One Health Outlook

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Meta-analysis of the prevalence of tuberculosis in cattle and zoonotic tuberculosis in humans in sub-Saharan Africa

Alfred Ngwira[1,3,4*], Samuel Manda[2], Esron Daniel Karimuribo[1,4] and Sharadhuli Iddi Kimera[1,4]

Abstract

Background Tuberculosis (TB) in cattle negatively affects the cattle economy in Africa, with zoonotic TB posing drug-resistance issues in humans. The burden of TB in cattle and zoonotic TB in humans in sub-Saharan Africa (SSA) is not well understood. This study aimed to determine the prevalence of both TB in cattle and zoonotic TB in humans in SSA through meta-analysis.

Methods Research on TB prevalence was sourced from multiple databases. A random effects meta-analysis model estimated TB prevalence in SSA and its regions, while meta-regression identified risk factors. The analysis included 114 studies for cattle and 59 for humans.

Results The estimated TB prevalence in cattle was 5.06% (95% CI: 3.76–6.78), with a higher burden in West Africa. The prevalence was greater on farms than at abattoirs. Among humans, *M. bovis* prevalence was 0.73% (95% CI: 0.53–1.01), increasing to 1.56% (95% CI: 1.04–2.33) in TB incident cases, especially in the West and East Africa. Higher prevalence was noted among livestock workers, and in drug-resistant cases. Significant factors influencing TB prevalence varied for cattle and humans, including country, diagnostic methods, and study populations.

Conclusion Focusing interventions on farms and livestock workers could help reduce the disease burden.

Keywords Bovine tuberculosis, Cattle, Zoonotic tuberculosis, *M. Bovis*, Sub-Saharan Africa

Introduction

Tuberculosis (TB) in cattle is primarily caused by *Mycobacterium bovis (M. bovis)*, part of the *Mycobacterium tuberculosis* complex (MTBC). The economic impact of livestock TB is significant, leading to cattle deaths, meat condemnations, and reduced production. In humans, zoonotic TB tends to be associated with drug resistance [1]. While TB in cattle is more prevalent in developed regions like the Americas and Europe [2], zoonotic TB prevalence in humans due to *M. bovis* is notably higher in Africa [3]. This disparity in animal TB in cattle is linked to differences in disease monitoring and farming practices; intensive farming is typical in developed continents. On the other hand, extensive farming is common

*Correspondence:
Alfred Ngwira
alfred.ngwira@sacids.org
[1]Department of Veterinary Medicine and Public Health, Sokoine University of Agriculture, Morogoro, Tanzania
[2]Department of Statistics, University of Pretoria, Pretoria 0002, South Africa
[3]Department of Basic Sciences, Lilongwe University of Agriculture and Natural Resources, Lilongwe, Malawi
[4]SACIDS Foundation for One Health, SACIDS Africa Centre of Excellence for Infectious Diseases, Sokoine University of Agriculture, Morogoro, Tanzania

in Africa. Multiple risk factors contribute to the higher incidence of zoonotic TB in Africa, including the consumption of infected animal products [3] and regional sociocultural practices, such as the Maasai's consumption of raw cattle blood [4].

Estimating the prevalence of TB in cattle and zoonotic TB in humans in sub-Saharan Africa remains challenging due to limited country-level studies and lack of resources. This results in an information gap that affects regional epidemiology, which could guide interventions from organizations such as the Africa Centres for Disease Control and Prevention (Africa CDC). This study aimed to estimate the prevalence of animal TB in cattle and zoonotic TB in humans within sub-Saharan Africa, utilizing meta-analysis to identify factors affecting TB prevalence.

Materials and methods

Search strategy

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Supplementary Table S1) [5] were followed to search various databases, including PubMed, African Journals Online (AJOL), Web of Science, Scopus, and Embase, with the last search in April 2024. For the prevalence of TB in cattle, key terms, such as "bovine tuberculosis," "*Mycobacterium bovis*," and "sub-Saharan Africa" were used in Boolean combinations to create search phrases.

For zoonotic TB caused by *M. bovis* in humans, the same strategy was adopted, replacing "cattle" with "humans" and excluding "bovine tuberculosis." Additional terms, such as "molecular," "characterization," and "*Mycobacterium tuberculosis* complex" were included in this search.

Eligibility criteria

The study for cattle TB prevalence considered: (i) published journal articles, (ii) research in sub-Saharan Africa, (iii) any form of cattle TB, and (iv) valid diagnostic methods. Exclusions included unpublished reports, studies on wildlife or other livestock, and review articles. For humans, inclusion criteria focused on published journal articles that investigated zoonotic TB caused by *M. bovis* in sub-Saharan Africa, with valid diagnostic methods. Studies published without peer review were excluded. In both instances, there was no limitation regarding the year the study was published. This was due to the limited number of studies, especially human studies, because of the limited capacity to diagnose *M. bovis* in many countries.

