestock, matched to cases from the same village Age: 15 to 24 years old: 9, 25 to 34 years old: 45, 35 to 44 years old: 17, 45 to 54 years old: 8, 55 years and above: 6 Sex: male: 71, female: 14 BCG vaccination: yes: 76 (89.4%), no: 9 Type of work: not reported					
Tschopp 2009 (6)	Ethiopia, November 2006 to May 2007	Cross-sectional	450 cattle owners (demographic information not reported) TB case in the household (confirmed, TB or EPTB): 86 households Animals 2,216 cattle	Measurement of exposure: interview Cattle housing at night: - outside shed: 11% (48 out of 499) - indoor with people: 46% (209 out of 449)	Humans: clinical diagnosis, testing regimen otherwise not reported Animals: skin test	Differential tests performed: no Humans: *M. bovis* or *M. TB* Animals: *M. bovis*	Odds of TB in people who house cattle indoors (univariate analysis, reference = free-roaming cattle, implied direction of transmission unclear)	OR: 1.00 (95% CI: 0.40 to 2.60, p=0.20)

Table D.4. Studies of TB transmission in people working with animals

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
Bapat 2017 (1)	India, March 2014 to June 2015	Prospective cohort	Group A: -105 farmers, dairy workers and livestock keepers - 25 samples PCR positive (23.8%) - age: less than 18 years= 2 (1.9%), 18 to 40 years= 62 (59.1%), more than 40 years= 41 (39%) - sex: 72 male (68.6%), 33 female (31.4%) Group B: -45 zoo-keepers and animal handlers - 11 samples PCR positive (24.4%) - age: less than 18 years = 0 (0%), 18 to 40 years = 11 (24.4%), more than 40 years = 34 (75.6%) - sex: 41 male (91.1%), 4 female (8.9%) One sample corresponded to one individual.	Measurement of exposure: questionnaire Animal contact: - group A: 82 (78.1%) - group B: 36 (80%) - group C: 49 (32.5%)	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)	Differential tests performed: yes (genotyping) *M. bovis*: Group A: 12 (11.4%) Group B: 4 (8.9%) *M.TB*: Group A: 13 (12.4%) Group B: 7 (15.6%)	Odds of TB in people in contact with animals (reference = no contact)	Group A (farmers): OR: 0.2237 (95% CI: 0.0642 to 0.7790, p=0.0187) No adjustment for potential confounding variables
							Odds of TB in people in contact with animals (reference = no contact)	Group B (zookeepers): OR: 2.6308 (95% CI: 0.1297 to 53.3659, p = 0.5288) No adjustment for potential confounding variables
Fetene 2011 (11)	Ethiopia, December 2007 to May 2008	Case-control	**Cases:** - 105 cattle owners with TB and 212 cattle - 80 cases with PTB and 25 cases with EPTB (combined demographics for both TB types) Age: less than 18 years: 19, 18 to 40 years: 60, more than 40 years: 26 Sex: 44 (42%) female, 61 male (58%)	Measurement of exposure: questionnaire Contact with cattle: - cases: yes:94, no: 11 - controls: yes:96, no: 9	Humans: CXR, sputum staining and culture, lymph node aspiration, ultrasound and other unspecified methods Animals: comparative intradermal tuberculin test	Differential tests performed: yes (colony morphology and nitrate reduction test) Humans: *M. TB* (35 cases), *M. bovis* (8 cases), other unspecified atypical mycobacteria (4 cases)	Difference in prevalence of TB in people who reported contact with cattle and people who did not report contact with cattle	p=0.647

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			Controls: - 105 cattle owners with 212 cattle who visited the same hospital as cases for 'any reason other than TB' Age: less than 18 years: 22, 18 to 40 years: 58, more than 40 years: 25 Sex: 37 female (35%), 68 male (65%)			Animals: not reported		
Jabeen 2024 (9)	Pakistan, not reported	Case-control	**Cases:** - 85 people with TB who owned livestock, recruited from hospitals - Age: 15 to 24 years old: 20, 25 to 34 years old: 13, 35 to 44 years old: 16, 45 to 54 years old: 8, 55 years and above: 28 Sex: male: 40, female: 45 BCG vaccination: yes: 48 (56.5%), no: 37 Type of work: not reported **Controls:** - 85 people without TB who owned livestock, matched to cases from the same village Age: 15 to 24 years old: 9, 25 to 34 years old: 45, 35 to 44 years old: 17, 45 to 54 years old: 8, 55 years and above: 6 Sex: male: 71, female: 14	Measurement of exposure: interview using questionnaire Cases: - work at cattle farm: yes: 53, no: 32 - cattle at home: yes: 31, no: 54 - contact with sick cattle: yes: 13, no: 72 - contact with coughing cattle: yes: 10, no: 75 Controls: - work at cattle farm: yes: 26, no: 59 - cattle at home: yes: 11, no: 74 - contact with sick cattle: yes: 3, no: 82 - contact with coughing cattle: yes: 2, no: 83	Cases: symptoms, CXR Controls: "no clinical signs of TB like illness at the time of visit"	Differential tests performed: no *M. bovis* or *M.TB*	Odds of TB in people working at a cattle farm (univariate analysis, reference = no to working at a cattle farm)	OR: 4.85 (95% CI: 2.15 to 10.9, p=0.00014)
							Odds of TB in people working at a cattle farm (multivariate analysis, reference = no to people working at a cattle farm)	OR: 4.2 (95% CI: 1.08 to 16.56, p=0.038) Adjusted for gender, raw milk consumption and living in a large family

