Spatiotemporal transmission and socio-climatic factors related to paediatric tuberculosis in north-western Ethiopia

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Abstract

The burden of tuberculosis (TB) in children reflects continuing and recent transmission within a population. This study aimed to identify spatiotemporal and socio-climatic factors associated with paediatric TB in north-western Ethiopia. Multivariate Poisson regression models were computed using a Bayesian framework. Estimates of parameters were generated using Markov chain Monte Carlo simulation. A total of 2,240 children aged under 15 years diagnosed with TB during the years 2013-2016 were included in the analysis. The annual TB incidence rates were 44 and 28 per 100,000 children, for children aged under 15 and 5 years, respectively. Spatial clustering of TB was observed in the border area of north-western Ethiopia. The spatio-temporal transmission of childhood TB was found to be associated with district level socio-climatic factors such as urbanisation [relative risk (RR): 1.8; 95% credible interval (CrI): 1.2, 2.6], lower educational status (RR: 1.5; 95% CrI: 1.0, 2.1), a high percentage of internal migration (RR: 1.3; 95% CrI: 1.0, 1.6), high temperature (RR: 1.3; 95% CrI: 1.0, 1.7) and high rainfall (RR: 1.5; 95% CrI: 1.1, 2.0). We conclude that interventions targeting hotspot districts with a high proportion of childhood TB are important to reduce TB transmission in northwest Ethiopia.

Introduction

Tuberculosis (TB) is an infectious disease caused by bacteria of the *Mycobacterium tuberculosis* complex transmitted via airborne spread of droplet nuclei produced by patients with infectious pulmonary or laryngeal TB (Sia and Wieland, 2011). The worldwide distribution of the disease, which varies by time period and place (Tiwari *et al.*, 2006; Touray *et al.*, 2010; Li *et al.*, 2013; Nana *et al.*, 2014; Dangisso *et al.*, 2015b; Woldeyohannes and Abera, 2015), is partly determined by ecological level factors such as socio-economic (Leung *et al.*, 2004; Nana *et al.*, 2014), demographic (Feske *et al.*, 2011), climatic (Li *et al.*, 2014) and other environmental factors (Sun *et al.*, 2015).

Young children, particularly those aged under 15 years of age, are a vulnerable group for TB infection and disease (Perez-Velez and Marais, 2012). Due to the long latency period in infected adults, and the uncertainty around when and where exposure occurred, it is difficult to infer ongoing transmission in communities from the incidence of TB in adults. Because children tend to progress rapidly to active TB following initial infection, the incidence of TB in children is a very good indicator of continuing and recent TB transmission within a population (Middelkoop *et al.*, 2008; Myers *et al.*, 2006; Newton *et al.*, 2008; Shingadia and Novelli, 2003; WHO, 2013). Children usually acquire TB infection when they are exposed to an infectious adult in their close environment, either in the household or in the community (Ferrarini *et al.*, 2016; Triasih *et al.*, 2015). The rate at which latent TB infection progresses to active disease varies by age

group and immune status. In the first year after initial infection, the risk of progression of latent TB infection to active TB disease in immunocompetent children aged less than 1 year is approximately 60%, for children age less than 5 years about 10%, and for children aged less than 15 years approximately 20% (Marais *et al.*, 2004a, 2004b, 2006; Newton *et al.*, 2008).

The transmission of TB and subsequent development of active TB disease is determined by ecological and individual-level factors (Escombe *et al.*, 2008; Loudon and Spohn, 1969). Individual-level clinical, behavioural, socio-economic and demographic risk factors have been well described (Coker *et al.*, 2006; Lienhardt Christina *et al.*, 2003b, 2005; Nava-Aguilera *et al.*, 2009). However, information about community-level and ecological factors is also important when implementing public health interventions based on the local context. Previous studies have described ecological-level socio-economic, demographic and climatic factors associated with TB transmission (Myers *et al.*, 2006; Rao *et al.*, 2016), however those studies have been conducted in high-income settings with low rates of TB transmission, or they have used both adult and childhood cases of TB that makes it impossible to differentiate whether the cases were due to primary infection, reinfection or reactivation of an old one (Chiang and Riley, 2005; Cohen *et al.*, 2007; Lambert *et al.*, 2003). In addition, there have been few spatial analyses of TB in endemic countries (Alene *et al.*, 2017; Jia *et al.*, 2008; Touray *et al.*, 2010; Wang *et al.*, 2012). Such analyses can help identify clusters, or transmission hotspots. This information is useful when targeting surveillance activities and public health interventions (Kolifarhood *et al.*, 2015; Souza *et al.*, 2007; Tsai, 2011). Therefore, the aim of this study was to investigate the spatio-temporal patterns of paediatric TB and to identify socio-economic and climatic factors associated with childhood TB incidence leading to a better understand the factors driving TB transmission in high-burden settings.