Data screening and extraction

Articles were downloaded and screened in two stages: initial reviews of titles and abstracts, followed by full-text evaluations of eligible articles. Data gathered included author, publication year, country, region, diagnostic methods, sample sizes, number of cases, and study populations, including type of TB infection based on drug resistance and site of infection in humans. Studies in multiple countries by the same author were treated as separate entries. Summarized results were compiled in tables (Supplementary Tables S2 and S3).

Quality evaluation

Articles were assessed based on the established quality criteria [6, 7], evaluating the clarity of study objectives, sampling methods and risk factors among others. Each criterion received one point and articles scored from 0 to 5, with scores of 0 or 1 considered low quality.

Statistical analysis

Random effects meta-analysis using logit-transformed proportions was conducted. Forest plots visually represented the overall and individual study prevalence estimates, while heterogeneity was assessed using the Cochran Q-statistic [8] and Higgins I-squared statistic [9]. To identify potential sources of heterogeneity, we performed univariate and multivariate meta-regression, including subgroup analysis, with meta-regression helping determine factors associated with TB prevalence using a 25% significance level to tackle the low power of tests due to the limited number of studies [2]. Independent variables in the meta-regression for TB prevalence in cattle included region, country, publication year, method of diagnosis, sample size, and study population. Similar variables were used for zoonotic TB caused by *M. bovis* in humans, including type of TB based on drug resistance and site of infection. Multivariate meta-regression was performed while incorporating all prior variables and addressing multicollinearity between country and region. We used a funnel plot to check for publication bias and conducted Egger's regression test [10]. Sensitivity analysis assessed the robustness of estimates by running meta-analyses while excluding individual studies. Statistical analyses were carried out using R packages "metafor" and "meta."

Results

Selection of studies

Figure 1 illustrates the article selection process for the meta-analysis. A total of 142 articles on tuberculosis (TB) in cattle were identified after screening the titles and abstracts. Twelve articles were eliminated due to duplication. During a thorough review of the full texts, 130 articles were considered. Sixteen of these studies did not meet the selection criteria, and one was excluded because of poor quality. Ultimately, 113 articles were selected for the meta-analysis on TB prevalence in cattle. Notably, one of the selected articles included two studies:

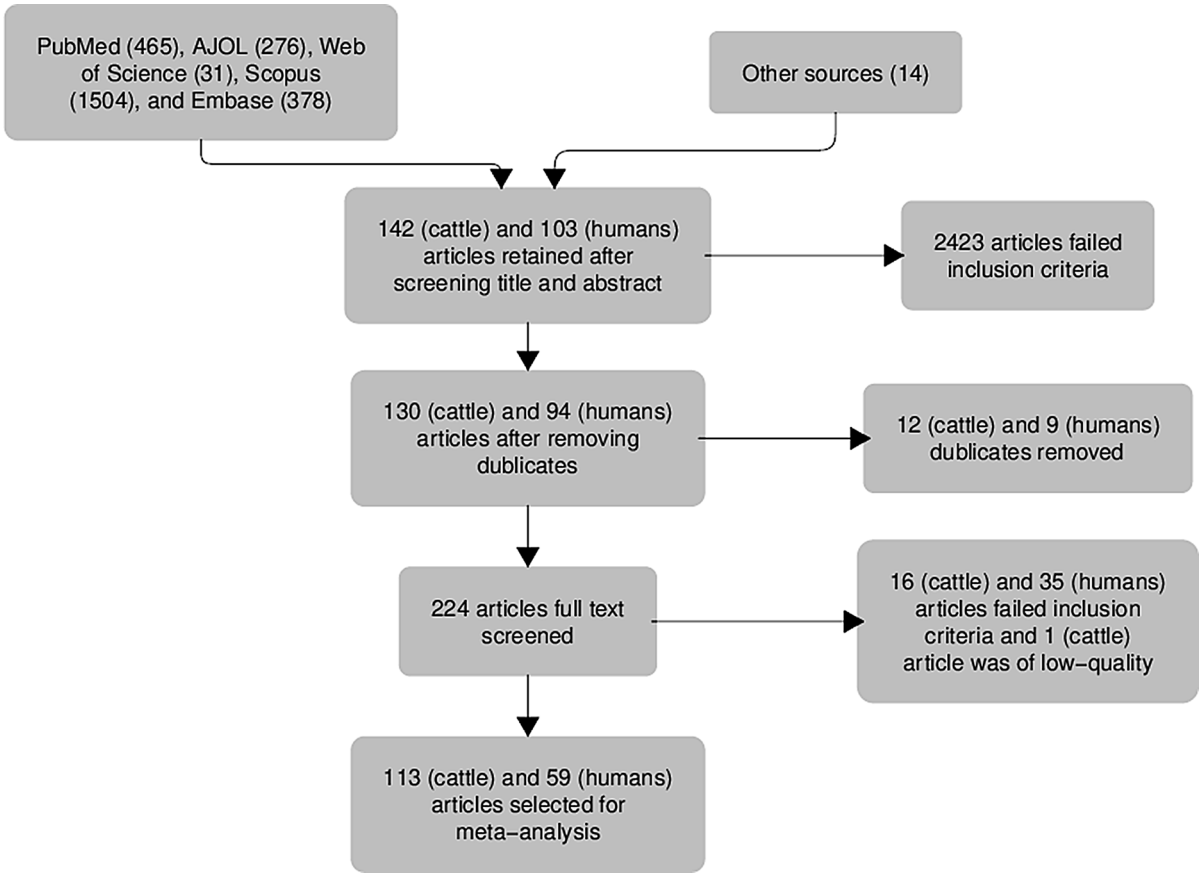

Fig. 1 PRISMA selection of articles about the prevalence of TB in cattle and *M. bovis* in humans

one conducted in Tanzania and another in Kenya, bringing the total number of studies analysed for TB in cattle to 114.

For zoonotic TB caused by *M. bovis* in humans, 103 studies were initially identified after screening the titles and abstracts. Nine of these were removed due to duplication, and 35 studies did not meet the inclusion criteria after full-text review, resulting in a total of 59 studies available for the meta-analysis of zoonotic TB in humans.

Characteristics of studies

The characteristics of studies about prevalence of TB in cattle and zoonotic TB caused by *M. bovis* in humans are detailed in Supplementary Tables S2 and S3, respectively. By region, the majority of studies on TB in cattle were conducted in East Africa ($n = 51$), followed by West Africa ($n = 32$), Southern Africa ($n = 20$) and Central Africa ($n = 11$). Ethiopia contributed the most studies on TB in cattle ($n = 25$), followed by Nigeria ($n = 14$), Ghana ($n = 8$) and Zambia ($n = 8$). For humans, many studies on zoonotic TB caused by *M. bovis* were conducted in Ethiopia ($n = 13$), Nigeria ($n = 9$), Ghana ($n = 6$) and Cameroon ($n = 5$). The regional distribution of studies on zoonotic TB in humans also showed a concentration in East and West Africa.

The most common diagnostic method for TB in cattle was the tuberculin test ($n = 58$), which included the comparative cervical test (CCT) ($n = 53$), single intradermal test (SIT) ($n = 4$), and caudal fold tuberculin (CFT) ($n = 1$). Additionally, molecular techniques ($n = 14$) and post-mortem examinations ($n = 15$) were the frequently used diagnostic methods. Other techniques included microscopy, culture, and enzyme-linked immunosorbent assays (ELISA), such as the lateral flow technique, immunochromatography, and interferon-gamma assay (IFN-γ). In this study, a positive result for the tuberculin test was defined as a skin thickness greater than 4 mm. Additionally, research on cattle was primarily conducted in farm or field settings ($n = 64$) compared to studies conducted in abattoirs ($n = 50$).

For humans, molecular techniques were the most commonly employed diagnostic methods for zoonotic TB caused by *M. bovis.* Pulmonary TB cases were more frequently studied than extrapulmonary TB. Additionally, most human studies involved TB patients ($n = 50$) rather than livestock-related workers ($n = 9$) as the study population.

Prevalence of TB in cattle and *M. bovis* in humans

The estimated prevalence of TB in cattle in sub-Saharan Africa was 5.06% (95% CI: 3.76–6.78) (Fig. 2). Among regions (Fig. 2), West Africa showed a higher prevalence of TB in cattle compared to Southern Africa, East Africa and Central Africa. Table 1 provides subgroup estimates for types of diagnosis, sample sizes, study populations and countries. Countries with a high prevalence of TB in cattle were Burundi, Chad, Benin, Madagascar and Somaliland. Moderate prevalence levels were observed in Mozambique, Nigeria, Ghana and Ethiopia. The cattle TB prevalence estimates decreased by an increase in sample size, where higher prevalence estimates were obtained for sample sizes of 250 or less. Cattle tested on the farms exhibited a higher prevalence of TB than those tested at the abattoirs. Diagnostic methods showed the highest prevalence of TB with ELISA and the lowest prevalence with postmortem examinations.