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			BCG vaccination: yes: 76 (89.4%), no: 9 Type of work: not reported					
Meisner 2019 (3)	Uganda, 2014 to 2016	Cross-sectional	493 livestock owners - sex: 250 males (50.7%) - age: mean = 40.8 (SD: 14.0) - 184 people with TB (37.3%) No TB reactors in cattle herd (n=405) - 200 (49.4%) - age: mean = 40.8 (SD: 14.2) At least one TB reactor (n=88) - 50 (56.8%) - age: mean = 40.7 (SD: 13.3) Type of work: not reported (other than livestock keeping, which may or may not be their type of work)	Measurement of exposure: questionnaire No cattle reactors in herd: mean = 2.5 (SD: 3.0) At least one reactor: mean = 0.18 (SD: 0.4) Presence of *M. bovis*-positive cattle in herd: - 29 of 184 (15.8%) people who were people with TB - 59 of 309 (19.1%) people who were people without TB	Humans: TST only Animals: caudal fold test	Differential tests performed: no (reported as human tuberculosis, no species reported)	Prevalence ratio (PR) of TST positivity in people without any TB reactors in their herd (multivariate analysis, total effect, reference = TB reactors in herd)	PR: 0.87 (95% CI: 0.62 to 1.22) adjusted for religion
							PR of TST positivity in people with TB reactors in herd (multivariate analysis, direct effect, reference = no TB reactors in herd	PR: 0.87 (95% CI: 0.62 to 1.22) adjusted for religion and TST positivity in other household members
							PR of TST positivity in males (modifier) without any TB reactors in their heard (multivariate analysis, total effect, reference = males with TB reactors in herd)	PR: 0.66 (95% CI: 0.49 to 0.87) adjusted for religion
							PR of TST positivity in males (modifier) without any TB reactors in their heard (multivariate analysis, direct	PR: 0.68 (95% CI: 0.52 to 0.89) adjusted for religion and TST positivity in other household members

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
							effect, reference = males with TB reactors in herd)	
							PR of TST positivity in females (modifier) without any TB reactors in their heard (multivariate analysis, total effect, reference = females with TB reactors in herd)	PR: 1.21 (95% CI: 0.76 to 1.95) adjusted for religion
							PR of TST positivity in females (modifier) without any TB reactors in their heard (multivariate analysis, direct effect, reference = females with TB reactors in herd)	PR: 1.24 (95% CI: 0.79 to 1.97) adjusted for religion and TST positivity in other household members
Monde 2023 (4)	Zambia, April 2020 to December 2021	Cross-sectional	Humans: - 255 people recruited from TB outpatient clinics, 26 of which (10.2%) were infected with *M. TB* Sex: 150 males, 105 females Age: - 0 to 24 years: 38 cases - 25 to 44 years: 132 cases - more than 45 years: 85 cases HIV status: - reactive*: 100 (of which 11 were people with TB) - non-reactive: 149 (of which 19 were people with TB)	Measurement of exposure: questionnaire Handling beef products: - yes = 67, people with TB = 6 (9.0%) - no = 188, people with TB = 20 (10.6%) Main source of meat: - buy from others = 239, people with TB = 22 (9.2%) - own cattle = 16, people with TB = 4 (25.0%) Animal contact: - yes = 71 (6 people with TB)	Humans: not reported Animals: PCR	Differential tests performed: for animals only (genotyping) Humans: *M. TB* (assumed) Animals: *M. bovis*	Odds of TB in 71 people who have contact with animals (univariate analysis, reference: 184 people with no contact with animals, implied direction of transmission unclear)	OR: 0.76 (95% CI: 0.29 to 1.97), p=0.567
							Odds of TB in people who handled beef products (6 people	OR: 1.21 (95% CI: 0.46 to 3.11), p=0.696

