One Health 19 (2024) 100905

Contents lists available at ScienceDirect

One Health

journal homepage: www.elsevier.com/locate/onehlt

Identification of common spatial and temporal trends in the epidemiology of cattle bovine tuberculosis and human extrapulmonary and drug-resistant tuberculosis in Malawi

Alfred Ngwira [a,c,d,*], Samuel Manda [b], Esron Daniel Karimuribo [a,d], Sharadhuli Iddi Kimera [a,d]

[a] Department of Veterinary Medicine and Public Health, Sokoine University of Agriculture, Morogoro, Tanzania
[b] Department of Statistics, University of Pretoria, Pretoria 0002, South Africa
[c] Department of Basic Sciences, Lilongwe University of Agriculture and Natural Resources, Lilongwe, Malawi
[d] SACIDS Africa Centre of Excellence for Infectious Diseases, SACIDS Foundation for One Health, Sokoine University of Agriculture, Morogoro, Tanzania

ARTICLE INFO

Keywords:
Common animal and human disease spatial effects
Log of count data
Zoonotic TB
One Health

ABSTRACT

Background: Identification of common spatial disease trends between cattle bovine tuberculosis (BTB) and human extrapulmonary tuberculosis (EPTB) and drug-resistant tuberculosis (DRTB) can support integrated disease control and monitoring programmes. We employed the recently developed multivariate disease mapping methods to examine whether the diseases exhibited any spatial correlation.

Methods: A retrospective study of cattle BTB and human EPTB and DRTB cases from 2018 to 2022 was conducted. Bivariate shared spatiotemporal components models were fitted to a) cattle BTB and human EPTB and b) cattle BTB and human DRTB at the district level in Malawi, with cattle density, human density and climatic variables as independent variables.

Results: Disease specific spatial effects were higher in the southern half of the country, while the shared spatial effects were more dominant in both the south and western parts of the country. The shared temporal effects showed constant trends, while disease specific temporal effects showed an increasing pattern for cattle BTB and a constant pattern for human EPTB and DRTB. The predicted disease incidence pattern for all forms of TB in the period without data showed a constant pattern over the years. Cattle density was positively associated with cattle BTB (β: 0.022; 95% Credible Interval (CI): 0.004, 0.042). Human density was positively associated with human EPTB (β: 0.005; 95% CI: 0.001, 0.009).

Conclusion: Cattle BTB and human EPTB and DRTB have a common spatial pattern in the west and southern parts of Malawi. Integrated interventions targeting high-density areas for cattle and human may have positive impacts on cattle BTB and human EPTB and DRTB.

1. Introduction

Bovine tuberculosis (BTB) is listed as one of the priority diseases to control in Malawi [1,2]. The disease results in significant economic losses to farmers and the country due to reduced animal productivity and meat condemnations at abattoirs. The disease has also public health implications since it also affects humans as zoonotic TB. In cattle, the prevalence of BTB has been estimated at 5.62% [3]. In Malawi, the distribution of BTB has shown to vary by district, where an earlier nationwide tuberculin study [4], showed a higher burden in the northern than central and southern region. A recent study that used case reports from the central veterinary laboratory [5], showed an even trend across the three regions. Based on an earlier report [4], the prevalence of zoonotic TB in humans was as high as 42.8% in some areas. A recent study has shown the zoonotic contribution of 3.3% of all human TB cases [6]. Bovine tuberculosis control is currently passive since there is no vaccination program against BTB in cattle. There is also no regular cattle testing and slaughter due to the cost of testing and the inability of government to compensate farmers. In this regard, Malawi is considered to be a third-tier country, where cattle BTB control is a policy, but it is not or is poorly implemented [7].

Assessment of common spatial and temporal disease trends plays an important role in providing extra epidemiologic information over and above that from disease specific trends, which offer an additional insight

* Corresponding author at: Department of Veterinary Medicine and Public Health, Sokoine University of Agriculture, Morogoro, Tanzania.
E-mail address: alfred.ngwira@sacids.org (A. Ngwira).

https://doi.org/10.1016/j.onehlt.2024.100905
Received 23 March 2024; Accepted 26 September 2024
Available online 5 October 2024

into disease aetiology, especially if the epidemiology of the disease in question is similar to the epidemiology of another disease. In this regard, other risk factors of a disease are known based on the risk factors of another disease that exhibit a similar pattern [8]. The information can be used in integrated disease control programmes to design integrated interventions [9,10]. The integrated disease control programmes in turn result in cost effective benefits compared to single disease control programmes [10]. Common disease trend analysis between cattle BTB and human extrapulmonary TB (EPTB) and drug-resistant TB (DRTB) has been motivated by their similar epidemiology and the absence of the actual zoonotic TB cases due to the limited laboratory testing by government. Most of the zoonotic BTB cases in humans tend to be associated with EPTB and DRTB [11,12]. Some of their risk factors are also similar, for example, cattle and wildlife buffalo density [13,14] and climatic factors such as humidity and precipitation [15,16].

Univariate spatiotemporal statistics approaches could be considered in modelling several interrelated diseases. Common and divergent trends could then be identified from the estimated spatial and temporal patterns. However, univariate approaches are incapable of being used to assess interactions and dependencies between the related diseases. Spatial and temporal disease models that consider the correlation between diseases improve the estimates of disease risks through increased statistical power [17]. Several joint spatial and spatiotemporal models exist for modelling multiple interrelated diseases simultaneously [18,19]. In this study, we employed the shared spatiotemporal components model for a) BTB in cattle and EPTB in humans and b) BTB in cattle and DRTB in humans. Using this modelling approach, we estimated the disease-specific spatial and temporal patterns and the shared spatial and temporal patterns common to the two diseases in either a) or b). Considering the interrelated BTB in cattle and human EPTB, and BTB in cattle and human DRTB, it could help public health interventions to be more integrated, thus better decision-making and evaluation.

2. Materials and methods

2.1. Study area and population

The study focussed on districts in Malawi (Fig. 1). There are 28 districts including four cities, namely, Blantyre, Zomba, Lilongwe and Mzuzu. Malawi is in the south and eastern part of Africa at −13.254308 latitude and 34.301525 longitude. It is 840 km long with its breadth varying between 10 and 160 km. The country covers a total area of 118,484 km^2 with land area of 94,449 km^2 and water area of 24,035 km^2. It is bordered by Tanzania to the north-east, Zambia to the north-west and central-west and Mozambique to the south.

The study population for cattle BTB was cattle that went for slaughter at an abattoir and the study outcome was the number of cattle reported to have BTB at an abattoir. The study sites were the major abattoirs in the regional cities of Blantyre, Lilongwe and Mzuzu. The choice of the major abattoirs from these cities was the fact that cattle originated from different districts thereby giving a good regional and national coverage. The study population for human EPTB and DRTB was human population with TB in each district and the outcome was the number of humans with either EPTB or DRTB in a district and year. Likoma Island was not included in the study since cattle farming is almost negligible. Neno district was part of Mwanza since the map that was used did not have a separate polygon for Neno.