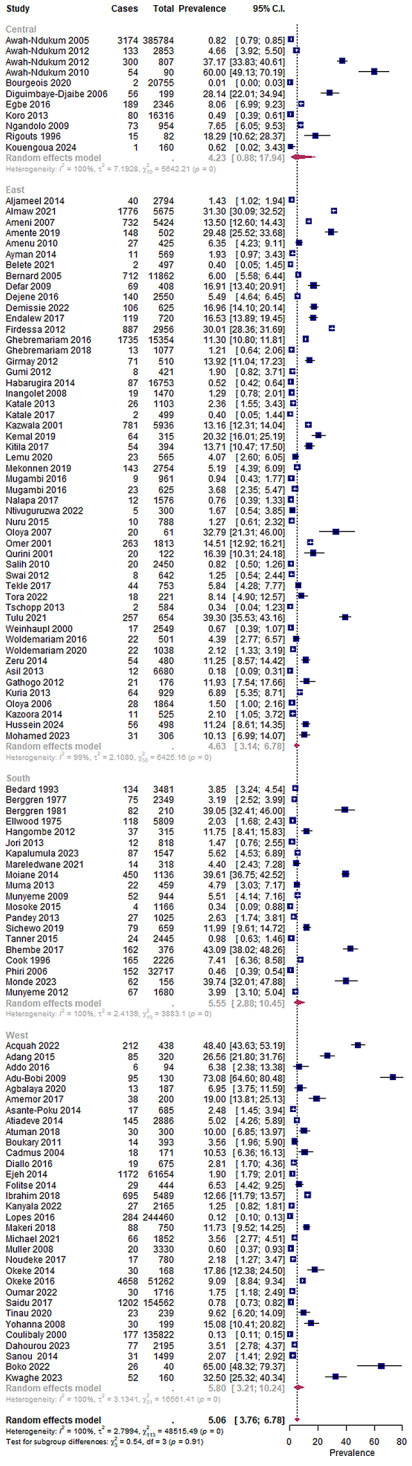

Fig. 2 Forest plot of TB prevalence in cattle in regions of sub-Saharan Africa

In humans, the estimated prevalence of zoonotic TB caused by *M. bovis* among the entire population in sub-Saharan Africa was 0.73% (95% CI: 0.53–1.01) (Fig. 3). Comparatively, the prevalence of *M. bovis* among human TB cases was 1.56% (95% CI: 1.04–2.33) (Fig. 4). The regional prevalence of *M. bovis* in humans was higher in the East and West Africa than in the Southern and Central Africa (Fig. 3). This trend was mirrored in the prevalence among human TB cases, which was again higher in the East, West and Southern Africa than in Central Africa (Fig. 4).

Table 2 includes prevalence estimates for subgroups outside of regional classification. Countries with a higher prevalence of zoonotic TB caused by *M. bovis* among the general human population were predominantly in East and West Africa, including, Nigeria, Burkina Faso, Tanzania, Uganda, and Madagascar. Among human TB cases, additional countries with higher prevalence of *M. bovis* included South Africa, Mozambique, Zambia, Chad, and Ethiopia. The distribution of *M. bovis* in the entire human population showed a higher burden among extrapulmonary TB (EPTB) cases compared to pulmonary TB (PTB) cases. This trend was also observed in the proportion of *M. bovis* among TB cases, where EPTB and drug-resistant TB (DRTB) patients showed a higher prevalence than those with pulmonary TB. Furthermore, livestock-related workers had a higher prevalence of *M. bovis* compared to TB patients. It was also notable that the prevalence of *M. bovis* in humans decreased with increasing sample size.

Sensitivity analysis and publication bias

Supplementary Figs. S1-S9 involve sensitivity and publication bias analysis about TB prevalence. The prevalence of TB in cattle remained stable, as sensitivity analyses showed minor changes when omitting individual studies (Supplementary Fig. S1). Publication bias assessment revealed no significant bias overall, but significant bias was detected in East Africa (t = -4.01, $p < 0.001$) and borderline bias in Central Africa ($t = 2.59$, $p = 0.054$). Conversely, there was a presence of publication bias in