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			- no difference (p=0.680) was identified in the number of people who were HIV reactive and people with TB Type of work: - farmer: 117 cases - trader: 47 cases - others: 91 cases Cattle: - 156 cattle carcasses tested, 62 of which (39.7%) were infected with M. bovis - 90 out 156 (57.7%) male - median age: 9.47 years	- no = 184 (20 people with TB)			with TB, 9.0%) (univariate analysis, reference: do not handle beef products, 20 people with TB, 10.6%)	
Murphree 2011 (15)	USA, 2006 to 2009	Retrospective cohort	Humans: - sample size: 46 employees included (57 contacted, 11 previous employees could not be reached) - all had at least one previous negative TST result. Sex: - 31 (67%) females - 15 (33%) males Age (mean): - 38 (range 20 to 65 years) Type of work: - 30 caregivers - 11 administrators - 5 maintenance workers - BCG vaccination: not reported - HIV status: not reported	Measurement of exposure: telephone interview Total cohort (46 cases) Close contact with elephants: - yes = 11, TST conversion = 2 (18.0%) - no = 35, TST conversion = 7 (20.0%) Quarantine area exposure during 2009: - yes = 13, TST conversion = 8 (62.0%) - no = 33, TST conversion = 1 (3.0%) Sub-group of employees who worked in the quarantine area in the outbreak period in 2009 (13 cases) Close contact with elephants: - yes = 3, TST conversion = 1 (33.3%) - no = 10, TST conversion = 7 (70.0%) Participated in elephant trunk washes:	Humans: TST Animals: culture genotyping (standard methods recommended by the Centres for Disease Control and Prevention)	Differential tests performed: yes (genotyping, elephants only) *M. TB* in elephant	Prevalence of TB	9 employees had positive TST results with indurations between 12 to 24 mm, but none were identified as having active TB - of all 13 employees who worked in the quarantine area for 4 hours or more and "observed their work practices in more detail" (of which 5 were elephant caregivers, 2 were maintenance workers, and 3 were administrators), one had a positive TST result after close contact with any elephant housed in the sanctuary - By the end of 2005, all elephants living at the refuge were *M. TB* negative from culture
							Risk of TB in the total cohort of	RR: 0.91 (95% CI: 0.22 to 3.75)

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			Animals: - 15 elephants housed in the sanctuary - one elephant with active TB (elephant L)	- yes = 1, TST conversion = 0 - no = 12, TST conversion = 8 (66.7%) Pressure washing barn walls and floors: - yes = 8, TST conversion = 5 (62.5%) - no = 5, TST conversion = 3 (60.0%) N95 respirator fit tested annually: - yes = 5, TST conversion = 2 (40.0%) - no = 8, TST conversion = 6 (75.0%) “Always” compliant with N95 wear: - yes = 5, TST conversion = 2 (40.0%) - no = 8, TST conversion = 8 (100.0%)			employees (n=46) who had contact with elephants	No adjustment for potential confounding variables
							Risk of TB in the total cohort of employees (n=46) who were exposed to the quarantine area during 2009	RR: 20.31 (95% CI: 2.81 to 146.69) No adjustment for potential confounding variables
							Risk of TB in employees with quarantine area exposure (n=13) who had close contact with elephants	RR: 0.48 (95% CI: 0.09 to 2.48) No adjustment for potential confounding variables
							Risk of TB in employees with quarantine area exposure (n=13) who pressure washed barn walls and floors	RR: 1.04 (95% CI: 0.43 to 2.55) No adjustment for potential confounding variables
							Risk of TB in employees with quarantine area exposure (n=13) who completed an N95 respirator fit test annually	RR: 0.53 (95% CI: 0.17 to 1.68) No adjustment for potential confounding variables
							Risk of TB in employees with quarantine area exposure (n=13) who reported themselves as 'always' compliant with N95 wear	RR: 0.53 (95% CI: 0.17 to 1.68) No adjustment for potential confounding variables

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
Sichewo 2019 (16)	South Africa, August to September 2017	Cross-sectional	Overall: - 150 people - sex: 94 male (62%), 56 female (38%) Age: - 16 to 64 years: 140 - over 64 years: 10 HIV prevalence: 55 (36%) positive Households with *M. bovis*-positive cattle: - 75 people Age: - 16 to 64 years: 68 - over 64 years: 7 Type of work: cattle farmers HIV: 40% (30 out of 75) positive Households with *M. bovis*-negative cattle: - 75 people Age: - 16 to 64 years: 72 - over 64 years: 3 Sex: not reported Type of work: cattle farmers HIV: 33% (25 out of 75) positive Animals: - cattle infected with *M. bovis*, numbers not reported. - 30 milk samples and 99 nasal	Measurement of exposure: questionnaire Completed by 71 participants (42 households with *M. bovis*-positive cattle [59%] and 41 households with *M. bovis* negative cattle [41%]). - involved in herding: yes = 100%, no =0% - involved in milking cows: yes =86%, no = 14% Family history of TB: - history of TB diagnosis in the family: 31 out of 71 (43.7%)* - no history of TB diagnosis in the family: 40 out of 71(56.3%)* Study reported rounded percentages, exact percentages calculated in this review.	Humans: PCR, culture Animals: IGRA conducted prior to study	Differential tests performed: yes (genotyping) Humans: unspecified mycobacterium TB complex organism (9 cases), *M.TB* (1 case) Animals: *M. bovis* (isolated from 9 nasal swabs (9% prevalence), and 2 milk samples (6.6%)	Prevalence of TB	Households with *M. bovis*-positive cattle: 7 PCR positive, one confirmed M. TB Households with *M. bovis*-negative cattle: 3 PCR positive, none confirmed with have TB