Materials and Methods

Study setting

The study was conducted in North Gondar Zone, Ethiopia. This is the largest zone in the Amhara region located in north-western Ethiopia, with an estimated mean elevation of 1,422 metres above the mean sea level (Figure 1). This region has four distinct seasons: summer (rainy season) from June to August, autumn (harvest season) from September to November, winter (dry season with frost in the morning) from December to February, and spring (the hottest season) from March to May. North-western Ethiopia contains 23 administrative districts and borders Sudan in the West and Eritrea in the North. Three of the districts were excluded from the study due to unavailability of data.

In Ethiopia, the district is the smallest administrative unit where both routine disease surveillance and national census data can be linked and geo-referenced. The average population size of a district in north-western Ethiopia is 146,481 people (CSA, 2007). According to the Ethiopian census report, there were 1.28 million children under 15 years of age and 430,844 children under 5 years of age in this region in 2007 (CSA, 2007).

Study participants

All new cases of TB in children aged under 15 years who were reported to the surveillance system for the period July 2013 to June 2016 were included in the study. Separate but similar models were constructed for children aged under 5 years and under 15 years since as TB in the former category mainly represents household transmission, whereas TB in the latter group represents both household and community transmission (Swaminathan and Rekha,
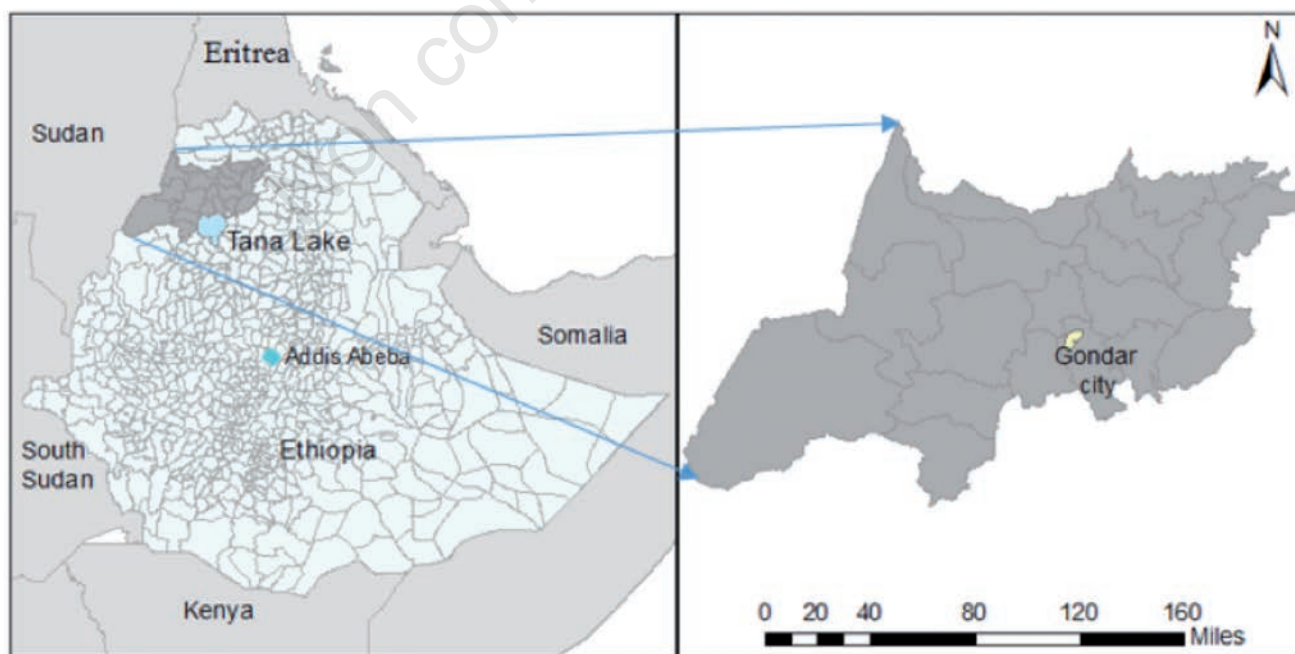
Figure 1. The geographical location of the study area (the study was conducted in the shaded part of Ethiopia, *i.e.*, north-western Ethiopia).

2010). In the analysis, the group under-15 included the group under-5.

Data collection and management

TB data for 20 districts were obtained from the Tuberculosis Control and Prevention Office, North Gondar Health Department. In Ethiopia, children with TB are usually detected either passively, *i.e.* they present to a health care service with signs and symptoms suggestive of TB, or actively as a result of contact tracing of infectious adults. TB is diagnosed based on a clinical examination, a medical history and if feasible through bacteriological confirmation (MOH, 2012). Both clinically and bacteriologically confirmed cases of TB are notified to the surveillance system on a quarterly basis and data are stored in an electronic health management information system (HMIS). Since the laboratory diagnosis of TB in children is generally difficult due to difficulties in obtaining sputum for smear microscopy, and the unavailability of chest radiography, the majority of TB diagnoses in children are based on clinical examination and medical history (MOH, 2008). In this study, we included both clinically and bacteriologically confirmed new cases of TB in children aged under fifteen years.