Table 1 Subgroup estimates of prevalence of TB in cattle in sub-Saharan Africa

Variable	Category	n	Prevalence, % (95% CI)	Heterogeneity	
				χ^2 $(p-\text{value})$	I^2(%)
Method of diagnosis	Culture	7	2.58 (0.77, 8.30)	822.09 (< 0.01)	99.3
	ELISA	6	14.59 (3.93, 41.63)	381.63 (< 0.01)	98.7
	IFN-γ	5	5.68 (2.68, 11.66)	57.98 (< 0.01)	93.1
	Postmortem	15	1.24 (0.47, 3.27)	18882.52 (< 0.01)	99.9
	Microscopy	7	10.57 (2.60, 34.34)	518.75 (< 0.01)	98.8
	Molecular	14	8.54 (2.76, 23.50)	1437.92 (< 0.01)	99.1
	Tuberculin	58	5.59 (4.13, 7.54)	6315.71 (< 0.01)	99.1
	Biochemical	2	6.37 (0.67, 40.76)	48.67 (< 0.01)	97.9
Sample size	< 100	5	31.97 (12.61, 60.49)	68.66 (< 0.01)	94.2
	100–250	15	18.09 (11.08, 28.14)	310.67 (< 0.01)	95.5
	250–500	20	8.01 (4.58, 13.63)	789.97 (< 0.01)	97.6
	500–1000	25	5.32 (3.26, 8.57)	1549.21 (< 0.01)	98.5
	1000–1500	8	2.41 (0.87, 6.50)	1167.48 (< 0.01)	99.4
	> 1500	41	2.25 (1.37, 3.68)	39186.28 (< 0.01)	99.9
Study population	Abattoir	50	4.01 (2.28, 6.96)	25131.10 (< 0.01)	99.8
	Field/Farm	64	6.12 (4.55, 8.18)	6787.36 (< 0.01)	99.1
Country	Malawi	5	5.97 (1.92, 17.07)	435.36 (< 0.01)	99.1
	Mozambique	2	7.49 (0.13, 83.13)	384.07 (< 0.01)	99.7
	South Africa	4	6.18 (0.73, 37.05)	248.04 (< 0.01)	98.8
	Zambia	8	5.36 (2.09, 13.05)	1117.97 (< 0.01)	99.4
	Botswana	1	1.47 (0.83, 2.57)	-	-
	Burundi	1	18.29 (11.34, 28.15)	-	-
	Chad	2	15.22 (3.77, 45.13)	60.78 (< 0.01)	98.4
	DRC	1	0.01 (0.00, 0.04)	-	-
	Cameroon	7	5.14 (1.00, 22.50)	4792.67 (< 0.01)	99.9
	Nigeria	14	8.88 (5.17, 14.83)	8431.08 (< 0.01)	99.8
	Burkina Faso	5	1.16 (0.37, 3.53)	744.07 (< 0.01)	99.5
	Benin	2	16.82 (0.26, 93.91)	115.06 (< 0.01)	99.1
	Ghana	8	8.28 (1.72, 31.82)	4900.64 (< 0.01)	99.9
	Mali	2	1.30 (0.28, 5.78)	23.51 (< 0.01)	95.7
	Niger	1	3.56 (2.12, 5.92)	-	-
	Ethiopia	25	8.28 (5.20, 12.92)	2207.18 (< 0.01)	98.9
	Eritrea	3	6.14 (1.29, 24.73)	88.39 (< 0.01)	97.7
	Sudan	4	0.81 (0.29, 2.22)	46.38 (< 0.01)	93.5
	Tanzania	6	1.59 (0.57, 4.39)	362.51 (< 0.01)	98.6
	Madagascar	1	16.39 (10.83, 24.05)	-	-
	Rwanda	2	0.86 (0.28, 2.65)	6.45 (< 0.01)	84.5
	Kenya	3	6.74 (3.48, 12.66)	16.33 (< 0.01)	87.7
	Somaliland	1	10.13 (7.22, 14.05)	-	-
	Uganda	6	3.08 (0.95, 9.58)	217.28 (< 0.01)	97.7

the estimation of *M. bovis* prevalence among the entire human population (t = -2.82, p = 0.007), although trim and fill analysis showed a minor deviation of the adjusted estimate from the original estimate. Furthermore, sensitivity analyses confirmed stability in the original prevalence estimates. Regional assessment of publication bias in the estimation of *M. bovis* prevalence among humans also showed a significant bias in East Africa (t = -2.34, p = 0.032). There was no evidence of publication bias in the estimation of the prevalence of *M. bovis* among human TB cases.

Factors of prevalence of TB in cattle and *M. Bovis* in humans

Meta-regression (Table 3) identified sample size (26.55%) as the primary determinant of heterogeneity in cattle TB prevalence, followed by country (15.45%) and diagnostic method (11.48%). Meta-regression analysis revealed that the most influential factors contributing to the heterogeneity of *M. bovis* prevalence among humans were sample size (45.06%), country (28.74%), type of TB infection (23.39%), and region (14.78%). Moreover, multivariate meta-regression demonstrated that these various factors