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			samples collected Context: The cattle owners were from 4 villages (Mnqobokasi, Makhasa, Mduku and Nibela), where *M. bovis* testing of cattle had been carried out as part of a research project in 2016 and 2017, so cattle TB status was known prior to the study.					
Silva 2018 (14)	Brazil, March 2008 to February 2010	Case-control (nested within previous cross-sectional study)	Cross-sectional study demographics: - 189 people - housing area: urban area = 185, rural = 4 - recruited from 2 public referral centres for human TB treatment Nested case-control study demographics 45 selected for inclusion in nested case-control study Cases: - 3 people (1.6%) co-infected with both *M. TB* and *M. bovis* - 2 EPTB, 1 PTB - sex: not reported (but matched to controls) - age: not reported (but matched to controls) - BCG vaccine: yes = 1, no = 2- HIV or AIDs status: all negative Controls (14 controls matched for each case): - 42 people, infected with *M. TB* only - 5 EPTB, 37 PTB	Measurement of exposure: interview Zoonotic potential exposures: - cases = 3 out of 3 - controls = 14 out of 42	Cases and controls: culture (details not reported)	Differential tests performed: yes (genotyping) Cases: *M. bovis* and *M. TB* (co-infected) Controls: *M. TB* only	Odds of M. bovis in people who reported zoonotic exposure (univariate analysis, reference = no zoonotic exposure, all TB negative)	OR*: 5.71 (95% CI: 2.827 to 40.99), p=0.024 (two-tailed), likelihood ratio: 5.92 *Haldane's correction applied for variables with zero frequency
							Odds of M. bovis in people who were HIV positive (univariate analysis, reference = HIV negative)	OR: not reported, 0 cases positive, p=0.71 (two-tailed), likelihood ratio: 0.12

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
			- sex: not reported, but matched to cases - age: not reported, but matched to cases (SD: 10 years) - BCG vaccine: yes = 9, no = 33 - HIV or AIDS status: 4 positive, 34 negative, 8 not reported					
Torres-Gonzalez 2013 (5)	Mexico, 2009 to 2011	Cross-sectional	Humans: - overall cohort: 311 dairy farm workers - median age: 36 years (IQR: 27 to 45 years) - 78% male (244 out of 311) Type of work: 268 dairy farm workers, 34 dairy farm worker household contacts, 9 abattoir workers Subgroup of 190 people with confirmed LTBI status (both TST and IGRA positive or TST and IGRA negative): - LTBI positive: 149 - LTBI negative: 41 - mean age: 37.1 years (SD: 11.5 years) - 81% male (153 out of 190) - BCG scar: yes = 160, no = 23, unknown = 7 Cattle: Of 1,561 routine necropsies performed during the study period on dead cattle, 154 had *M. bovis*	Measurement of exposure: questionnaire In people with confirmed LTBI status: - 70 out of 189 (37%) reported high exposure to cattle (direct contact in closed spaces, 1 exposure unknown), of which 65 out of 148 were LTBI positive and 18 out of 41 were LTBI negative - 111 out of 190 (58%) reported more than 4 hours of daily contact with cattle, of which 65 out of 148 were LTBI positive, 5 out of 41 were LTBI negative - 178 out of 190 (94%) reported more than one year stay at the facility, of which 140 out of 149 were LTBI positive, 38 out of 41 were LTBI negative	Humans: LTBI confirmed by TST and IGRA, active TB confirmed by CXR and culture in participants with respiratory or systematic symptoms. Animals: post-mortem culture	Differential tests performed: yes (genotyping) *M. bovis*	Odds of high exposure activities (direct contact with livestock in closed spaces) among people with LTBI compared to people with no LTBI (multivariable analysis, reference = people who tested LTBI negative)	OR: 6.09, 95% CI: 2.04 to 18.23, p < 0.001 Adjusted for age, sex, more than 4 hours of daily contact with cattle, more than 1 year of stay at the facility, consumption of raw dairy products, BCG scar and previous contact with TB cases
							Odds of more than 4 hours of daily contact with cattle in people with LTBI compared to people with no LTBI (multivariable analysis, reference = people had exposure and tested negative)	OR: 0.85 (0.34 to 2.08), p not reported (assumed p > 0.05) Adjusted for age, sex, high exposure activity, more than 1 year of stay at the facility, consumption of raw dairy products, BCG scar and previous contact with TB cases
							Odds of having stayed at the facility for more than one year in people who had LTBI compared to people with no LTBI (multivariable analysis, reference	OR: 1.19 (95% CI: 0.27 to 5.20) Adjusted for age, sex, high exposure activity, more than 4 hours of daily contact with cattle, consumption of raw dairy products, BCG scar and previous contact with TB cases