2.2. Study design and data collection

The study used a retrospective sample study for the 2018 to 2022 period. In this regard, cases of BTB in cattle (Supplementary Table 1), including their place of origin and year were recorded from logbooks found at the selected abattoirs (Supplementary Fig. 1). The BTB cases

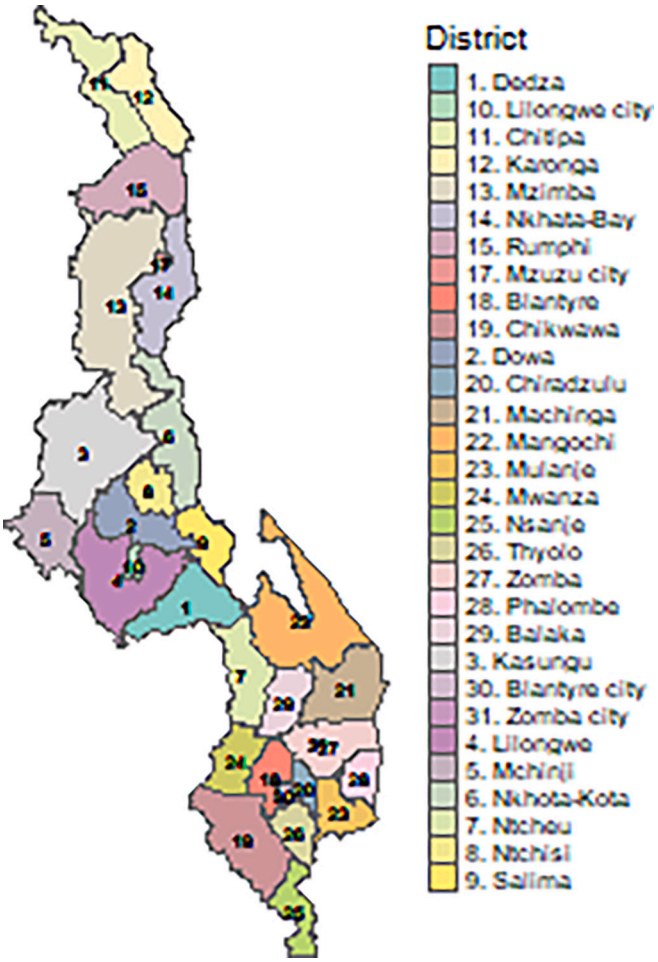

Fig. 1. Map of Malawi land mass showing districts and cities.

were also recorded from abattoir-based meat inspection monthly reports kept at theregional central veterinary laboratory offices (Supplementary Fig. 2). Using the place of origin, the cattle BTB cases were aggregated at district level and year to have the outcome of interest in this study. To avoid an overlap between logbooks and monthly reports, logbooks were used where monthly reports were not traceable, especially in the central and northern region. Diagnosis of cases was by postmortem examination. Data was also collected on cattle population for each district (Supplementary Table 2) from the 2006–2007 livestock census report [20]. The cattle population data for the study years 2018 to 2022 was projected by using the average national annual growth rate (Supplementary Table 3). Cattle population density was then calculated by dividing population by district area size in km^2. The area size of each district was recorded from the national human census report [21].

Human extrapulmonary and drug-resistant TB cases for each district and year from 2018 to 2022 (Supplementary Tables 4 and 5) were collected from National TB and Leprosy Programme after being granted permission (Supplementary Appendix A). These cases were based on TB cases recorded by the district hospital and health centres. The EPTB cases were bacteriologically or clinically confirmed. A positive lateral flow urine lipoarabinomannan assay (LF-LAM) test result without a concordant sputum sample was also classified as an EPTB case. For the EPTB cases that were clinically diagnosed, they were diagnosed based on the overall clinical presentation of the patient, the laboratory and radiological results [22]. Drug-resistant TB cases were confirmed by the Gene Xpert and TB culture diagnostic method. Human 2018 population data for each district was also collected from the 2018 human

population census report [21] (Supplementary Table 6), which also yielded the population density upon dividing population by area in km^2. Similar to cattle population, human population for the subsequent study years was found by using the annual growth rate.

District level data was also collected on climatic variables such as annual average temperature, maximum temperature, minimum temperature and precipitation (Supplementary Table 7). Climatic data was downloaded from WorldClim (https://www.worldclim.org/data). The data represented the district level averages based on data from 1970 to 2000 computed by the R *raster* package. WorldClim data was used since the annual weather data from Malawi meteorological department did not cover all districts. The use of WorldClim data is supported in the literature [23,24]. Permission to conduct the entire study and to collect BTB case data for cattle was granted by the department of animal health and livestock development in Malawi (#DAHLD/AHC/10/2022/1) (Supplementary Appendix B).

2.3. Statistical analysis

As the data were the observed counts of TB cases, an appropriate spatial model could have been based on the Poisson spatial model with a log-linear link function. However, the number of cattle exposed to TB at each abattoir could not be measured. Thus, we instead modelled the log of count in a linear spatial model, where we added a one to each count. Using a linear model allowed us to avoid the limitations of not having the exposed number of cattle. In application of the linear model, we initially compared the linear models with different constants added to count data with the negative binomial using simulation [25,26] (Supplementary Appendix C). In comparison, we also considered the linear model of log of count, after the zeros were replaced with 0.5.

Univariate linear spatiotemporal models of the number of cattle BTB and human EPTB and DRTB cases were fitted (Supplementary Appendix C). This was followed by fitting the bivariate shared component spatiotemporal linear models, one between BTB in cattle and EPTB in humans, and another between BTB in cattle and DRTB in humans (Supplementary Appendix C). We also fitted the bivariate spatiotemporal negative binomial model for comparison with the linear model on the predicted counts, considering that the linear model of log of count plus one tend to perform poorly under small counts [27]. In these models, we used the number of cases as the dependent variable, while district, year, cattle density, human density and climatic variables such as precipitation and temperature were used as independent variables. District, year and their interaction were modelled as spatial, temporal and spatiotemporal random effects respectively, representing the effects of unobserved factors of disease incidences. The choice of independent variables other than district and year was based on the literature [14,16]. For each bivariate model, three models were fitted, namely, the full model with all covariates, including district and year (Model 1), the reduced model with significant covariates, including district and year (Model 2), and the space-time model with only district and year without covariates (Model 3).

Model inference was Bayesian implemented in R using integrated nested Laplace approximation (INLA) [28]. The spatial and temporal effects were assigned the conditional autoregressive (CAR) distribution (Supplementary Appendix C). The other priors were based on Knorr-Held [29], G'omez-Rubio et al. [30] and Otiende et al. [31]. The map of posterior probability that the spatial effect was positive denoted as $p(s_i > 0)$, also known as exceedance probability was used to determine districts with high probability that the spatial effect had an increasing effect. To assess spatial, temporal and spatiotemporal dependence between BTB in cattle and EPTB and DRTB in humans, a correlation matrix of the weights of the shared effects was made. Model comparison was by the deviance information criterion (DIC). We also predicted disease mean counts for the years where there was no data.

