



# Hierarchical Bayesian modeling of spatio-temporal patterns of scrub typhus incidence for 2009–2013 in South Korea

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## ABSTRACT

This study aims to analyze spatio-temporal patterns of scrub typhus incidence and to identify environmental risk factors in South Korea from 2009 to 2013 using hierarchical Bayesian Poisson model. We classified 244 municipal areas into nine categories based on the posterior relative risks and their temporal trends and these patterns were visualized. Environmental covariates (i.e. land surface temperature, precipitation and vegetation) were compiled by season to reflect the seasonal behavior of trombiculid mites and rodents and by year to explain year-based environmental changes. A total of six covariates were incorporated in the regression model and environmental effects were evaluated. We found areas in the south, southwest, and southeast of South Korea that present relatively high risk, and the north and southeast parts show rapid increases during the study period. The spatio-temporal maps present similar patterns as well. A positive correlation is found between the scrub typhus risk and precipitation in summer, and normalized difference vegetation index in fall. In contrast, the scrub typhus risk is negatively correlated with land surface temperature in fall. This information has implications for prioritizing disease control resources on high-risk areas. Furthermore, the regression results might be utilized for predicting scrub typhus incidence and contribute to the design of disease control programs in the future.

## 1. Introduction

Scrub typhus, also called Tsutsugamushi disease, is an acute infectious human disease caused by pathogenic *Rickettsia Tsutsugamushi* (Kawamura, Tanaka, & Tamura, 1995). It occurs when pathogen-infected larval trombiculid mites bite humans. The clinical symptoms of scrub typhus are high fever, chills, and skin eruptions, and it can also cause death in cases of inappropriate treatment; thus, taking appropriate measures for the disease is needed (KCDC, 2012; Kawamura et al., 1995; Kong et al., 2007). Scrub typhus is prevalent in eastern Asia, the western Pacific, and northeastern Australia, called the Tsutsugamushi Triangle, and roughly one million people in this triangle are newly infected by *R. Tsutsugamushi* annually; South Korea is included in this triangle (Watt & Parola, 2003). After the first case in 1986, the number of scrub typhus infection in South Korea has drastically increased (KCDC, 2012, 2014; Kong et al., 2007; Kweon et al., 2009). Currently, it is one of the most common chigger-borne diseases in South Korea, with 34,787 cases reported between 2009 and 2013.

The epidemiology of scrub typhus depends on the interactions among three critical elements; (i) trombiculid mites, (ii) vertebrate hosts and (iii) the pathogen *R. Tsutsugamushi*. Larval trombiculid mites feed on the tissue fluids of vertebrate hosts (such as *Apodemus agrarius*, *Microtus fortis*, and *Micromys minutus*) and humans until they obtain enough nutrients from the fluids and drop off from the hosts to become

adult mites (Kawamura et al., 1995; Sasa, 1961). Transmission occurs when humans travel through vegetation and are exposed to infected larval trombiculid mites. Each generation of these mites harbors *R. Tsutsugamushi* in one of two ways: (i) either feeding on an infected vertebrate host, or (ii) ovarian transmission between female mites and their offspring.

Three critical elements actively interact one another and transmit scrub typhus under specific climate conditions, called scrub typhus nest (Kawamura et al., 1995; Reisen, 2010). Climatic conditions such as temperature and precipitation are important for the transmission of scrub typhus, as these factors form critical conditions for the development of vectors and vertebrate hosts (Gage, Burkot, Eisen, & Hayes, 2008; Gubler et al., 2001). Vectors such as mosquito, tick, and trombiculid mite are poikilothermic arthropods, very sensitive to climate conditions (Kawamura et al., 1995; Sasa, 1961; Yang et al., 2014). For trombiculid mites, in particular, temperature must attain certain ranges within the tolerances for the development, reproduction, behavior, and completion of their life cycle. Moreover, the previous research reveals that the activity of trombiculid mites depends on humidity (Kim & Jang, 2010; Sasa, 1961), which is closely related to the amount of precipitation. Furthermore, climate conditions are influential for vegetation to form and develop, and vegetation, in turn, provides habitats for both trombiculid mites and vertebrate hosts, and food for vertebrate hosts (Barrios et al., 2013; Reisen, 2010). As a result, scrub typhus nests

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are strictly restricted to specific locations in the certain climate conditions that are suitable for their survival.

Recent climate changes in South Korea have contributed to changes in ecology of vectors and hosts, which might affect the distribution of scrub typhus nests and the disease risk at the same time. Scrub typhus surveillance data from the Korea Centers for Disease Control & Prevention (KCDC) reported that a substantial increase in scrub typhus incidence was observed from 4995 in 2009 to 10,365 in 2013, potentially due to the climate changes in South Korea (KCDC, 2014). Significant increases in temperature and precipitation in South Korea have recently been observed (Kim & Kim, 2011; Kim, Kang, & Adams, 2012; Kug & Ahn, 2013; Yoo et al., 2011), and these changes may cause the increase in the population of trombiculid mites in scrub typhus nests, due to the increased habitat's suitability for their survival. To our knowledge, however, only few research has been conducted about the relationship between scrub typhus incidence and changes in climate and vegetation in South Korea (Kim & Kim, 2014; Kwak et al., 2015). Thus, it is necessary to investigate the ecology of scrub typhus in conditions under which the susceptibility to scrub typhus has dramatically increased over five years.