Study	Country, time period	Study type	Population	Exposure	Diagnostic method for TB	TB species	Outcome type	Result
							= people who had exposure and tested negative)	
Winthrop 2005 (7)	USA, May 2002	Cross-sectional	Humans - 88 people who potentially had contact with cattle during outbreak of *M. bovis* at a dairy farm Median age (range): - overall: 22 years (0 to 45 years) - dairy staff: 22 years (17 to 42 years) - family of dairy staff: 13 years (0 to 42 years) - slaughterhouse staff: 35 years (20 to 45 years) Sex: 53 male, 26 female, 9 unknown Birth place: Mexico = 53, US = 25, unknown = 10 Received BCG vaccine: - yes: 49 - no: 28 - unknown: 11 Animals: - approximately 3,500 cattle screened, of which 38 cattle were positive for *M. bovis*	Measurement of exposure: questionnaire Type of work: - dairy staff: 27 people - slaughter house employee: 13 people - not reported (family of diary staff): 48 people	Humans: TST, CXR if positive for TST and clinical evaluation Animals: screened with skin test and postmortem culture	Differential tests performed: no (however no human contacts tested positive for TB and lesions in infected cattle were consistent with *M. bovis*)	Prevalence of TB	By diagnostic test: - TST: 78 tested, 33 (42%) positive - CXR: all negative ((performed on 20 of the 33 [61%] positive for TST) - clinical evaluation: no contacts clinically suspicious for active TB TST positivity by occupational exposure: Family of dairy staff: - 11 (27%) people with TB Dairy staff: - 18 (72%) people with TB Slaughterhouse staff - 4 (33%) people with TB
							Risk of positive TST result in dairy staff (reference = family of dairy staff)	RR: 1.2 (95% CI: 0.6 to 2.1) Adjusted for being born in Mexico
							Risk of positive TST result in slaughterhouse staff (reference = family of dairy staff)	RR: 1.0 (95% CI: 0.4 to 2.5) Adjusted for being born in Mexico

Annexe E. Risk of bias assessment

Table E.1. Risk of bias assessment for cross-sectional studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Comments (including reason for no)
Gebre 2010 (2)	No	Yes	Unclear	Yes	No	No	No	No	Q1: Limited detail provided about criteria for inclusion in the study (only "pulmonary TB suspected patients requesting AFB"). Q3: Very limited information reported about measurement exposure without full reporting of raw data for all exposures, and potential for information bias in self-reported exposures. Q5 and 6: No confounding factors identified. Q7: Smear positivity alone is not sufficient to definitively diagnose active TB. Q8: X^2 for associations only, no regression analysis performed.
Meisner 2019 (3)	Yes	Yes	No	Yes	Yes	Yes	No	No	Q3: Potential for information bias in self-reported exposures Q7: TST only not sufficient to definitively diagnose TB Q8: Study notes that cattle herd size was a potential confounder of raw milk consumption and TST positivity association, but this was not adjusted for because a large amount of data was missing for this variable (169 out of 493 observations missing)
Monde 2023 (4)	Yes	Yes	No	Unclear	No	No	No	Yes	Q3: Potential for information bias in self-reported exposures Q4: Did not explicitly state testing regimen for TB in human cases Q5 and 6: No confounding factors identified. Q7: Outcome measurement not reported
Sichewo 2019 (16)	Yes	Yes	No	Yes	N/A	N/A	Yes	No	Q3: Potential for information bias in the reporting of family history of TB and other variables Q5/6/8: Statistical comparison of the outcome of interest for this review (TB prevalence among households with M bovis positive cattle) was not conducted, prevalence of TB only reported. However, study authors did perform statistical comparison for other outcomes such as for those with a family history of TB.
Torres-Gonzalez 2013 (5)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Q3: Potential for information bias in self-reported exposures
Tschopp 2009 (6)	Yes	No	No	Yes	No	No	Unclear	Yes	Q2: Limited reporting of study subject demographics Q3: Potential for information bias in self-reported exposures Q5 and 6: No confounding factors identified. Q7: Measurement method of outcome not detailed
Winthrop 2005 (7)	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Q3: Potential for information bias in self-reported exposures Q10: Only confounding variable adjusted for was place of birth (Mexico), other confounders should have been considered

Critical appraisal was done using the JBI checklist for cross-sectional studies (18)

List of questions

Q1: Were the criteria for inclusion in the sample clearly defined?
Q2: Were the study subjects and the setting described in detail?
Q3: Was the exposure measured in a valid and reliable way?
Q4: Were objective, standard criteria used for measurement of the condition?
Q5: Were confounding factors identified?
Q6: Were strategies to deal with confounding factors stated?
Q7: Were the outcomes measured in a valid and reliable way?
Q8: Was appropriate statistical analysis used?