3. Results

Fig. 2 shows the time series plot of the number of BTB cases in cattle and EPTB and DRTB cases in humans. There were 828 cases of BTB in cattle recorded in the study period. The average of BTB cases was 6 and the standard deviation was 27. The total number of cases for EPTB and DRTB in humans in the study period was 26,852 and 545 respectively. The mean number of human EPTB cases was 207 and the standard deviation was 291. The average number of human DRTB cases was 4, while the standard deviation was 5. In this regard, there was high heterogeneity among the cattle BTB and human EPTB cases. The number of BTB cases in cattle had been increasing, while the number of EPTB and DRTB cases in humans had been fluctuating in the study period. The number of BTB cases in cattle and DRTB cases in humans had been low compared to the number of EPTB cases in humans. A map of the number of cases (Fig. 3), showed an almost similar south-north gradient of BTB in cattle and EPTB and DRTB in humans, with a greater number of districts in the southern half of the country having more cases compared to districts in the northern half. The pattern for cattle BTB cases also showed west-east gradient, with more cases in the west than in the east. Districts with high number of cases in terms of both cattle BTB and human EPTB and DRTB were Chikwawa, Chiradzulu, Mchinji and Mzimba.

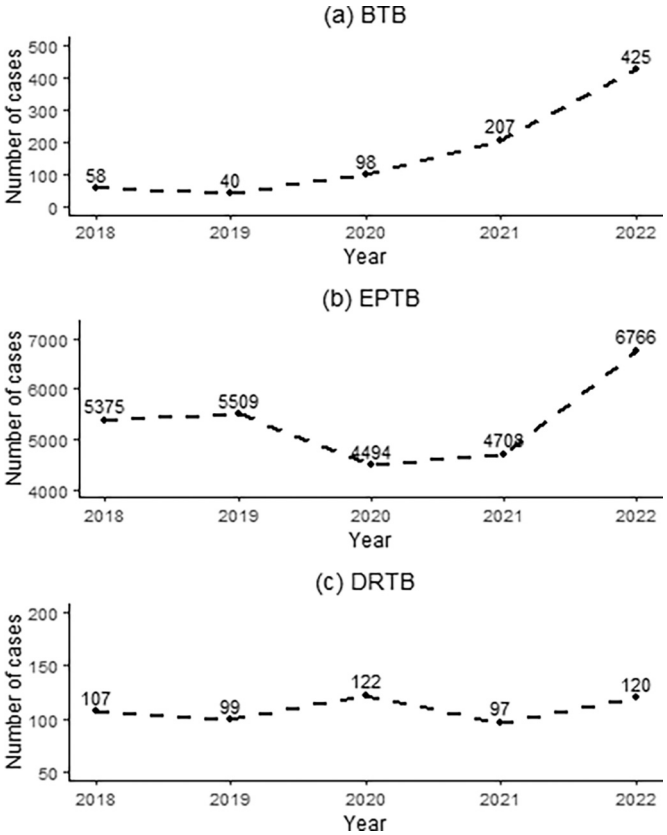

Fig. 2. Annual trends in cattle BTB and human EPTB and DRTB cases.

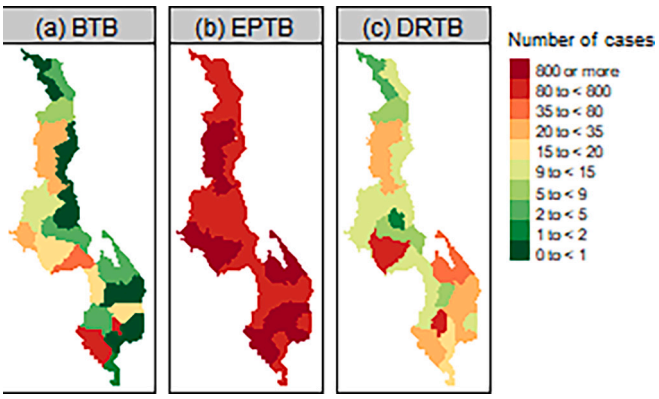

Fig. 3. Spatial trends in cattle BTB and human EPTB and DRTB cases, 2018 to 2022.

Fig. 4 shows the mean bias and root mean square error of the log of count models and the negative binomial model. The negative binomial model showed the minimum bias throughout the confidence interval of the true mean of cattle BTB cases. The log of count plus one, log of count plus half and the log of count with zeros replaced with half model had a higher positive bias for the mean count less than the average of cattle BTB cases and a higher negative bias for the mean count more than average of cattle BTB cases, meaning the models had the tendency to overestimate small counts and underestimate higher counts. Despite this behaviour, the log of count plus one and the log of count plus half model were indistinguishably unbiased in terms of estimating the point mean value of cattle BTB cases, which was 6 and they had the minimum RMSE. Although the log of count plus 0.001 model had the smaller bias below and above the point true mean value and was close to the standard model of counts, the negative binomial, it was biased in terms of estimating the point average value of cattle BTB cases. Due to this reason, further univariate and bivariate spatiotemporal modelling was based on the log of count plus one model. For comparison purposes, bivariate spatiotemporal prediction of disease counts using the negative binomial was also done.

Table 1 and Tables 2 and 3 show results of univariate and bivariate spatiotemporal linear models of the log transformed number of cases respectively. There was no difference in terms of the number of significant predictors between univariate and bivariate models. In both cases, cattle density was a significant risk factor of cattle BTB and human density was a significant risk factor of human EPTB. Human density was a borderline significant factor of DRTB. Precipitation was also a borderline significant common risk factor of cattle BTB and human EPTB and DRTB cases. Cattle density was positively associated with cattle BTB cases. Similarly, human density was positively associated with human EPTB and DRTB cases. On the contrary, precipitation was negatively associated with the number of cattle BTB and human EPTB and DRTB cases. In general, bivariate models fitted the data better than univariate models since they had smaller DIC. Due to this reason and for the sake of estimating both the shared and disease specific trends, further statistical inference was based on the bivariate models. A comparison of a bivariate model with all significant covariates, including space and time, with the space-time model, showed the space-time model fitting the data better when we jointly modelled cattle BTB and human DRTB. To have comparable shared patterns between BTB and EPTB and between BTB and DRTB, and also for the reason of having a less adjusted spatial pattern which can be compared to the raw spatial pattern in Fig. 3, further inference was based on the space-time linear model. For comparison with the standard count data model, results on the predicted counts based on the negative binomial model were included in the supplementary materials (Supplementary Figs. 3 & 4).

Figs. 5 and 6 show the spatial effects on cattle BTB and human EPTB and DRTB and their posterior probability. The distribution of disease specific spatial effect on BTB in cattle showed an increasing effect in the west than in the east. The disease specific spatial effect on human EPTB

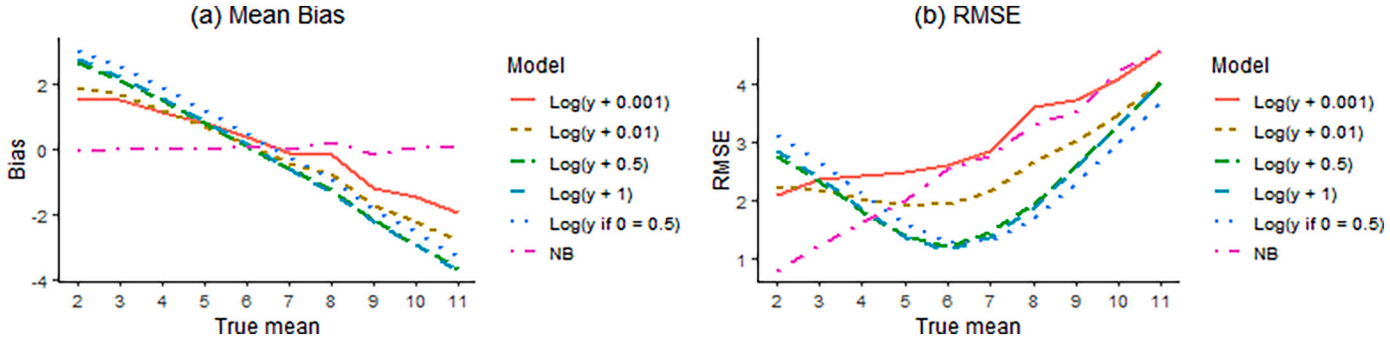

Fig. 4. Mean bias and root mean square error from count data models fitted to negative binomial simulated data based on parameters of the empirical cattle BTB data.