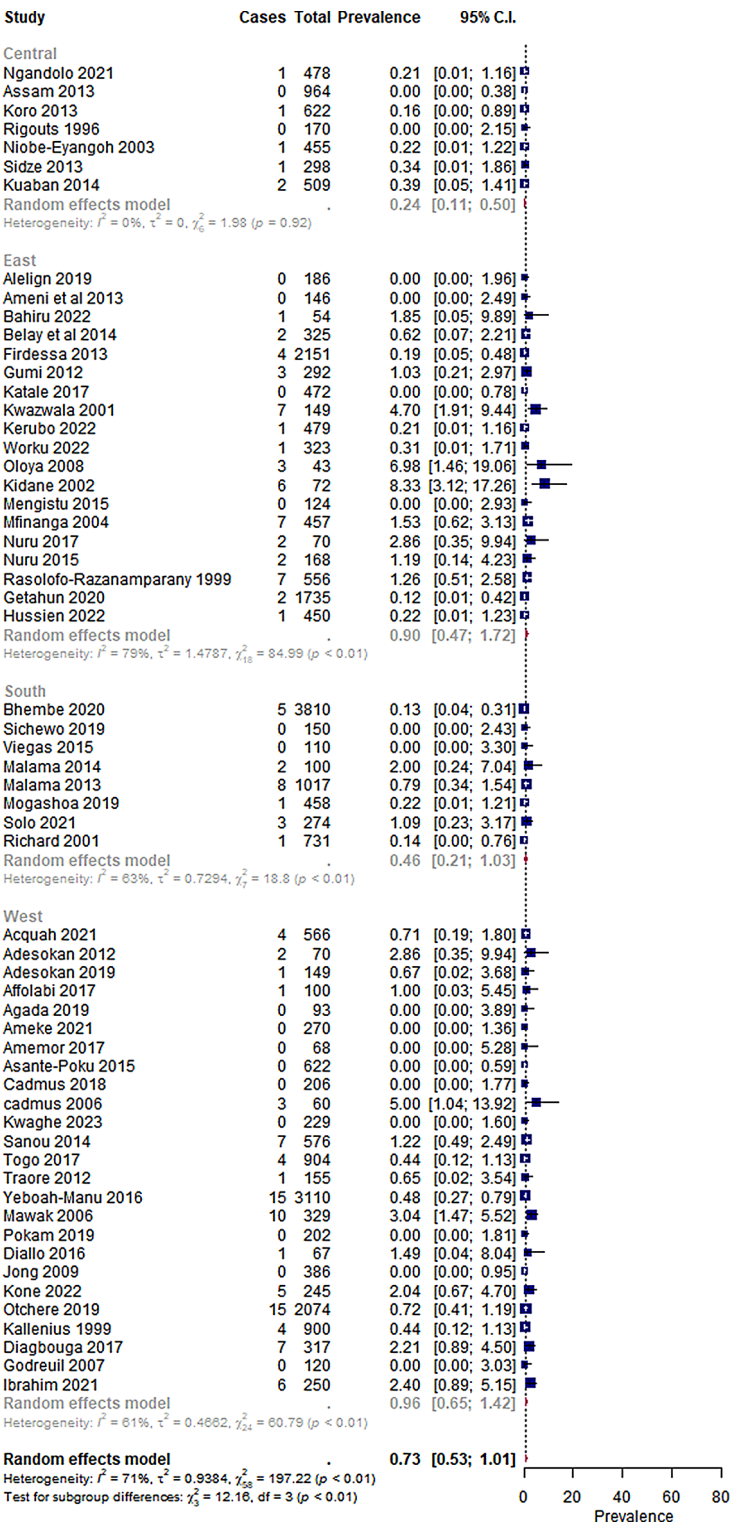

Fig. 3 Forest plot of *M. bovis* prevalence in all humans in regions of sub-Saharan Africa