Recent increases in scrub typhus incidence and vulnerability imply that mapping the spatio-temporal patterns of scrub typhus incidence within a given interval is required to identify high-risk areas (Lawson, 2013). An analysis of scrub typhus risk from both spatial and temporal perspectives highlights high-risk areas where the disease is endemic and identify their temporal changes. Thus, the resulting map can provide implications for prioritizing disease control resources in high-risk areas and enable us to develop effective disease control strategies (Cromley & McLafferty, 2011; Dickin, Schuster-Wallace, & Elliott, 2014; Hsueh, Lee, & Beltz, 2012; Kuo, Huang, Ko, Lee, & Wang, 2011; Richardson, Thomson, Best, & Elliott, 2004).

A Bayesian spatio-temporal model proposed by Bernardinelli et al. (1995) is appropriate for the analysis of scrub typhus risk and its temporal variations (Bernardinelli et al., 1995). Using this model, disease risk can be divided into three main components: (i) a spatial pattern within the specific time period, (ii) a temporal trend over the study areas, and (iii) a space-time interaction effect within the certain area (Bernardinelli et al., 1995; Law, Quick, & Chan, 2014; Li, Haining, Richardson, & Best, 2014). Not only can this Bayesian framework highlight high-risk areas but also identify temporal changes in disease risk within each areal unit over the study period. Furthermore, the Bayesian model has the advantages in that it can control two major statistical issues: (i) overdispersion, which occurs when the variance in the count data modeled by Poisson distribution is larger or smaller than the mean and (ii) the small sample size problem, which gives rise to unstable estimates because of low counts of disease occurrence (Beale, Lennon, Yearsley, Brewer, & Elston, 2010; Bernardinelli et al., 1995; Haining, Law, & Griffith, 2009). With these advantages, the Bayesian approach has been applied to the analysis of vector-borne diseases such as Lyme disease (Barrios et al., 2013; Chen, Stratton, Caraco, & White, 2006, pp. 777–784; Waller et al., 2007), malaria (Alegana et al., 2013; Villalta, Guenni, & Rubio-Palis, 2013), and dengue fever (Lowe et al., 2011). However, limited attention has been paid to the Bayesian analysis of scrub typhus risk.

This study aims to investigate the spatio-temporal patterns of scrub

typhus incidence in South Korea from 2009 to 2013 and to identify its environmental risk factors using a Bayesian spatio-time framework. Resources for preventing scrub typhus are limited, and only 34 out of 251 municipal areas are running scrub typhus control programs in South Korea (KCDC, 2012). Thus, prioritizing resources on high scrub typhus risk areas is required for the design of disease control plans. To achieve this, we fractionized the study areas based on the relative risks and their temporal trends. Specifically, in the first stage all municipal areas were classified by their relative risk of scrub typhus: high, moderate, or low. Secondly, these areas were reclassified by the local trend: increasing, similar to the overall trend, or decreasing. This classification can highlight both high-risk areas and moderate-risk areas with increasing trends and yield bases in order to focus resources on these areas. Furthermore, to identify risk factors for scrub typhus, we incorporated seasonal (summer and fall) and annual (from 2009 to 2013) environmental covariates (land surface temperature, precipitation and vegetation) that are potentially associated with the epidemiology of scrub typhus. With the analysis of the spatio-temporal patterns of scrub typhus risk within a given time, this study is expected to provide increased understanding of scrub typhus incidence and theoretical backgrounds for disease control strategies.

## 2. Materials and methods

### 2.1. Disease incidence data and seasonal covariates

Mainland South Korea and Jeju-do are the study area for this analysis. Minor small islands (7 of 251 municipal areas in 2013) were excluded from this analysis because of the ecological differences between the mainland and the islands (such as climate, vegetation, and soil). Scrub typhus count data taken from 2009 to 2013 were provided by the Korea Centers for Disease Control (KCDC). Original data include patient information such as submunicipal-level address, age and gender. All records were geocoded and aggregated to municipal level to protect patients' personal information and to reflect the administrative area boundary changes between the 2009 and the 2013 census.

To explain scrub typhus incidence patterns, environmental covariates were selected based on previous research (Kim & Kim, 2014; Kong et al., 2007; Kuo et al., 2011; Wardrop et al., 2013). Environmental risk factors are composed of three main components: (i) land surface temperature (LST) (°C), (ii) rainfall (mm), and (iii) normalized difference vegetation index (NDVI) (Table 1). We used LST in this research as trombiculid mites and rodents live on the ground surface so LST might reflect the ecology of the disease better than the air temperature. NDVI was incorporated to investigate the vegetation effects on scrub typhus incidence (Pettorelli et al., 2005). Data were collected and compiled for summer (from June to August) and fall (from September to November) to reflect the ecological behavior of trombiculid mites, which hatch in late summer and feed the tissue fluids in fall. Furthermore, data were assembled by year (from 2009 to 2013) to explain the annual variations in the ecological factors that affect scrub typhus incidence. Thus, each environmental risk factor contains a total of ten temporal datasets (Fig. 1).

The land surface temperature (LST) in summer and fall over five years was calculated using satellite images (MOD11A1) collected by a

**Table 1**  
List and brief descriptions of the seasonal (summer and fall) covariates used in this study.

Season	Covariates	Description
Summer	Land surface temperature	Female mites lay eggs at favorable temperature (25–32 °C) and hatch them in two weeks (Sasa, 1961)
	Precipitation	Heavy precipitation can eliminate trombiculid mite eggs or scrub typhus nests
	NDVI	Habitat index for vertebrate hosts and trombiculid mites
Fall	Land surface temperature	Feeding activity is more active at high temperatures in fall (Kawamura et al., 1995)
	Precipitation	The amount of precipitation is related to humidity in habitats and food availability (Gubler et al., 2001)
	NDVI	Habitat index for vertebrate hosts and trombiculid mites

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