Table 1
Estimates of univariate linear model of cattle BTB and human EPTB and DRTB.

Parameter	BTB	EPTB	DRTB
Fixed	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Cattle density	0.023* (0.004, 0.042)	0.011 (−0.008, 0.030)	0.002 (−0.014, 0.020)
Human density	0.000 (−0.004, 0.003)	0.005* (0.001, 0.008)	0.003† (0.000, 0.006)
Temperature	0.040 (−0.173, 0.255)	0.037 (−0.199, 0.275)	0.032 (−0.164, 0.231)
Precipitation	−0.002† (−0.003, 0.000)	−0.002† (−0.004, 0.000)	−0.001† (−0.003, 0.000)
Random			
Spatial	2.381 (1.295, 4.951)	3.597 (2.183, 6.711)	2.165 (1.218, 4.329)
Temporal	0.063 (0.020, 0.380)	0.017 (0.001, 0.122)	0.001 (0.000, 0.023)
Spatiotemporal	0.452 (0.353, 0.595)	0.094 (0.074, 0.124)	0.287 (0.224, 0.375)
DIC	−840.57	−842.10	−837.99

* Statistically significant at 5% significance level and †borderline significance.

Table 2
Estimates of bivariate linear model of cattle BTB and human EPTB.

Parameter	Model 1		Model 2		Model 3	
	BTB	EPTB	BTB	EPTB	BTB	EPTB
Fixed	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Cattle density	0.022* (0.004, 0.042)	0.011 (−0.008, 0.030)	0.022* (0.005, 0.040)	–	–	–
Human density	0.000 (−0.004, 0.003)	0.005* (0.001, 0.009)	–	0.004† (0.000, 0.008)	–	–
Temperature	0.039 (−0.170, 0.250)	0.040 (−0.194, 0.274)	–	–	–	–
Precipitation	−0.002† (−0.003, 0.000)	−0.002† (−0.004, 0.000)	−0.002† (−0.003, 0.000)	−0.002† (−0.004, 0.000)	–	–
Random						
Disease specific						
Spatial	2.370 (1.289, 4.950)	3.597 (2.169, 6.667)	2.193 (1.208, 4.505)	3.367 (2.045, 6.098)	3.300 (1.919, 6.289)	4.098 (2.545, 7.246)
Temporal	0.063 (0.019, 0.383)	0.001 (0.000, 0.083)	0.061 (0.019, 0.392)	0.016 (0.004, 0.458)	0.068 (0.021, 0.411)	0.001 (0.000, 0.070)
Spatiotemporal	0.452 (0.353, 0.596)	0.093 (0.071, 0.124)	0.452 (0.353, 0.597)	0.093 (0.072, 0.125)	0.452 (0.353, 0.596)	0.092 (0.071, 0.123)
Shared						
Spatial	0.001 (0.000, 0.065)		0.001 (0.000, 0.071)		0.001 (0.000, 0.066)	
Temporal	0.001 (0.000, 0.054)		0.001 (0.000, 0.057)		0.001 (0.000, 0.074)	
Spatiotemporal	0.000 (0.000, 0.008)		0.000 (0.000, 0.009)		0.000 (0.000, 0.009)	
Weights of shared						
Spatial	21.4 (0.009, 132)	24.8 (0.010, 150)	25.3 (0.010, 154)	23.3 (0.009, 144)	23.6 (0.010, 144)	22.4 (0.010, 138)
Temporal	2.00 (0.003, 14)	5.16 (0.620, 17.3)	3.38 (0.000, 24.9)	4.19 (0.001, 30.7)	1.81 (0.001, 12.7)	5.57 (0.614, 19.4)
Spatiotemporal	5.51 (0.018, 38.1)	1.70 (0.002, 11.9)	5.57 (0.019, 38.6)	1.52 (0.002, 10.7)	5.94 (0.020, 41.1)	1.66 (0.002, 11.6)
DIC	−1369.95		−1306.78		−1309.191	

* Statistically significant at 5% significance level and †borderline significance.

Table 3
Estimates of bivariate linear model of cattle BTB and human DRTB.

Parameter	Model 1		Model 2		Model 3	
	BTB	DRTB	BTB	DRTB	BTB	DRTB
Fixed	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Cattle density	0.022* (0.003, 0.041)	0.002 (−0.014, 0.019)	0.022* (0.005, 0.040)	–	–	–
Human density	0.000 (−0.004, 0.003)	0.003† (0.000, 0.006)	–	0.003† (0.000, 0.006)	–	–
Temperature	0.038 (−0.170, 0.247)	0.031 (−0.161, 0.224)	–	–	–	–
Precipitation	−0.002† (−0.003, 0.000)	−0.001† (−0.003, 0.000)	−0.002† (−0.003, 0.000)	−0.001† (−0.003, 0.000)	–	–
Random						
Disease specific						
Spatial	2.369 (1.295, 4.950)	2.151 (1.220, 4.310)	2.188 (1.208, 4.484)	1.969 (1.131, 3.846)	3.300 (1.927, 6.329)	2.049 (1.185, 3.906)
Temporal	0.059 (0.017, 0.384)	0.001 (0.000, 0.023)	0.058 (0.017, 0.415)	0.001 (0.000, 0.022)	0.056 (0.015, 0.492)	0.001 (0.000, 0.022)
Spatiotemporal	0.388 (0.234, 0.652)	0.248 (0.088, 1.464)	0.394 (0.220, 0.764)	0.203 (0.064, 1.25)	0.395 (0.227, 0.730)	0.175 (0.046, 1.721)
Shared						
Spatial	0.001 (0.000, 0.065)		0.001 (0.000, 0.062)		0.001 (0.000, 0.067)	
Temporal	0.001 (0.000, 0.029)		0.001 (0.000, 0.027)		0.000 (0.000, 0.034)	
Spatiotemporal	0.001 (0.000, 0.121)		0.001 (0.000, 0.118)		0.001 (0.000, 0.121)	
Weights of shared						
Spatial	22.3 (0.009, 137)	23.6 (0.009, 143)	22.7 (0.009, 140)	23.2 (0.009, 142)	21.7 (0.009, 134)	21.6 (0.009, 133)
Temporal	120 (0.006, 497)	1.50 (0.006, 9.81)	172 (0.001, 561)	1.47 (0.007, 9.45)	224 (0.005, 822)	1.68 (0.022, 9.46)
Spatiotemporal	77.0 (0.044, 457)	20.8 (0.005, 148)	115 (0.015, 598)	82.7 (0.008, 470)	81.0 (0.025, 473)	35.7 (0.023, 247)
DIC	−856.31		−862.97		−889.63	

* Statistically significant at 5% significance level and †borderline significance.