Table E.2. Risk of bias assessment for case-control studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Comment
Coker 2006 (8)	Unclear	Unclear	No	No	Yes	Yes	Yes	Yes	Yes	No	Q1 and 2: No reporting of demographic information for cases and controls, cannot determine if matched appropriately despite the study reporting that matching was performed. Q3:The study reported that cases were confirmed with culture but did not report how they confirmed that controls were TB-negative. Q4: Potential for information bias in self-reported exposures Q10: No adjustment for basic confounding variables such as age or sex (adjusted for: diabetes, relative with TB, possession of household assets, living with others, employment, shortage of food, financial security, smoking habit, alcohol drinking habit, illicit drug use, history of imprisonment)
Fetene 2011 (11)	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Q4: Potential for information bias in self-reported exposures Q6 and Q7: confounders were not identified and no adjustment for potential confounders
Gebremichael 2018 (13)	Yes	No	Unclear	No	Yes	Yes	Yes	Unclear	Yes	Yes	Q2: cases and controls were not matched; however, demographics were similar. Q3: controls were not confirmed by diagnostic tests to not have TB Q4: Potential for information bias in self-reported exposures
Getachew 2023 (Preprint) (12)	Yes	No	No	No	Yes	Unclear	Unclear	Yes	Yes	Yes	Q2: Matching not performed, but demographics reported for each. Q3: Cases were confirmed via laboratory testing, while controls were not lab-tested for TB. Q4: Potential for information bias in self-reported exposure Q6 and Q7: Some confounders mentioned, but study also reports 'other potential confounders' without specifying
Gompo 2020 (10)	Yes	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	No	Q3: Did not report how TB diagnosis was made. Q4: Potential for information bias in self-reported exposures

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Comment
											Q10: No inclusion of basic demographics (such as age and sex) in multivariable model (adjusted for smoking habit and previous TB history only)
Jabeen 2024 (9)	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Q3: Cases were confirmed to have TB by symptom assessment and CXR, controls were reported as TB negative without same level of clinical investigation ("no clinical signs of TB like illness at the time of visit") Q4: Potential for information bias in self-reported outcomes
Silva 2018 (14)	Yes	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Yes	Yes	Q2: limited reporting of demographics Q3: cases diagnosed with culture, method of diagnosis for controls unclear Q4: Potential for information bias in self-reported exposures Q6 and 7: Study reports ‘adjusting for potential confounding factors' without specifying what was adjusted for

Critical appraisal was done using the JBI checklist for case-control studies (18)

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.3. Risk of bias assessment for cohort studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Comment
Bapat 2017 (1)	Yes	Yes	No	No	No	Unclear	Yes	Yes	Yes	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. Q10: No strategies to address incomplete follow-up were used.
Murphree 2011 (15)	Yes	Yes	No	No	No	N/A	No	Yes	Yes	N/A	Yes	Q3: potential for information bias in the self-reported exposures. Q4 and Q5: No adjustment for potential confounders. Q6and10: Retrospective study. Q7: TST only not sufficient to diagnose TB.

Critical appraisal was done using the JBI checklist for cohort studies (18)

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: CI: confidence interval, OR: odds ratio, PR: prevalence ratio, RR: risk ratio

Table F.1. Risk of TB in people who consumed raw dairy products compared to risk of TB in people who did not consume raw dairy products

Certainty assessment							Effect	Certainty
Number of studies and endnote references	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Effect estimate (95% CI)**	
Odds of TB in people who consumed raw milk compared to people who did not consume raw milk (multivariate analysis)								
4 (8, 9, 12, 13)	Case-control	very serious [note 1]	serious [note 2]	not serious	serious [note 3]	strong association (large magnitude of effect, OR more than 2.0 in 2 or more studies)	OR ranged from 2.75 to 9.97 95% CI ranged from 1.67 to 59.35	⨁◯◯◯ Very low
Odds of TB in farmers or zookeepers who consumed raw milk compared to people who did not consume raw milk (univariate analysis)								
1 outcome reported for 2 groups within one study (farmers and zookeepers) (1)	Prospective cohort	very serious [note 4]	serious [note 2]	not serious	very serious [note 3] [note 5]	none	OR ranged from 1.76 to 6.34 95% CI ranged from 0.07 to 42.6	⨁◯◯◯ Very low
Odds of TB in people who had contact with sick cattle or consumed raw dairy products compared to people who did not have contact with sick cattle or consume raw dairy products (multivariate analysis)								
1 (10)	Case-control	serious [note 6]	not assessed [note 7]	serious [note 8]	not serious	none	OR 3.9 (2.1 to 7.4)	⨁◯◯◯ Very low
Prevalence of TB in people who consumed raw milk compared to people who did not consume raw milk (multivariate analysis)								
1 (3)	Cross-sectional	very serious [note 9]	not assessed [note 7]	not serious	Serious [note 5]	none	PR 0.87 (0.64 to 1.39)	⨁◯◯◯ Very low
Odds of TB in people who consumed raw milk on a daily or weekly basis compared to consumption of raw milk when needed (multivariate analysis)								
1 (4)	Cross-sectional	serious [note 9]	not assessed [note 7]	serious [note 10]	not serious	none	OR 2.72 (1.73 to 4.28)	⨁◯◯◯ Very low
Odds of TB in people who consumed above median levels of raw milk compared to people who did not consume above median levels of raw milk (univariate analysis)								
1 (14)	Case-control	serious [note 9]	not assessed [note 7]	not serious	serious [note 5]	none	OR: 3.58 (2.02 to 24.13)	⨁◯◯◯ Very low
Odds of TB in people who consume raw milk compared to people who did not consume raw milk (univariate analysis)								
1 (6)	Cross-sectional	serious [note 9]	not assessed [note 7]	not serious	serious [note 5]	none	OR: 0.30 (0.50 to 1.80)	⨁◯◯◯ Very low