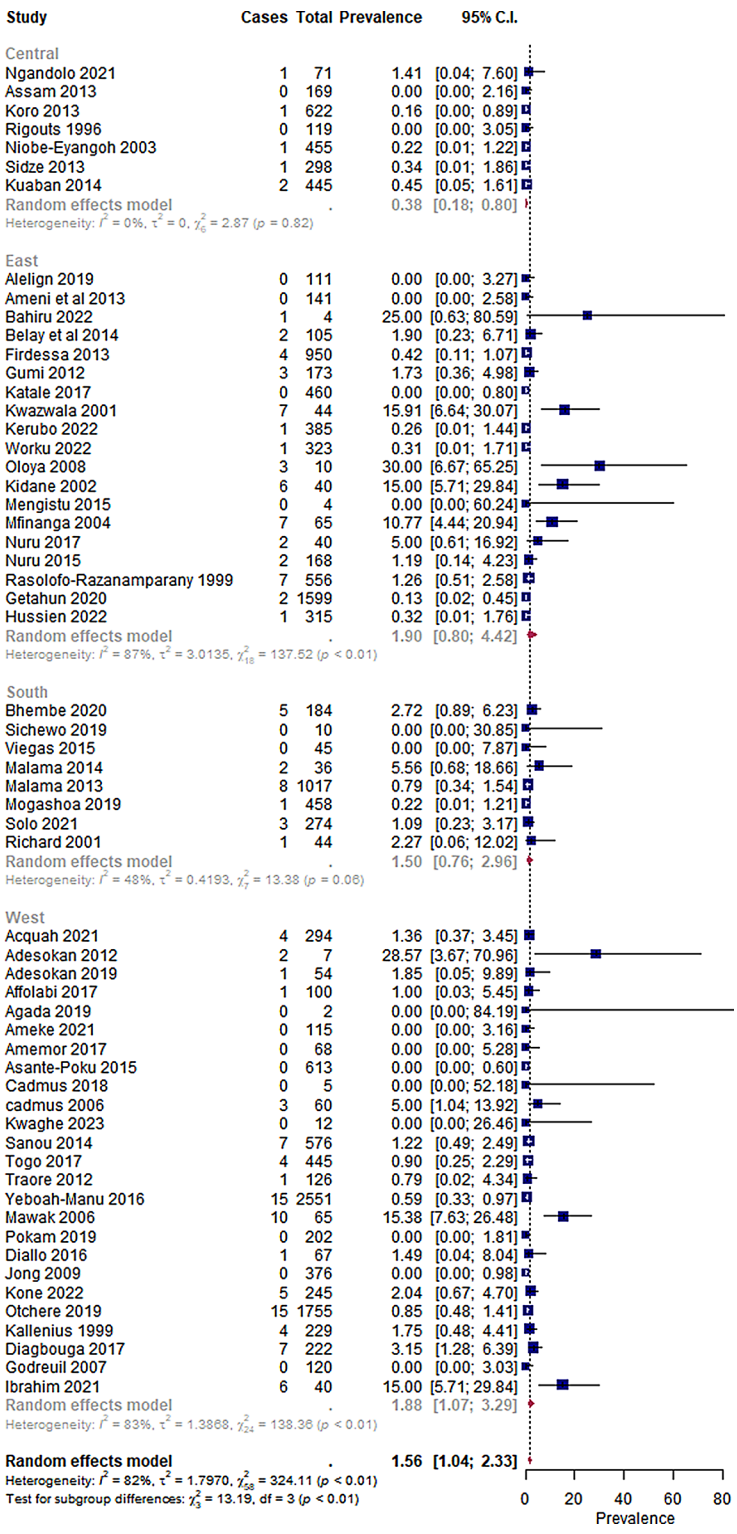

Fig. 4 Forest plot of *M. bovis* prevalence among human TB cases in regions of sub-Saharan Africa

Table 2 Subgroup estimates of prevalence of *M. Bovis* in humans in sub-Saharan Africa

Variable	Category	n	Prevalence, % (95% CI)		Heterogeneity	
			All humans	Human TB cases	χ^2 $(p-\text{value})$	I^2(%)
Method of diagnosis	Conventional	11	1.23 (0.70, 2.16)	2.21 (0.88, 5.48)	31.85 (< 0.01)	68.6
	Molecular	48	0.64 (0.44, 0.92)	1.42 (0.90, 2.21)	145.18 (< 0.01)	67.6
Sample size	< 100	9	3.88 (2.27, 6.56)	9.65 (4.41,19.80)	10.03 (0.26)	20.2
	200–250	17	0.91 (0.50, 1.64)	1.98 (1.00, 3.87)	24.31 (0.08)	34.2
	250–500	17	0.69 (0.40, 1.21)	1.15 (0.50, 2.64)	41.15 (< 0.01)	61.1
	500–1000	10	0.51 (0.30, 0.87)	1.05 (0.74, 1.49)	17.36 (0.04)	48.2
	> 1000	6	0.34 (0.17, 0.66)	0.68 (0.35, 1.32)	20.45 (< 0.01)	75.6
Type of TB infection	DRTB	1	0.13 (0.05, 0.31)	2.72 (1.14, 6.36)	-	-
	PTB	42	0.66 (0.48, 0.91)	1.26 (0.79, 2.00)	85.12 (< 0.01)	51.8
	EPTB	6	2.02 (0.60, 6.52)	9.19 (4.26, 18.70)	23.37 (< 0.01)	78.6
	PTB & EPTB	10	0.89 (0.39, 2.02)	1.25 (0.49, 3.12)	40.21 (< 0.01)	77.6
Study population	Patients	50	0.72 (0.51, 1.03)	1.28 (0.84, 1.95)	191.00 (< 0.01)	74.3
	Livestock workers	9	0.86 (0.39, 1.88)	7.66 (2.96, 18.40)	6.18 (0.63)	0.0
Country	Mozambique	1	0.45 (0.03, 6.79)	1.09 (0.07, 15.14)	-	-
	South Africa	2	0.14 (0.06, 0.33)	2.85 (1.24, 6.40)	0.39 (0.53)	0.0
	Zambia	4	0.85 (0.50, 1.43)	1.55 (0.63, 3.77)	5.08 (0.17)	40.9
	Botswana	1	0.22 (0.03, 1.53)	0.22 (0.03, 1.53)	-	-
	Burundi	1	0.29 (0.02, 4.50)	0.42 (0.03, 6.30)	-	-
	Chad	1	0.21 (0.03, 1.47)	1.41 (0.20, 9.33)	-	-
	Cameroon	5	0.24 (0.11, 0.56)	0.30 (0.13, 0.69)	1.95 (0.75)	0.0
	Nigeria	9	1.87 (1.03, 3.38)	7.96 (3.59, 16.70)	13.33 (0.10)	40.0
	Burkina Faso	3	1.54 (0.87, 2.72)	1.70 (0.70, 4.10)	2.20 (0.33)	8.9
	Benin	1	1.00 (0.14, 6.75)	1.00 (0.14, 6.75)	-	-
	Ghana	6	0.58 (0.42, 0.80)	0.74 (0.52, 1.03)	4.05 (0.54)	0.0
	Mali	4	0.98 (0.40, 2.39)	1.35 (0.74, 2.43)	5.60 (0.13)	46.4
	Gambia	1	0.13 (0.01, 2.03)	0.13 (0.01, 2.08)	-	-
	Guinea Bissau	1	0.44 (0.17, 1.18)	1.75 (0.66, 4.56)	-	-
	Ethiopia	13	0.70 (0.32, 1.53)	1.43 (0.55, 3.63)	56.00 (< 0.01)	78.6
	Tanzania	3	1.37 (0.23, 7.80)	3.68 (0.20, 41.92)	9.61 (< 0.01)	79.2
	Uganda	1	6.98 (2.27, 19.51)	30.00 (9.98, 62.37)	-	-
	Madagascar	1	1.26 (0.60, 2.62)	1.26 (0.60, 2.62)	-	-
	Kenya	1	0.21 (0.03, 1.47)	0.26 (0.04, 1.82)	-	-