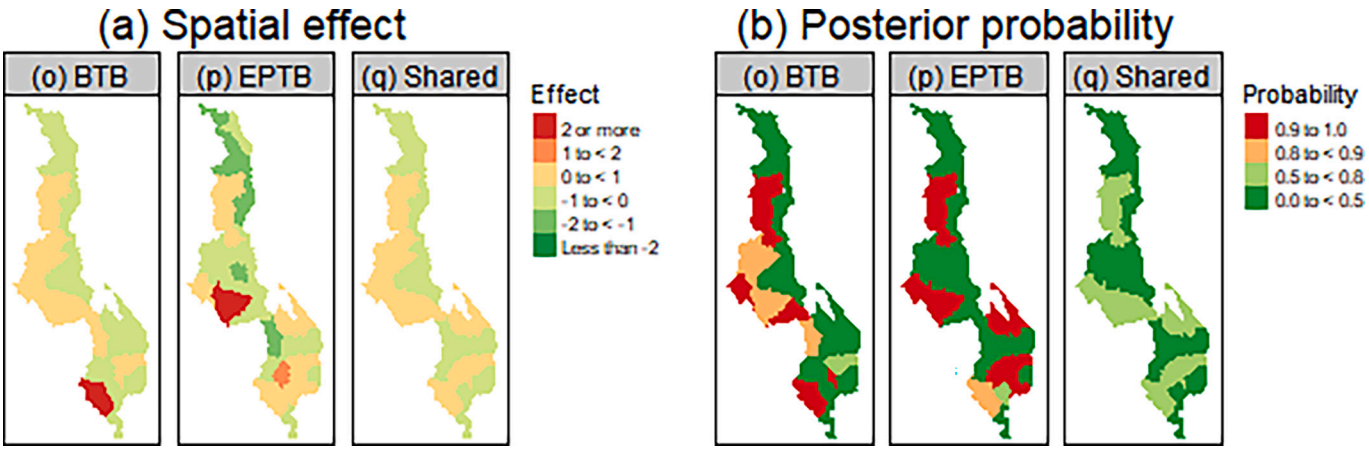

Fig. 5. Disease specific and shared spatial effect on cattle BTB and human EPTB (a) and their posterior probability (b).

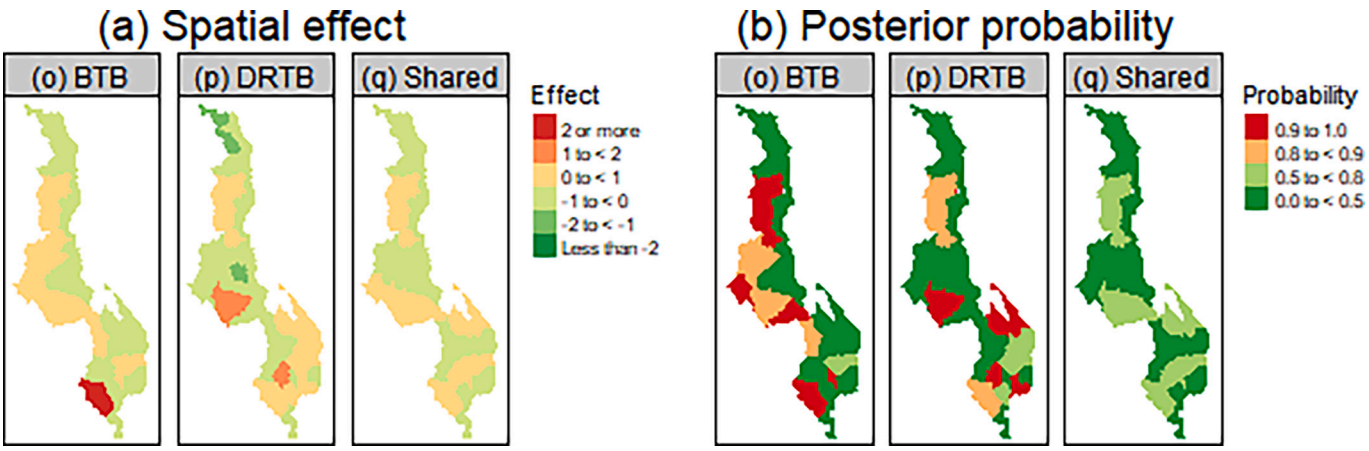

Fig. 6. Disease specific and shared spatial effect on cattle BTB and human DRTB (a) and their posterior probability (b).

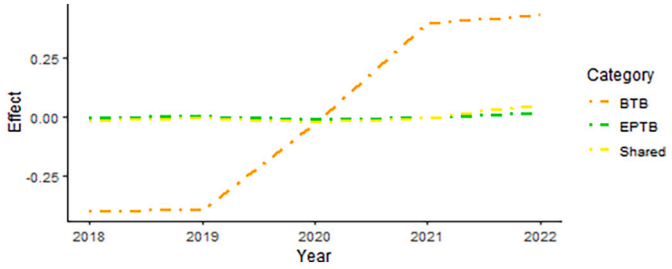

Fig. 7. Disease specific and shared temporal effect on cattle BTB and human EPTB.

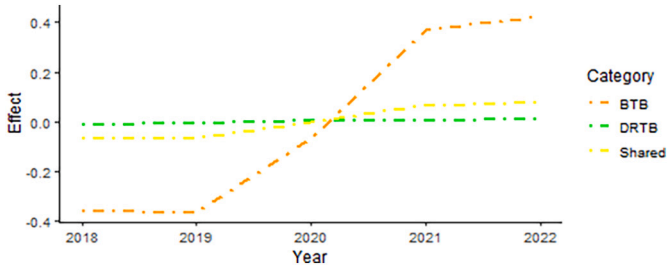

Fig. 8. Disease specific and shared temporal effect on cattle BTB and human DRTB.

and DRTB showed more districts in the southern half of the country having an increasing effect than those in the northern half. The gradient of the shared spatial effect on cattle BTB and human EPTB was west-east, with districts in the west having an increasing effect than those in the east. The gradient of the shared spatial effect on BTB and DRTB was south-north. The posterior probability regarding the shared spatial effect on cattle BTB and human EPTB or cattle BTB and human DRTB showed low probability that the spatial effect was positive. Figs. 7 and 8 show the temporal effects on cattle BTB and human EPTB and DRTB. The temporal effect on cattle BTB showed a reducing effect from 2018 to 2020 and an increasing effect thereafter. The disease specific temporal effects on human EPTB and DRTB were constantly close to zero, implying insignificance. The shared temporal effects on cattle BTB and human EPTB or cattle BTB and human DRTB were also close to zero. Spatiotemporal prediction (Fig. 9) in the study period showed an increasing pattern for cattle BTB and a constant pattern for human EPTB and DRTB. The gradient for all forms of TB in each year was approximately south-north. The predicted counts in years with no data showed a constant trend for all forms of TB over time (Fig. 10). Prediction of counts in years with no data based on the negative binomial model (Supplementary Fig. 4) also showed similar patterns with minor differences. In this regard, the predicted mean cattle BTB cases under the linear model (Fig. 10) were lower than those predicted under the negative binomial model (Supplementary Fig. 4). The predicted cattle BTB cases under the negative binomial model also showed an increasing pattern over the years.