Certainty assessment							Effect	Certainty
Number of studies and endnote references	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Effect estimate (95% CI)**	
Risk of TB in people who consumed raw milk compared to people who did not consume raw milk (multivariate analysis)								
1 (7)	Cross-sectional	serious [note 11]	not assessed [note 7]	not serious	serious [note 5]	none	RR 1.5 (0.8 to 3.0)	⨁◯◯◯ Very low

Explanations

Note 1: The studies were at high risk of bias in one or more critical areas, such as differences in how cases and controls were identified and the potential for bias in the measurement of the exposure.
Note 2: There was a wide variance in point estimates.
Note 3: 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.
Note 4: The study was at high risk of bias in one or more critical areas, such as some participants having TB at the start of the study, no adjustment for confounding variables and no discussion of loss to follow up.
Note 5: The confidence intervals cross the line of no effect.
Note 6: The study was mostly at low or unclear risk of bias, however there was potential for bias in the measurement of the exposure and confounding bias caused by variables not included in the analysis.
Note 7: Only one study reported this outcome, not possible to assess inconsistency.
Note 8: The outcome of interest (risk of TB after raw milk consumption) has not been directly measured (unclear if TB transmission occurred from raw milk consumption or contact with animals).
Note 9: The study was at high risk of bias in one or more critical areas, including the potential bias in the exposure and the outcome measurement, or confounding bias caused by variables not included in the analysis.
Note 10: The comparator of interest (no raw milk consumption) has not been directly measured.
Note 11: The study was mostly at low or unclear risk of bias, however there was potential for bias in the measurement of the exposure and the method for measurement of the outcome was not reported.

Table F.2. Risk of TB in people who lived with animals compared to people who did not live with animals

Certainty assessment							Effect	Certainty
Number of studies and endnote references	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	
Odds of TB in children who lived with animals compared to children who did not live with animals (multivariate analysis)								
2 (12, 13)	Case-control	very serious [note 1]	serious [note 2]	not serious	very serious [note 3] [note 4]	none	OR ranged from 1.75 to 8.11 95% CI ranged from 0.86 to 53.58	⨁◯◯◯ Very low
Odds of TB in people who co-house with cattle at night compared to people who did not co-house with cattle at night (univariate analysis)								
1 (9)	Case-control	very serious [note 5]	not assessed [note 6]	not serious	serious [note 3]	none	OR 2.5 (1.2 to 5.2)	⨁◯◯◯ Very low
Odds of TB in people who house cattle indoors compared to people who did not house cattle indoors (univariate analysis)								
1 (6)	Cross-sectional	very serious [note 7]	not assessed [note 6]	not serious	serious [note 4]	none	OR 1.0 (0.4 to 2.6)	⨁◯◯◯ Very low

Explanations

Note 1: The studies were at high risk of bias in one or more critical areas, including the identification of cases and controls, potential bias in the exposure, as well as confounding bias caused by variables not included in the analysis.
Note 2: The point estimates varied widely between the studies.
Note 3: 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.
Note 4: Confidence intervals cross the line of no effect.
Note 5: The study was at high risk of bias in one or more critical areas, including the potential for bias in the identification of cases and controls, the measurement of the exposure and no adjustment for confounding variables in this analysis.
Note 6: Only one study reported this outcome, not possible to assess inconsistency.
Note 7: The study was at high risk of bias in one or more critical areas, including no adjustment for confounding variables in this analysis and not reporting how the outcome was measured.

Table F.3. Risk of TB in people who had contact with animals through occupational exposure compared to people who do not have contact with animals through occupational exposure

Certainty assessment							Effect	Certainty
Number of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	
Odds of TB in people in contact with animals through occupation (farmers and zookeepers, univariate analysis)								
1 (1)	Prospective cohort study	very serious [note 1]	Serious [note 2]	not serious	very serious [note 3] [note 4]	none	OR ranged from 0.22 to 2.63 95% CI range: (0.0642 to 53.3659)	⊕◯◯◯ Very low
Risk of TB in people in contact with animals through occupation (slaughterhouse workers and dairy staff, multivariate analysis)								
1 (7)	Cross-sectional study	Serious [note 5]	not serious	not serious	Serious [note 4]	none	RR ranged from 1.0 to 1.2 95% CI range: (0.6 to 2.5)	⊕◯◯◯ Very low
Odds of TB in people working at a cattle farm compared to people not working at a cattle farm (multivariate analysis)								
1 (9)	Case-control study	very serious [note 6]	not assessed [note 7]	not serious	serious [note 3]	none	OR 4.20 (1.08 to 16.56)	⊕◯◯◯ Very low
Prevalence ratio of TB in people with TB reactors in herd compared to people with no TB reactors in herd (multivariate analysis)								
1 (3)	Cross-sectional study	very serious [note 8]	not assessed [note 7]	serious [note 9]	serious [note 4]	none	PR 1.12 (0.82 to 1.54)	⊕◯◯◯ Very low
Odds of TB in people who have contact with animals compared to people who do not have contact with animals (univariate analysis)								
1 (4)	Cross-sectional study	very serious [note 9]	not assessed note 7]	not serious	Serious [note 4]	none	OR 0.76 (0.29 to 1.97)	⊕◯◯◯ Very low
Risk of TB in zoo employees who had contact with elephants kept in the zoo compared to zookeepers who did not have contact with elephants (univariate analysis)								
1 (15)	Retrospective cohort	very serious [note 10]	not assessed [note 7]	not serious	very serious [note 3] [note 4]	none	RR 0.91 (0.22 to 3.75)	⊕◯◯◯ Very low