District-level demographic variables (*i.e.*, residence, education, illiteracy rate and internal migration); socioeconomic factors (*i.e.*, economic inactivity and unemployment rate); housing conditions (*i.e.*, average number of families in a house); indoor air pollution (*i.e.*, traditional kitchen inside the house with charcoal, firewood and dung used for cooking) were obtained from the 2007 Ethiopian census report (CSA, 2007) (Table 1). Monthly climatic data, including minimum, maximum and mean temperatures as well as mean rainfall were obtained from the global climate website, Worldclim (http://worldclim.org/version2). Since TB data were collected quarterly, the monthly climatic data were also aggregated into quarters. The population density of each district was calculated as the total population living in the district divided by the area of the district in km².

The incubation period of TB in children (*i.e.*, the period from initial infection to clinical manifestation of signs and symptoms) can vary from weeks to months (Esposito *et al.*, 2013,

Swaminathan and Rekha, 2010) and the delay in seeking health care can vary according to the health seeking behaviour of the parents (Gelaw *et al.*, 2014). The lag time between climatic exposure and reporting of active TB disease was assessed by performing a preliminary analysis. In this preliminary analysis, the association between the incidence of TB and minimum temperature, maximum temperature, mean temperature and rainfall were determined by cross-correlation plots using a moving average filter to decompose time trends. The relationship between TB and temperature was better explained by mean temperature rather than minimum and maximum temperature. Therefore, to avoid the effects of multicollinearity in meteorological variables, minimum and maximum temperature were excluded from the models, and only the mean temperature, with a six-month lag, was included.

Data analysis

Tuberculosis incidence rate

The cumulative incidence rate of childhood TB was calculated by dividing the total number of new paediatric TB cases between 2013 and 2016, by the population of the same age group in the corresponding districts, multiplied by 100,000 to obtain a rate per 100,000 population. Since the independent variables, including population density, average number of families in a house, mean temperature and mean rainfall have different units and scales of measurement that would have produced unknown threshold effects, we calculated the arithmetic mean and standard deviation (SD) for each of the district-level independent variables and standardised them to a z-scale on the basis of their mean and SD, *i.e.* (X-mean)/SD. This method also helps with identifiability in the estimation of the posterior distribution of the coefficients. A similar technique has been used in previous research to address this problem (Myers *et al.*, 2006).

Spatial analysis

TB data were geo-referenced and linked to the district level socio-economic, demographic and climatic data using geographical information system (GIS) using ArcGIS software (ESRI, Redlands, CA, USA). Spatial clustering of paediatric TB was

Table 1. Descriptive characteristics of twenty census districts in north-western Ethiopia.

Variable	Definition	Mean	SD	Range
Internal migration (%)	Percentage of population that had immigrated to a district within the last five years of the census	13.4	15.4	3.3-57.1
No schooling (%)	Percentage of people 5 years and older who never attended school	70.5	7.5	50.0-80.0
Urban residence (%)	Percentage of urban residence in the districts	17.0	16.2	0-63.3
Unemployment (%)	Percentage of unemployed people aged 10 years and older in the labour force	3.0	3.8	0.3-16.5
Non-active economically (%)	Percentage of population 10 years and older neither engaged in nor available for production of economic goods and services	32.1	10.8	14.1-48.6
Household crowding (n)	Average number of families in a house	1.0	0.01	1.02-1.05
Population density (n)	Number of people per km²	102.9	77.6	11.9-349.8
Traditional cooking inside house (%)	Percentage of the population using a traditional kitchen inside the house	11.5	6.0	4.3-27.5
Burning charcoal for heating food (%)	Percentage of the population using charcoal for cooking	17.9	15.8	2.9-57.1
Burning wood use for heating food (%)	Percentage of the population using firewood for cooking	88.2	4.8	76.0-96.3
Burning dung for heating food (%)	Percentage of the population using dung for cooking	64.3	30.0	4.4-95.3
Temperature (°C)	Monthly average environmental mean air temperature	21.1	5.2	7.2-29.9
Rainfall (mm)	Monthly average mean rainfall	82.0	92.2	0-316.6

SD, standard deviation.

assessed on a global scale using Moran's *I* statistic to gauge the presence, strength and direction of spatial autocorrelation over the whole study area and to test the assumption of spatial independence when implementing spatial pattern analysis (Appendix 1). Spatial clustering was also assessed at the local scale using the Anselin Local Moran's *I* statistic, and the Getis-Ord statistic (Anselin, 1995; Getis and Ord, 1992).

Spatiotemporal analysis

Since the number of children with TB in each district was a count variable, we assumed that it followed a Poisson distribution. We accounted for extra-Poisson variation by using covariates and random effects. Four different spatiotemporal Poisson regression models were constructed in a Bayesian framework, using the WinBUGS software, version 1.4 (Medical Research Council Biostatistics Unit, Cambridge, UK). The models were constructed with and without covariates to ascertain the ability of socio-climatic covariates to describe the spatiotemporal dependency of the data. The following models were used: I) without covariates; II) with covariates and unstructured random effects; III) with covariates and spatially structured (*i.e.*, correlated) random effects; and IV) with covariates and spatially structured and unstructured random effects.