The contribution in amount of variation due to random factors (Tables 2 & 3, Model 3), showed that much of the variation in cattle BTB when we modelled cattle BTB and human EPTB was due to disease specific spatial (86%) and spatiotemporal (12%) factors. For human EPTB, the variation due to disease specific spatial factors was substantial (98%). In the bivariate spatiotemporal modelling of cattle BTB and DRTB, much of the random variation in BTB was due to disease specific spatial (88%) and spatiotemporal factors (11%), while much of the variation in human DRTB was due to disease specific spatial factors (92%). An evaluation of spatial, temporal and spatiotemporal correlation of the random factors of cattle BTB and human EPTB and DRTB using the bivariate correlation of weights of the shared effects (Table 4 &

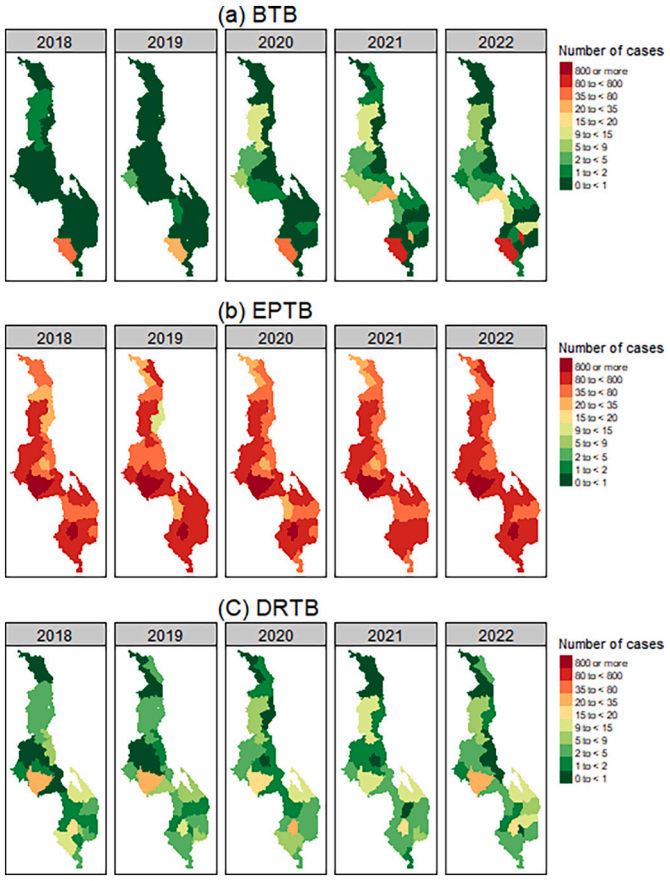

Fig. 9. Predicted cattle BTB and human EPTB and DRTB, 2018 to 2022.

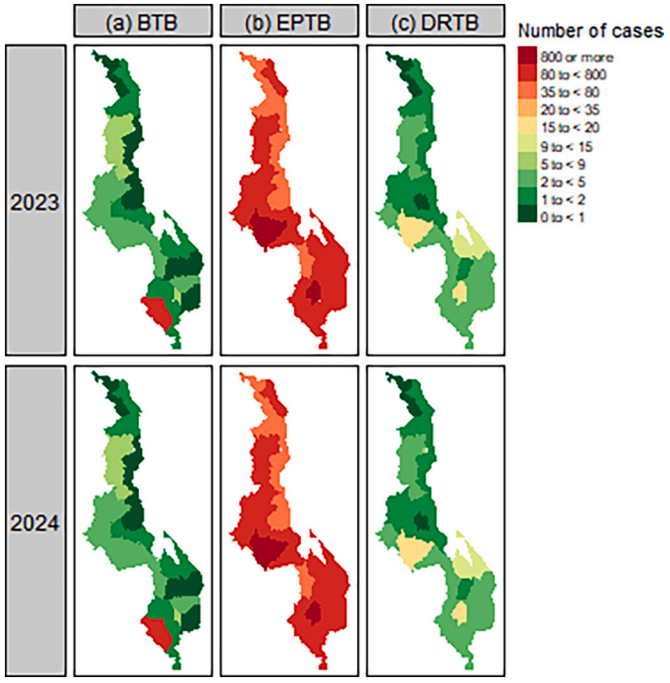

Fig. 10. Predicted cattle BTB and human EPTB and DRTB in 2023 and 2024.

Supplementary Table 8), showed a significant positive temporal correlation of cattle BTB and human EPTB random factors. There was also significant positive temporal and spatiotemporal correlation of the

Table 4
Assessment of spatial, temporal and spatiotemporal correlation.

		BTB & EPTB					
		Spatial		Temporal		Spatiotemporal	
		BTB	EPTB	BTB	EPTB	BTB	EPTB
Spatial	BTB		−0.051[a]	0.191	0.119	0.020	0.207
	EPTB	−0.051[a]		0.034	−0.023	0.074	0.173
Temporal	BTB	0.191	0.034		0.230[b]	0.144	0.124
	EPTB	0.119	−0.023	0.230[b]		0.013	0.025
Spatiotemporal	BTB	0.020	0.074	0.144	0.013		−0.059[c]
	EPTB	0.207	0.173	0.124	0.025	−0.059[c]	

		BTB & DRTB					
		Spatial		Temporal		Spatiotemporal	
		BTB	DRTB	BTB	DRTB	BTB	DRTB
Spatial	BTB		0.000[a]	−0.189	0.373	0.211	−0.032
	DRTB	0.000[a]		−0.210	0.087	0.343	0.033
Temporal	BTB	−0.189	−0.210		0.170[b]	−0.293	−0.044
	DRTB	0.373	0.087	0.170[b]		−0.083	−0.286
Spatiotemporal	BTB	0.211	0.343	−0.293	−0.083		0.750[c]
	DRTB	−0.032	0.033	−0.044	−0.286	0.750[c]	

[a] Spatial correlation.
[b] Temporal correlation.
[c] Spatiotemporal correlation.

random factors of cattle BTB and human DRTB. Positive temporal correlation means that the random factors of cattle BTB and human EPTB and DRTB were similar over the study period. The observed positive spatiotemporal correlation means that the random factors of cattle BTB and human DRTB were similar over space and time.

4. Discussion

This paper has investigated common and disease specific spatial and temporal trends in the epidemiology of cattle bovine tuberculosis and human extrapulmonary and drug-resistant tuberculosis in Malawi. We applied the recently developed multivariate spatiotemporal models for several related disease outcomes. The shared spatiotemporal components model was used and estimated by Bayesian methods. We used cattle BTB data from the central veterinary laboratory offices and abattoirs and human EPTB and DRTB data from National TB and Leprosy Programme. Higher common disease spatial effects were found in the western and southern parts of the country.