Certainty assessment							Effect	Certainty
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	
Risk of TB in zoo employees who were exposed to the quarantine area (which housed a people with TB elephant) compared to those who did not have quarantine area exposure (univariate analysis)								
1 (15)	Retrospective cohort	very serious [note 10]	not assessed [note 7]	not serious	Serious [note 3]	None	RR 20.31 (2.81 to 146.69)	⊕◯◯◯ Very low
Odds of TB in people who reported zoonotic exposure compared to people who reported no zoonotic exposure (univariate analysis)								
1 (14)	Nested case-control	very serious [note 6]	not assessed [note 7]	not serious	Serious [note 3]	none	OR 5.71 (2.82 to 40.99)	⊕◯◯◯ Very low
Odds of TB high exposure activities in people who tested positive for TB compared to people who tested negative for TB (multivariable analysis)								
1 (5)	Cross-sectional	not serious	not assessed [note 7]	serious [note 13]	serious [note 3]	none	OR 6.09 (2.04 to 18.23)	⊕◯◯◯ Very low
Odds of TB in children who consumed raw meat compared to children who did not consume raw meat (univariate analysis)								
1 (13)	Case-control	very serious [note 6]	not assessed [note 7]	not serious	not serious	none	OR 1.67 (1.01 to 2.73)	⊕◯◯◯ Very low
Odds of TB in people who handled beef products compared to people who do not handle beef products (univariate analysis)								
1 (4)	Cross-sectional	very serious [note 10]	not assessed [note 7]	Serious [note 14]	very serious [note 3] [note 4]	none	OR 1.21 (0.46 to 3.11)	⊕◯◯◯ Very low
Odds of TB in people who consume raw meat compared to people who do not consume raw meat (univariate analysis)								
1 (6)	Cross-sectional	very serious [note 15]	not assessed [note 7]	not serious	Serious [note 4]	none	OR 1.1 (0.6 to 2.0)	⊕◯◯◯ Very low

Explanations

Note 1: The study was at high risk of bias in one or more critical areas, such as some participants having TB at the start of the study, no adjustment for confounding variables and no discussion of loss to follow up.

Note 2: There was a wide variance in point estimates.

Note 3: 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.

Note 4: Confidence intervals cross the line of no effect.

Note 5: The study was mostly at low or unclear risk of bias, however there was potential for bias in the measurement of the exposure and the outcome.

Note 6: The study was at high risk of bias in one or more critical areas, including the potential for bias in the identification of cases and controls, the measurement of the exposure and no adjustment for confounding variables in this analysis.

Note 7: Only one study reported this outcome, not possible to assess inconsistency.

Note 8: The study was at high risk of bias in one or more critical areas, including the potential bias in the exposure and the outcome measurement, as well as confounding bias caused by variables not included in the analysis.

Note 9: The presence of TB reactors in herd does not necessarily mean that people had direct contact with animals.

Note 10: The study was at high risk of bias in one or more critical areas, including the potential bias in the exposure and the outcome measurement, as well as confounding bias caused by variables not included in the analysis.

Note 11: The study was at high risk of bias in one or more critical areas, including the potential bias in the exposure measurement as well as confounding bias caused by variables not included in the analysis.
Note 12: Having a family history of TB is not directly relevant to the outcome of TB transmission, and presence of reactor cattle in herd does not necessarily mean people had direct contact with infected cattle.
Note 13: The outcome is odds of high exposure activities (being an abattoir worker, veterinary personal performing cattle necropsies, foremen, or milker), by people with TB result, rather than odds of TB by high exposure activities compared to low / no exposure activities.
Note 14: This outcome is a result of an indirect exposure.
Note 15: The study was at high risk of bias in one or more critical areas, including no adjustment for confounding variables in this analysis and not reporting how the outcome was measured.

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UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation heath secure.

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Prepared by Katie Kerr, Stefano Brini, Jennifer Hill, Mikhailia McIntosh Maman and Serena Carville

For queries relating to this document, please contact: enquiries@ukhsa.gov.uk

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