Model 4, which includes all the components in the preceding models, was constructed as follows:

$$Y_{i,j} \sim \mathrm{dPoissson}(\mu_{ij})$$

where $Y_{i,j,}$ is the observed number of paediatric TB cases at the district level *i* and quarter *j*, was assumed to follow a Poisson distribution with mean μ_{ij}; The log of the mean value was modelled as:

$$\mathrm{Log}\,(\mu_{ij}) = \log(E_{ij}) + \alpha + \beta_k X_{ijk} + \gamma\,t + U_i + V_i$$

where E_{ij} is the expected number of paediatric TB cases in district *i* and quarter *j*, α the intercept, β_k the coefficient for covariate $X_{k,}$ γ the temporal trend in the outcome variable, t the 16 quarters of the annual period 2013-2016, *Ui* unstructured random effects and V_i spatially structured random effects.

The spatially structured random effects were modelled using a conditional autoregressive (CAR) structure (Besag *et al.*, 1991). The neighbourhood structure for the modelling of spatial correlation was based on the queen definition, whereby two areas are considered neighbours if they share a common boundary or vertex. Prior probability distributions for the coefficients β were assumed to have normal distributions with a mean=0 and a precision (*i.e.*, inverse of variance)=1×10^{-6}. For the intercept α, flat prior distributions were used (*i.e.*, a non-informative, improper prior with bounds $-\infty$ and $+\infty$). The prior for the precision of the unstructured and spatially structured random effects were assigned a non-informative gamma distribution with shape and scale parameters equalling 0.001.

The posterior parameters were estimated using a Bayesian Markov Chain Monte Carlo (MCMC) simulation. Convergence of the models was determined by visual inspection of posterior kernel densities and history plots. The model was run for 300,000 iterations and convergence occurred within the first 100,000 iterations. The models with best fit were selected on the basis of deviance information criteria (DIC) value, whereby a model with a lower DIC value was considered to be a better-fitting model. Details of the model construction are presented in Appendix 2.

Results

A total of 2,240 new cases of paediatric TB in children under 15 were reported to the zonal health department surveillance system through the HMIS from June 2013 to June 2016. Twenty-two percent (484) of the children were under 5 years, and 53% (1,180) were male. The largest proportion of cases was from Gondar Town (17%, 391) and Metema District (11%, 250). The annual incidence rate for new cases of paediatric TB was 44 per 100,000 children for children under 15 years and 28 per 100,000 children, for children under 5. The spatial distribution of TB for both age groups of children in north-western Ethiopia is presented in Figure 2. The TB incidence rate ranged from 13 to 317 per 100,000 children for children under 15 years and from 5 to 198 per 100,000 children for children under 5. The highest TB incidence rates were observed in West Armacho District (317 and 198 per 100,000 children, for children under 15 and 5 years, respectively) and Metema District (147 and 119 per 100,000 children, for children under 15 and 5 years, respectively) (Figure 2).

Data from the Ethiopian national census report indicated that the mean proportion of the population who were immigrants within the last five years of the census was 13.4 % (SD: 15.4%). The majority of the population (70.5%, SD: 7.5) were generally illiterate and 17.0% (SD: 7.5) lived in urban areas. The mean temperature and rainfall for the study area were 21°C (SD: 5.2) and 82 mm (SD: 92.2), respectively (Table 1).

Temporal trends of paediatric tuberculosis

The number of paediatric TB cases peaked in the 4th quarter, during the spring season, in all years (Figure 3). The number of cases was highest in 2013 and declined over the study period (Relative Risk (RR): 0.96; 95% CI: 0.95, 0.97). Trends in mean temperature and mean rainfall reflected trends in the number of children diagnosed with TB and were confirmed by the cross-correlation graph (Figure 3). The final model showed that the 6-month lag temperature (RR: 1.3; 95% CrI: 1.0-1.7) and rainfall (RR: 1.5; 95% CrI: 1.1-1.9) were significantly associated with TB in children less than 15 years, but not in children under 5 (Table 2).

Spatio-temporal patterns of paediatric tuberculosis

Paediatric TB was clustered in north-western Ethiopia (Global Moran's *I*=0.14; P=0.007). A high-high cluster of cases was observed in Metema and West Armacho Districts, and a hotspot for new cases of TB for both age groups was observed in Metema District (Figure 4). When the socio-climatic variables were incorporated into the model, spatial clustering was not apparent in the residuals (Global Moran's *I*=-0.18; P=0.17), indicating that the covariates could explain the spatial clustering in childhood TB counts. Based on the lowest DIC value, the model that contained covariates with an unstructured random effect was the best-fitting model for both age groups of children (Table 2).

Table 2 shows the fitted model for both age groups. In the best-fitting model for children aged under 15, lower (illiterate) educational status (RR: 1.5; 95% CrI: 1.0, 2.1), urbanisation (RR: 1.8; 95% CrI: 1.2, 2.6), high temperature (RR: 1.3; 95% CrI: 1.0, 1.7) and high rainfall (RR: 1.5; 95% CrI: 1.1, 2.0) were significantly associated with paediatric TB. When the model was restricted to children aged under 5, female sex (RR: 1.6; 95% CrI: 1.3, 1.9), urbanisation (RR: 1.6; 95% CrI: 1.1, 2.2) and a high proportion of internal migrants (RR: 1.3; 95% CrI: 1.0, 1.6) were significantly associated with paediatric TB (Table 2).