Using multivariate spatiotemporal models to estimate cattle BTB and human EPTB and DRTB trends resonates well with One Health. The approach is encouraging in understanding comorbidity of zoonoses between humans and animals in sub-Saharan Africa, where their risk including BTB is high [6,32]. Nevertheless, the approach is likely to be hampered by lack of livestock disease data due to poor data monitoring systems in livestock health. Furthermore, zoonotic diseases in humans are not well monitored and hence forth their data is also hard to find. An improvement in both animal and human zoonotic data monitoring is required for the quality implementation of multivariate spatial modelling. The observed differences in the predicted cattle BTB counts in 2023 and 2024 between the linear model (Fig. 10) and the negative binomial model (Supplementary Fig. 4) may be attributed by the poor approximation by the linear model under small counts [27].

An explanation to the observed disease spatial and temporal trends is a matter of conjecture. Districts such as Chikwawa, Mchinji and Lilongwe among others have shown a similar disease increasing spatial effect on cattle BTB and human EPTB and DRTB probably due to similar zoonotic contextual risk factors such as high cattle population density. This is likely considering that previous studies have shown bovine density to be positively correlated with BTB in cattle and TB in humans [13,14]. Most districts with the observed increased shared spatial effect are known to have high cattle population [20]. Other similar contextual risk factors in play may be climatic conditions such as precipitation, temperature and humidity [15,16], and this study found precipitation as a possible common driver of cattle BTB and human EPTB and DRTB incidences based on the borderline significance [33]. Lack of the outright statistical significance of precipitation may be attributed by the low statistical power of a linear model compared to the classical count data models [34]. An explanation to the observed negative effect of precipitation on cattle BTB and human EPTB and DRTB incidences is that prolonged exposure to dry conditions tend to reduce production of protective mucus on the surface of the respiratory system which can make cattle and humans vulnerable to TB infection [15]. In addition, low precipitation may result in cattle competing for fewer waterholes and food, which, in turn, due to close contacts, may result in infections. This explanation is possible considering that a previous study found waterpoint density per unit surface being negatively associated with cattle BTB [35].

The observed west-east gradient of the shared spatial effect may be explained by the increase in cattle and human activities in the west than in the east, and some of these activities include cattle movements and markets. Cattle movement networks have been known to be positively associated with BTB infection [36]. Cattle markets may also put buyers and workers at risk of zoonotic TB which tends to be extrapulmonary. More cattle and human activities in the west than in the east may be attributed by the major national road M1. The observed divergent disease specific trends would be attributed by disease specific risk factors such as farming systems for BTB in cattle [37] and human socioeconomic factors such as living conditions for human DRTB [38]. For example, the increased spatial effect on cattle BTB in the southern tip of the country is probably due to the intensive farming system practiced by large farm owners who keep their animals in feedlots. Also, dissimilar trends of BTB in cattle and EPTB and DRTB in humans in Blantyre may be attributed by high human population density, which mainly affects humans other than cattle. This is evident from this study where human population density has been found as a significant determinant of EPTB in humans, but not BTB in cattle. The divergent disease trends may also be explained by other risk factors of EPTB and DRTB in humans which are not zoonotic such as HIV infection [39]. The south-north gradient of

EPTB and DRTB is likely to be caused by higher human population density in the south and centre than in the northern region. High burden of cattle BTB in some southern districts may also be attributed by high cattle population, especially in the southern tip of the country.

The increasing temporal pattern of BTB in cattle in the study period may be due to an increase in human population which has hence forth increased trading activities thereby increasing BTB incidences. It may also be attributed by the increasing overall cattle population in the country [40]. The other possible reason for the increasing temporal pattern of cattle BTB may be the lack of implementation of control measures, due to lack of resources such as human, financial and laboratory equipment [5,7]. A possibility of sampling biases due to the absence of a well organised data base system might also be the contributing factor to the observed cattle BTB temporal pattern. The constant temporal trend of human EPTB and DRTB, especially the random effect to be constantly zero or insignificant, may be related to the reduced zoonotic TB transmissions due to the dwindling animal population per capita [41]. Also, this may be due to the decreasing human HIV infections which tend to exacerbate TB infections [42].

The study has weaknesses including that data for BTB in cattle was not collected from a well organised electronic surveillance system which might have resulted into some spatial and temporal sampling biases. Diagnosis of cattle BTB cases was based on postmortem examination and hence forth some incidences might not be the true cases. Nevertheless, the study results make sense and are consistent with the previous studies [4,5]. In addition, the study did not use the actual zoonotic TB cases in humans due to their absence since they are usually not diagnosed due to the limited hospital testing capacity. Nonetheless, the EPTB cases acted as a good proxy for zoonotic TB cases since in most cases the two tend to be positively correlated. Future studies with enough financial resources may conduct a national representative laboratory sample survey of *M. bovis* in cattle and humans and then use multivariate shared component spatial modelling for joint spatial pattern analysis.

5. Conclusions

Districts with the increased shared spatial effect between cattle BTB and human EPTB or between cattle BTB and human DRTB were mostly on the west and southern half of the country. The distribution of disease specific human EPTB and DRTB spatial effects showed a south-north gradient. The spatial effect on cattle BTB showed a west-east gradient. The shared temporal effects were constantly close to insignificance. The predicted cattle BTB and human EPTB and DRTB cases in the period with no data showed a constant pattern over time. Cattle density was positively associated with BTB cases. Human density was positively associated with EPTB. Integrated programmes to control cattle BTB and human EPTB and DRTB may focus on the western and southern half of the country. The interventions may be prioritized in cattle and human densely populated districts.

CRediT authorship contribution statement

Alfred Ngwira: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Samuel Manda:** Supervision, Writing – review & editing. **Esron Daniel Karimuribo:** Supervision, Writing – review & editing. **Sharadhuli Iddi Kimera:** Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data is provided within the manuscript or supplementary information files.

Acknowledgements

Alfred Ngwira acknowledges Partnership for Skills in Applied Sciences, Engineering and Technology (PASET) through the Regional Scholarship and Innovation Fund (RSIF) for financial support to his PhD programme. PASET had no role in the study design, data collection and analysis, the decision to publish, or the preparation of the manuscript. The findings and conclusions of this study are those of the authors and do not necessarily represent the views of PASET.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2024.100905.