Table 3 Meta-regression of prevalence of TB in cattle and *M. Bovis* in humans in sub-Saharan Africa

Variable	Univariate			Multivariate	
	Proportion, % R^2	Wald chi-square	*P*-value	Wald chi-square	*P*-value
Cattle					
Region	0.00	0.528	0.913	1.960	0.581
Country	15.45	44.214	0.005**	33.495	0.073*
Publication year	0.00	3.848	0.572	1.692	0.890
Method of diagnosis	11.48	20.731	0.004**	9.073	0.248*
Sample size	26.55	42.509	< 0.001**	12.135	0.033**
Study population	0.69	1.736	0.188*	1.510	0.219*
Humans					
Region	14.78	8.416	0.038**	11.570	0.009**
Country	28.74	26.264	0.094*	21.976	0.233*
Publication year	31.17	12.852	0.005**	1.703	0.636
Method of diagnosis	4.59	2.438	0.118*	12.280	0.001**
Sample size	45.06	26.349	< 0.001**	31.731	< 0.001**
Study population	0.00	0.000	0.996	5.805	0.016**
Type of TB infection	23.39	11.125	0.011**	5.043	0.169*

*Significant at 25% significance level and **significant at 5% significance level

collectively explained a greater degree of heterogeneity in human TB prevalence compared to cattle TB.

Discussion

The study utilized meta-analysis following PRISMA guidelines to estimate the prevalence of TB in cattle and *M. bovis* in humans across sub-Saharan Africa. Results indicated higher TB prevalence in cattle in West Africa, while both West and East Africa reported higher *M. bovis* prevalence in humans. There was significant variation in *M. bovis* prevalence in humans at both regional and country levels, while TB prevalence in cattle showed significant variation only at the country level. The prevalence was greater in cattle on farms than at abattoirs and notably higher among livestock-related workers and in cases of extrapulmonary and drug-resistant TB.

Numerous meta-analyses have shown a significant degree of variability in prevalence, likely due to differences in study methodologies, clinical variations among cattle or humans [11], as well as discrepancies in diagnostic specificity and sensitivity [12]. The absence of significant publication bias was expected, as studies on prevalence are consistently published regardless of findings. However, some analyses indicated small study effects and the Egger's test may have been less effective with fewer than twenty studies [13]. The significant unaccounted variation in TB prevalence among cattle may be attributed to additional factors not considered, such as different farming systems and cattle breeds [14].

The variation in TB prevalence across countries may relate to differences in control measures, categorized into three tiers of TB management [15]. Countries like South Africa and Namibia implement strong control programs, while others have poorly managed policies. Variations in climate and cattle density may also affect prevalence, as *M. bovis* is known to thrive in warm and humid conditions. The consistency of findings regarding country-level cattle TB prevalence supports observations in prior literature [16], with similar farming systems likely explaining the minimal regional variations. Significant regional variation of zoonotic TB in humans may be attributed to differences in sociocultural factors such as those of the Maasai of drinking raw cattle blood [4]. In addition, HIV may be responsible for the variation in zoonotic TB in humans, as it is a risk factor of EPTB [17], which, in turn, is associated with zoonotic TB [18].

Due to the exclusion of non-journal case reports, the reliability of prevalence estimates could be affected as fewer studies were sampled, especially per country. Furthermore, some important factors of TB in cattle such as farming systems and type of animal breed [14] were not investigated due to the missing information. In addition, the overall prevalence estimates were based on studies with varying methodologies. Despite these shortcomings, the findings of this study are consistent with the literature [19, 20].

Conclusion

To reduce the burden of animal and zoonotic tuberculosis (TB) in sub-Saharan Africa, interventions should consider allocating resources based on the regional disease burden, particularly at the country level for TB in cattle, as there is significant variation among countries. The focus should be on cattle on farms and the livestock-related workers. Future studies could benefit from including raw disease reports to enhance country-level estimates.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s42522-024-00130-8.

Supplementary Material 1

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Author contributions
AN conceived the study, drafted and edited the manuscript. SM, EDK, and SIK supervised the study and edited the manuscript. All authors read and approved the manuscript.

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Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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