Discussion

The results presented fully explained observed spatial clustering of paediatric TB in the study area. The temporal trend of TB decreased over the study period, and the incidence was shown to have seasonal variation, with more TB observed in the spring. The decline of TB incidence in north-western Ethiopia over the study period might be due to improvements in TB treatment outcomes and TB care overall (Datiko and Lindtjørn, 2009; Dangisso *et al.*, 2015a). According to the World Health Organization (WHO), the TB treatment success rate for new cases increased in Ethiopia from 77% in 2010 to 89% in 2015 (WHO, 2012, 2016). This could be also associated with expansions of directly observed therapy (DOT) and other prevention programmes (MOH, 2008; Dangisso *et al.*, 2015a). The national TB programme report from the Ministry of Health (MOH) showed that the number of hospitals and health centres providing DOT services in the country increased by more than 62% between 2010 and 2013 (MOH, 2013).

The observed seasonal pattern, with a peak observed from March to May (*i.e.*, spring) could be a consequence of high rates of TB transmission during the winter season resulting in active TB developing several weeks or months later (Vynnycky and Fine, 2000; Marais *et al.*, 2004a). This is consistent with previous studies where high rates of TB transmission have occurred during the winter season (Thorpe *et al.*, 2004; Fares, 2011; Willis *et al.*, 2012), which could be due to seasonal variations in food availability and food intake (Roba *et al.*, 2015; Hirvonen *et al.*, 2016), indoor overcrowding (Parrinello *et al.*, 2012) and low exposure to sunlight and its subsequent impact on vitamin D levels (Webb *et al.*, 1988; Sherman *et al.*, 1990; Nnoaham and Clarke, 2008). In addition, during the winter season there are high levels of rainfall

and humidity, which may decrease airflow and favour TB transmission. This is supported by our results, whereby high rainfall recorded was associated with increased incidence of TB (Figure 3).

The observed seasonal pattern of TB could be related to migration patterns. In our study, the internal-migrant proportion of the population was associated with TB transmission. The majority of internal migrants are seasonal workers who come from different parts of the country and who are employed in the agricultural sector (Asfaw *et al.*, 2010). These people live, work and eat together in overcrowded living conditions, which may further facilitate TB transmission. Our study identified also urbanisation as a TB risk factor, which is supported by previous studies reporting that TB incidence is associated with urban residence, poor quality housing with overcrowding, lack of water and sanitation (Barnes *et al.*, 2011; Prasad *et al.*, 2016). Indeed, environmental factors that facilitate TB transmission may be more common in urban settings (Lienhardt Christian *et al.*, 2003a, 2003b; Narasimhan *et al.*, 2013).

Furthermore, socioeconomic status has been associated with TB. In districts where a high proportion of the population was illiterate, childhood TB rates were found to be high. This could be due to the fact that lower educational status may lead to a poorer understanding of the transmission of the disease and self-protective measures. It may also be associated with poor living conditions, including household overcrowding and other issues, such as poor access to healthcare. This may suggest that higher educational levels at the community level may reduce TB transmission and incidence. Wealth and levels of educational attainment have been associated with TB across many settings (Harling *et al.*, 2008; Suk *et al.*, 2009).

The present study is the first published study on the spatio-temporal distribution of paediatric TB in Ethiopia. The study included several

Table 2. Socio-climatic factors associated with tuberculosis in children in north-western Ethiopia in the period 2013-2016.