References

[1] Malawi Goverment and WHO, Joint external evaluation of IHR core capacities of the Republic of Malawi [Online]. Available: https://www.who.int/publications/i/item/WHO-WHE-CPI-2019.58, 2019.
[2] Malawi Government, Policy document on livestock in Malawi [Online]. Available: https://www.fao.org/faolex/results/details/en/c/LEX-FAOC169552, 2004.
[3] T.F. Kapalamula, et al., Prevalence and risk factors of bovine tuberculosis in slaughtered cattle, Malawi, Heliyon 9 (2023) e13647.
[4] B.G. Bedard, S.W. Martin, D. Chinombo, A prevalence study of bovine tuberculosis and brucellosis in Malawi, Prev. Vet. Med. 16 (1993) 193–205.
[5] P.E. Njoka, A.B. Dibaba, The status of bovine tuberculosis in Malawi, in Tuberculosis in animals: an African perspective, Springer, Cham, 2019.
[6] B. Müller, et al., Zoonotic Mycobacterium bovis induced tuberculosis in humans, Emerg. Infect. Dis. 19 (2013) 899–908.
[7] A.B. Dibaba, N.P.J. Kriek, The control of bovine tuberculosis in Africa, in Tuberculosis in animals: an African perspective, Springer, Cham, 2019, pp. 237–270.
[8] E.H. Tzala, C. Marshall, N. Best, Multivariate analysis of spatial and temporal variation in cancer mortality in Greece: ISEE-398, Epidemiology 14 (2003) S79–S80.
[9] Q. Du, M. Zhang, Y. Li, H. Luan, S. Liang, F. Ren, Spatial patterns of ischemic heart disease in Shenzhen, China: a Bayesian multi-disease modelling approach to inform health planning policies, Int. J. Environ. Res. Public Health 13 (2016) 436.
[10] K.A. Alene, et al., Spatial codistribution of HIV, tuberculosis and malaria in Ethiopia, BMJ Glob. Health 7 (2022) e007599.
[11] I. Khattak, et al., Incidence and drug resistance of zoonotic Mycobacterium bovis infection in Peshawar, Pakistan, Adv. Exp. Med. Biol. 1057 (2018) 111–126.
[12] M.R. Silva, et al., Risk factors for human Mycobacterium bovis infections in an urban area of Brazil, Mem. Inst. Oswaldo Cruz 113 (2018) e170445.
[13] K. Willgert, et al., Is bovine density and ownership associated with human tuberculosis in India? PLoS One 18 (2023) e0283357.
[14] J.M. Madden, G. Mcgrath, J. Sweeney, G. Murray, J.A. Tratalos, S.J. More, Spatial and spatiotemporal epidemiology models of bovine tuberculosis in the Irish cattle population, 2012-2019, Spat. Spatiotemporal. Epidemiol. 39 (2021) 100441.
[15] Y. Xiao, et al., The influence of meteorological factors on tuberculosis incidence in Southwest China from 2006 to 2015, Sci. Rep. 8 (2018) 10053.
[16] Q. Gong, et al., Prevalence of bovine tuberculosis in dairy cattle in China during 2010–2019: a systematic review and meta-analysis, PLoS Negl. Trop. Dis. 15 (2021) e0009502.
[17] R. Oliveira, A. Teixeira-Pinto, Analyzing multiple outcomes: is it really worth the use of multivariate linear regression? J. Biom. Biostat. 6 (2015) 4.
[18] G. Vicente, A. Adin, T. Goicoa, M.D. Ugarte, High dimensional order free multivariate spatial disease mapping, Stat. Comput. 33 (2023) 104.
[19] A. Corberán-Vallet, Prospective surveillance of multivariate spatial disease data, Stat. Methods Med. Res. 21 (2012) 457–477.
[20] National Statistical Office of Malawi, National census of agriculture and livestock 2006–2007 [Online]. Available: http://www.nsomalawi.mw, 2010.
[21] National Statistical Office of Malawi, Population and housing census [Online]. Available: http://www.nsomalawi.mw, 2018.
[22] Malawi Government, National Tuberculosis Control Programme Manual [Online]. Available: https://pdf.usaid.gov/pdf_docs/PA00KGDD.pdf, 2012.
[23] D.W. Redding, S. Tiedt, G. Lo Iacono, B. Bett, K.E. Jones, Spatial, seasonal and climatic predictive models of Rift Valley fever disease across Africa, Philos. Trans. R. Soc. B Biol. Sci. 372 (2017) 20160165.
[24] J. Nkamwesiga, et al., Spatiotemporal cluster analysis and transmission drivers for Peste des Petits ruminants in Uganda, Transbound. Emerg. Dis. 69 (2022) e1642–e1658.

[25] R.B. O'Hara, D.J. Kotze, Do not log-transform count data, Methods Ecol. Evol. 1 (2010) 118–122.
[26] M.B. Morrissey, G.D. Ruxton, Revisiting advice on the analysis of count data, Methods Ecol. Evol. 11 (2020) 1133–1140.
[27] S. Cabras, S. He, A Bayesian spatiotemporal model for predicting passengers occupancy at Beijing metro, Spat. Stat. 55 (2023) 100754.
[28] H. Rue, S. Martino, N. Chopin, Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations, J. R. Stat. Soc. Ser. B Stat Methodol. 71 (2009) 319–392.
[29] L. Knorr-Held, Bayesian modelling of inseparable space–time variation in disease risk, Stat. Med. 19 (2000) 2555–2567.
[30] V. G'omez-Rubio, F. Palmi-Perales, G. Lopez-Abente, R. Ramis-Prieto, P. Fern'andez-Navarro, Bayesian joint spatiotemporal analysis of multiple diseases, SORT 43 (2019) 51–74.
[31] V.A. Otiende, T.N. Achia, H.G. Mwambi, Bayesian hierarchical modeling of joint spatiotemporal risk patterns for human immunodeficiency virus (HIV) and tuberculosis (TB) in Kenya, PLoS One 15 (2020) e0234456.
[32] T. Allen, et al., Global hotspots and correlates of emerging zoonotic diseases, Nat. Commun. 8 (2017) 1124.
[33] A. Hackshaw, A. Kirkwood, Interpreting and reporting clinical trials with results of borderline significance, Br. Med. J. 343 (2011) d3340.
[34] A.R. Ives, For testing the significance of regression coefficients, go ahead and log-transform count data, Methods Ecol. Evol. 6 (2015) 828–835.
[35] G. Herrero-García, et al., Waterhole characteristics in tuberculosis positive and negative beef cattle farms from endemic regions in Spain, Rangel. Ecol. Manag. 92 (2024) 50–58.
[36] A. Palisson, A. Courcoul, B. Durand, Role of cattle movements in bovine tuberculosis spread in France between 2005 and 2014, PLoS One 11 (2016) e0152578.
[37] G.M. Shirima, R.R. Kazwala, D.M. Kambarage, Prevalence of bovine tuberculosis in cattle in different farming systems in the eastern zone of Tanzania, Prev. Vet. Med. 57 (2003) 167–172.
[38] N. Shartova, F. Korennoy, S. Makhazova, Spatial patterns of tuberculosis in Russia in the context of social determinants, Spat. Spatiotemporal. Epidemiol. 45 (2023) 100580.
[39] S. Gounden, R. Perumal, N. Magula, Extrapulmonary tuberculosis in the setting of HIV hyperendemicity at a tertiary hospital in Durban, South Africa, south. African, J. Infect. Dis. 33 (2018) 57–64.
[40] FAO, Livestock sector report–a review of the livestock sector in Malawi in 2021, Lilongwe, 2022. [Online]. Available: doi:10.4060/cc1073en.
[41] E.W. Chirwa, I. Kumwenda, C. Jumbe, P. Chilonda, I. Minde, Agricultural growth and poverty reduction in Malawi: past perfomance and recent trends [Online]. Available: https://pdf.usaid.gov/pdf_docs/PNADS611.pdf, 2008.
[42] H. Kanyerere, et al., The rise and fall of tuberculosis in Malawi: associations with HIV infection and antiretroviral therapy, Trop. Med. Int. Health 21 (2016) 101–107.