District-level variable	Children under 15 years			Children under 5 years		
	Model II[#]: Unstructured	Model III[§]: Structured	Model IV[^]: Unstructured and structured	Model II[#]: Unstructured	Model III[§]: Structured	Model IV[^]: Unstructured and structured
	RR (95% CrI)	RR (95% CrI)	RR (95% CrI)	RR (95% CrI)	RR (95% CrI)	RR (95% CrI)
Female	1.08 (0.99, 1.17)	1.08 (0.99, 1.17)	1.08 (0.99, 1.17)	1.60 (1.33, 1.92)	1.60 (1.33, 1.92)	1.60 (1.33, 1.92)
Education status illiterate (%)	1.47 (1.02, 2.06)	1.29 (0.86, 1.84)	1.41 (0.95, 2.02)	1.19 (0.85, 1.66)	1.09 (0.77, 1.52)	1.16 (0.81, 1.62)
New internal migrant (%)	1.09 (0.84 1.39)	1.18 (0.87, 1.55)	1.13 (0.85, 1.46)	1.29 (1.01, 1.60)	1.40 (1.07, 1.77)	1.32 (1.03, 1.67)
Use of firewood for cooking (%)	1.05 (0.84 1.29)	1.05 (0.76, 1.39)	1.04 (0.80, 1.32)	1.03 (0.84, 1.25)	1.06 (0.81, 1.38)	1.04 (0.82, 1.30)
Urban population (%)	1.85 (1.25, 2.62)	1.59 (1.03, 2.31)	1.76 (1.15, 2.58)	1.58 (1.14, 2.22)	1.40 (0.97, 1.97)	1.53 (1.06, 2.16)
Autumn (Sep-Nov)	0.74 (0.61, 0.88)	0.72 (0.58, 0.89)	0.73 (0.59, 0.88)	0.86 (0.60, 1.18)	0.88 (0.60, 1.23)	0.86 (0.60, 1.20)
Summer (Dec-Feb)	0.46 (0.20, 0.91)	0.42 (0.18, 0.84)	0.44 (0.19, 0.90)	0.41 (0.06, 1.41)	0.38 (0.05, 1.35)	0.40 (0.06, 1.43)
Spring (Mar-May)	1.14 (0.91, 1.41)	1.11 (0.88, 1.38)	1.13 (0.90, 1.40)	0.90 (0.55, 1.40)	0.88 (0.53, 1.38)	0.89 (0.53, 1.40)
Temperature (°C)	1.34 (1.04, 1.73)	1.37 (0.99, 1.88)	1.36 (1.02, 1.82)	1.20 (0.91, 1.59)	1.12 (0.81, 1.52)	1.19 (0.88, 1.59)
Rainfall (mm)	1.50 (1.11, 1.98)	1.56 (1.15, 2.08)	1.53 (1.12, 2.03)	1.68 (0.89, 2.88)	1.75 (0.90, 3.08)	1.72 (0.89, 3.03)
Temporal pattern (by quarter)	0.96 (0.95, 0.97)	0.96 (0.95, 0.97)	0.96 (0.95, 0.97)	0.94 (0.92, 0.96)	0.94 (0.92, 0.96)	0.94 (0.92, 0.96)
Constant	0.29 (-0.08, 0.67)	0.35 (0.01, 0.69)	0.31 (-0.07, 0.67)	0.30 (-0.32, 0.92)	0.35 (-0.27, 0.97)	0.32 (-0.32, 0.96)
Variance (unstructured)	7.05 (2.64, 14.0)	-	58.14 (2.99, 558.0)	16.69 (3.6, 53.9)	-	65.98 (3.91, 552.0)
Variance (spatially structured)	-	1.62 (0.60, 3.25)	127.40 (0.92, 1056.0)	-	7.33 (0.8, 21.6)	176.70 (1.5, 1283.0)
DIC	2839.45	2841.81	2842.42	1379.47	1383.14	1380.80
DIC (without covariate)°	2848.30	-	-	1383.74	-	-

DIC, deviance information criterion; RR, relative risk; CrI, credible interval. °Value obtained from Model I (*i.e.* the model without covariate); #model with covariates and unstructured random effects (*i.e.* fixed effects and non-spatial random effects); §model with covariates and structured random effects (*i.e.* fixed effects and spatially correlated random effects); ^model with covariates, structured and unstructured random effects (*i.e.* fixed effects, spatially correlated random effects and non-spatial random effects).
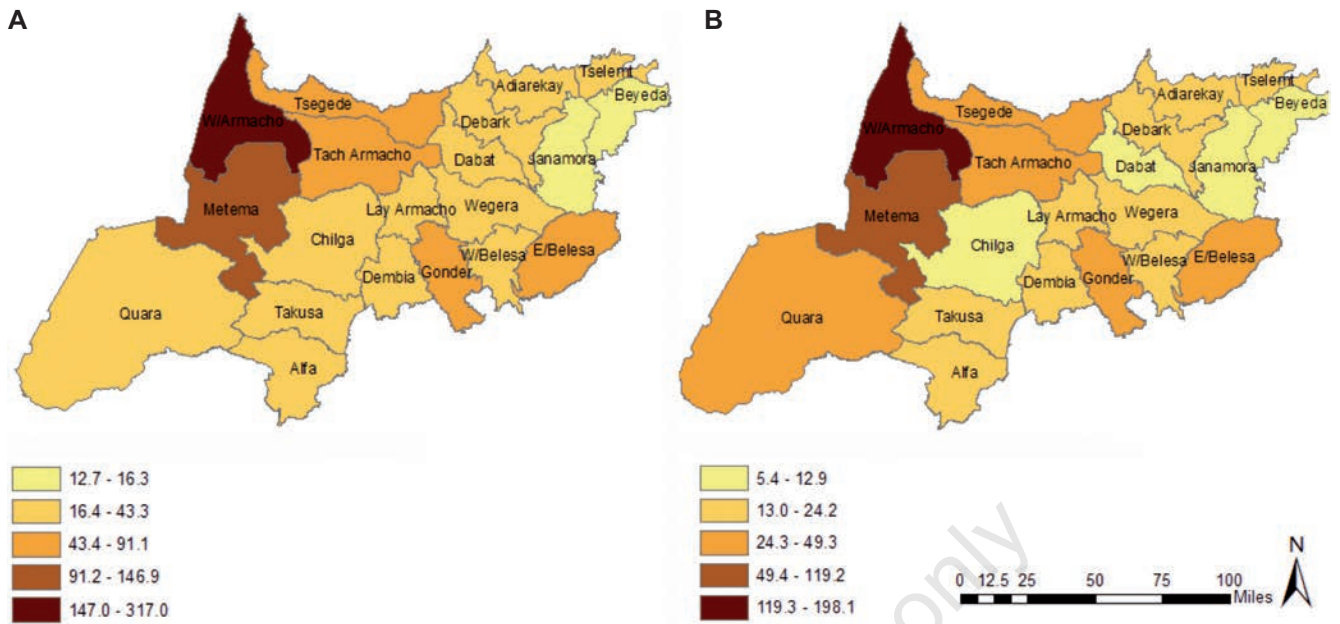
Figure 2. Paediatric tuberculosis annual incidence rates per 100,000 children in twenty districts of north-western Ethiopia: A) for children under fifteen years; B) for children under five years.
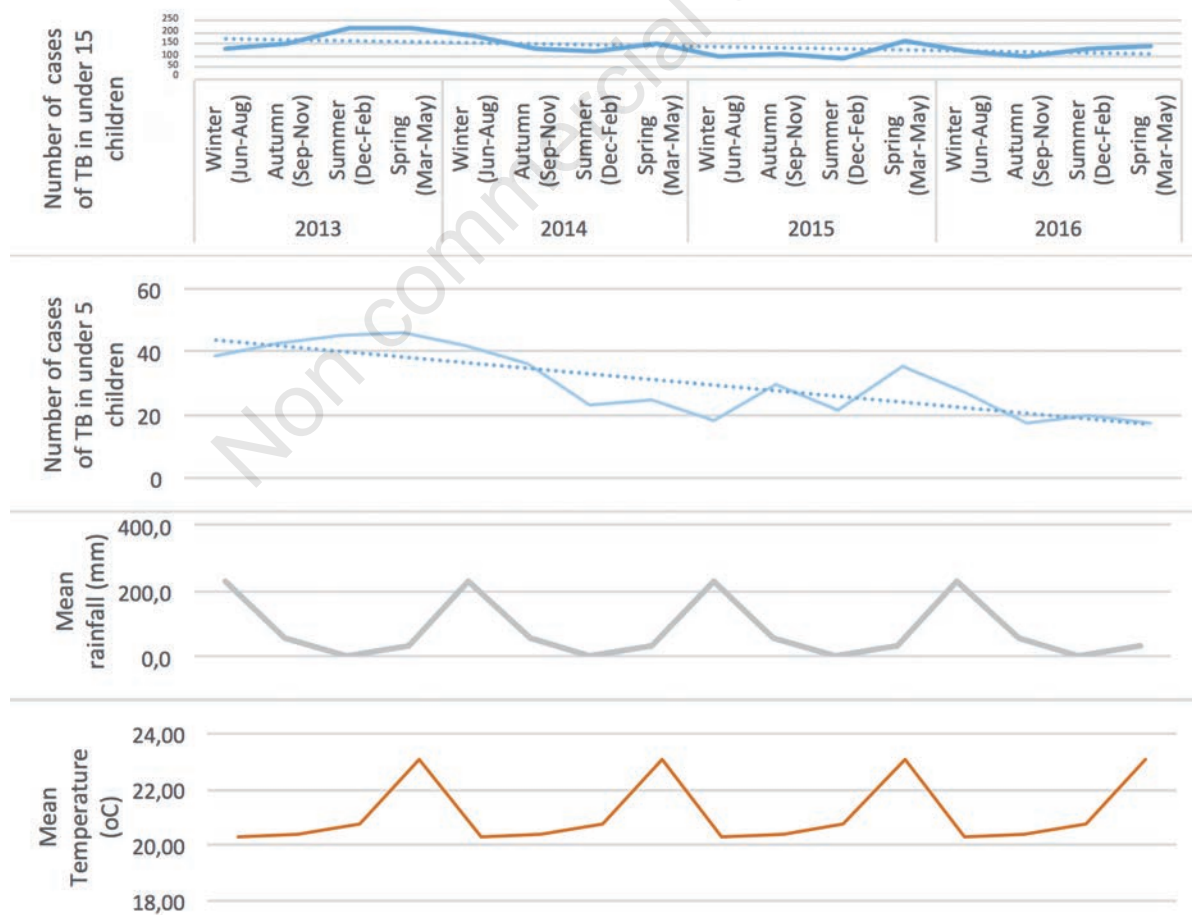

Figure 3. Tuberculosis diagnoses in children under fifteen years and in children under five years compared to temperature and rainfall in north-western Ethiopia by quarter over the period 2013-2016.

ecological variables that were associated with rates of TB, but all environmental variables plausibly associated with TB were not included. For instance, temperature and rainfall are not the only climatic factors that may be associated with TB transmission, other important meteorological variables such as hours of sunshine, wind speed and atmospheric pressure may also be associated (Rao *et al.*, 2016). However, since north-western Ethiopia is located in a tropical region, some climatic factors, such as hours of exposure to sunshine, are relatively homogenous in the study area. Additionally, it should be acknowledged that TB transmission is multi-factorial and heavily influenced by socio-economic factors, many of which we did not examine.

Given that this was an area-level analysis, it is important to acknowledge the ecological fallacy, whereby associations at one level of aggregation cannot be assumed to hold true at other levels, including for individual people in the study area. Under-detection and under reporting of paediatric TB are a potential limitation of the study, and the exact burden of TB among children in north-western Ethiopia is not be known. Finally, we have not incorporated some other important clinical risk factors into the analysis such as HIV infection, a potent risk factor for TB.
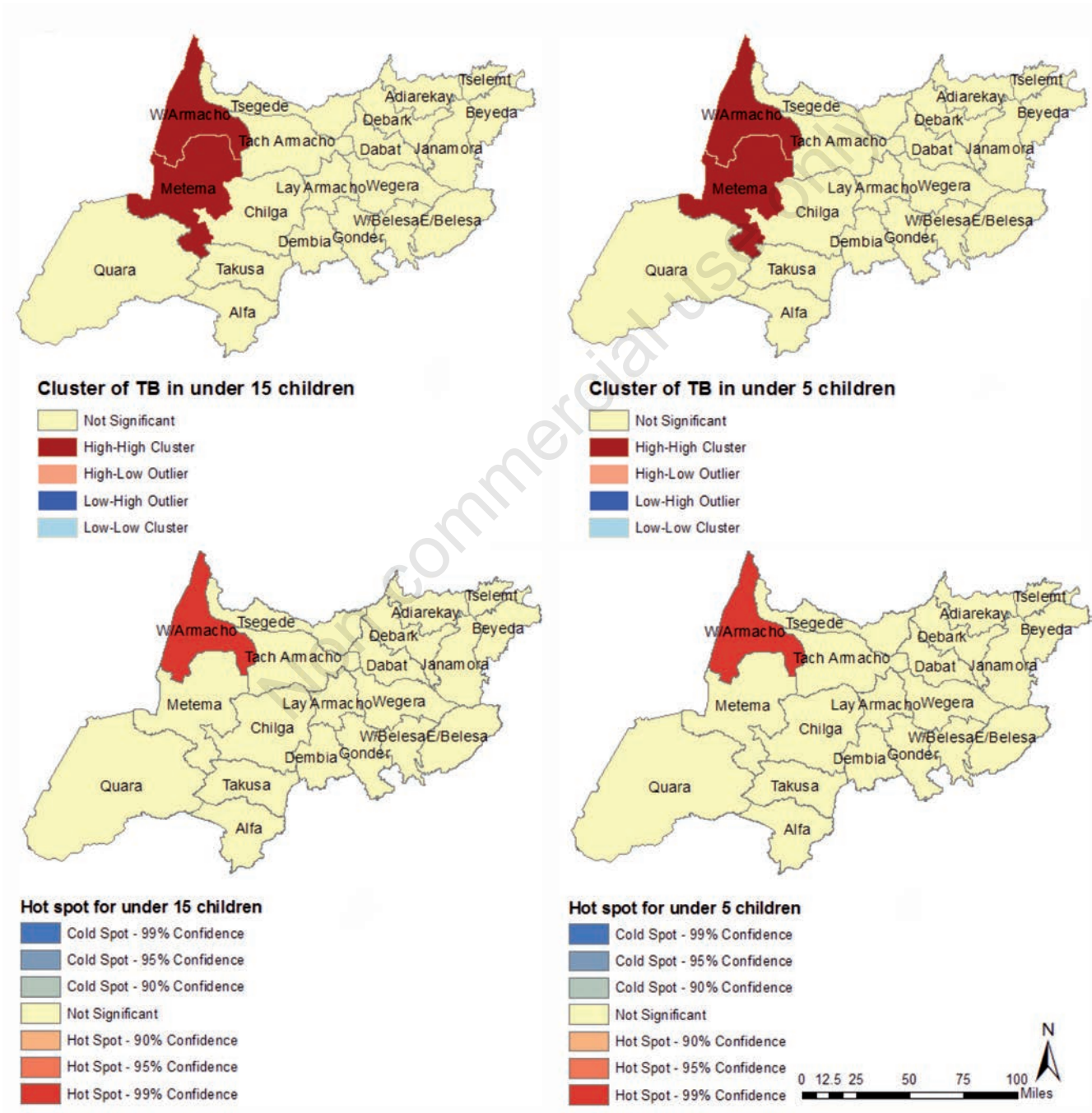

Figure 4. Spatial clusters tuberculosis incidence rate and hot spots for children in north-western Ethiopia in the period 2013-2016.

Conclusions

We found that paediatric TB was spatiotemporally clustered in north-western Ethiopia and that clustering was associated with several socio-climatic factors, including urbanisation, internal migration, educational status, rainfall, and temperature. The identification of paediatric TB clustering can help to identify TB transmission hotspots. Using this information, decision-makers may want to implement focused interventions for the control and prevention of TB in high-transmission districts.

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