A Comparative Analysis of Malaria Risk in Japan and the Republic of Korea: Current Trends and Future Risk in the Context of Climate Change*

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Abstract. Japan and the Republic of Korea (South Korea) are former malaria endemic areas, where malaria vectors are still present. This article compares the current situation in each country, analyses reasons for the differences, determines the main climatological parameters controlling malaria prevalence and makes predictions of the climatic suitability of further re-emergence in the region as a result of climate change. Future projections of risk are made using a climatically sensitive base-reproduction rate model for malaria. The results showed that South Korea experiences significantly more annual cases of malaria. Multiple regression analysis indicated that climatic variables have a statistically significant influence on the monthly malaria trends in South Korea ($R^2$ 11.1%) and no statistical influence on annual trends 1993–2010. The base reproduction rate model simulates the impact of climate on the biological processes involved in malaria transmission. Simulations of the biological base reproduction rate model Projected that the climate will become more suitable for malaria transmission in the future in all of the study areas. This model provides an important first step towards understanding the impact of climate change on malaria transmission.

Key Words: Malaria risk, Japan, Republic of Korea, climate change, infectious diseases, re-emergence

1. Introduction

Malaria is the most prevalent parasitic vector borne disease in the world, with an estimated 207 million reported cases per year (WHO, 2014). Despite increased global spending, there has not been a significant decrease in cases annually. In addition to this, the influence of the climate on a number of the parameters controlling transmission means that there is potential for malaria to spread to previously malaria free regions (van Lieshout et al., 2004). For this reason, it is important to investigate malaria trends in areas on the periphery of the current endemic region and determine the risk of re-emergence in these areas. Indigenous malaria was eradicated from Japan in 1961 and from South Korea in 1979. However, malaria (Plasmodium vivax strain) re-emerged in South Korea in 1993 (Feighner et al., 1998). The incidence of malaria outbreaks in South Korea has fluctuated since re-emergence, suggesting that re-emergence in similar geographic areas is possible (Feighner et al., 1998; Han et al., 2006). Research comparing reasons for differences in prevalence between countries is important for understanding the variables that control malaria prevalence, and has not been undertaken between South Korea and Japan.

Several studies that propose that there is a strong link between the climate and the distribution of malaria (van Lieshout et al., 2004; Jones and Morse, 2010; Parham and Michael, 2010). This is particularly true in terms of temperature, monthly rainfall and
humidity (Kleinschmidt et al., 2000). Changes to the climate are most likely to have an impact on the spatio-temporal distribution of malaria in areas at the fringes of current endemic regions (Lindsay and Birley, 1996; Martens et al., 1999). These are areas where climatic conditions are seasonally suitable for malaria outbreaks (Guerra et al., 2006), where malaria transmission vectors are present. With an anticipated increase of global temperatures of between 1.1–2.9°C and 2.4–6.4°C by 2100 (Representative Concentration Pathway (RCP) climate scenarios), the area of the world at risk from re-emerging malaria is expected to increase. Therefore, it is important to understand the relationship between malaria and the climate to identify areas at the pole-ward and altitudinal limit of malaria distribution which could be at risk to future epidemics.

Malaria can be controlled by anthropogenic factors, including medical treatments, vaccinations and control of potential vector populations (Han et al., 2006; Ermert et al., 2011). These all have financial costs. Therefore, being able to identify areas at different risk levels is vital in ensuring that financial resources are allocated to malaria control efficiently (Guerra et al., 2006). This is particularly relevant to South Korea and Japan, where increased international travel and the presence of malaria vectors (Anopheles sinensis mosquito) makes re-emergence through imported malaria a potential threat (Kano and Kimura, 2004).

The aim of this research is to compare the malaria situation in Japan and South Korea, and to analyse the risk of re-emergence occurring in Japan under climate change. The potential risk of malaria re-emergence in an area can be estimated by calculating the base-reproduction rate model (Lindsay et al., 2010). This model simulates the effect of temperature on the transmission rate of malaria (Lindsay and Birley, 1996). Therefore, it is an indicator of which areas could support transmission of malaria if subjected to an imported case, assuming the vector is present. A number of the parameters (human biting rate, gonotrophic cycle and sporogonic cycle) are temperature dependent. Thus, climate can be used as a predictor of risk.

2. Methods

A research framework was developed to compare and explain the differences between malaria transmission trends in Japan and South Korea and to project the future risk of outbreaks occurring in these areas as a result of climate change. An initial comparative analysis was conducted, including a quantitative analysis of the relationship between temperature and malaria transmission. Based upon this analysis, it was deemed appropriate to produce risk projections by combining a malaria transmission model with climate model outputs to identify changes in future risk from climate change. Finally, to identify the key uncertainties and focus future model improvement research, a full literature review of the sensitivity of the malaria transmission model components was conducted.

2.1 Direct comparison

Observational data of reported malaria cases were collated from the Korean Center for Disease Control (KCDC, 2014) and the Japanese Infectious Disease Surveillance Center (IDSC, 2014). A comparison of annual trends in Japan and South Korea was made to determine the differences in occurrence of malaria in both countries. In order to attempt to explain the differences, statistical analysis and a literature review were conducted.

2.2 Quantitative assessment of climatic factors

The initial comparison revealed the need for a more detailed analysis of annual and monthly trends of reported malaria cases in South Korea to be conducted. Particular focus was placed on the trend of malaria cases in relation to known factors in malaria transmission: near surface air temperature; precipitation; and relative humidity. Monthly values for minimum temperature, maximum temperature, precipitation and relative humidity (KMA, 2011) were obtained for each region for the period corresponding with the available malaria records (2001–2010). The relationship between each of these values and the number of malaria cases was then statistically analysed using regression analysis at a monthly and early level to assess the correlation between each variable and the number of malaria cases.
2.3 Base reproduction rate model risk projections

The statistical analysis revealed that it was appropriate to use a process-based malaria transmission model to project future risk of re-emergence in the region based upon monthly temperature projections. The principal theory behind the process-based method is the concept of the basic reproduction rate of malaria \( (R_0) \) (Lindsay and Thomas, 2001; Anderson and May, 1991). \( R_0 \) is calculated using an equation to represent the temperature dependent cycles in the process of malaria transmission. The value of \( R_0 \) represents the average number of infections that are produced from the introduction of a single infected individual into a potential host population (van Lieshout et al., 2004). Any \( R_0 \) value that is greater than 1 means that malaria can proliferate indefinitely. If the value of \( R_0 \) is less than 1 then the disease will die out without further external introductions (Parham and Michael, 2010).

The formula used to calculate the basic reproduction rate \( (R_0) \) is explained below (Lindsay and Birley, 1996; Lindsay et al., 2010; Lindsay and Thomas, 2001):

\[
R_0 = \frac{ma^2bp^n}{-\ln(p)r} \tag{1}
\]

Where \( m \) is the number of vectors per person and \( a \) represents the number of mosquito bites per person per day (Lindsay and Birley, 1996). When the population of mosquitoes is unknown then \( ma \) is assumed to be one (Lindsay and Thomas, 2001). When \( ma \) is assumed to be one, the female mosquito feeding rate \( (a) \) must be calculated. In this study, \( ma \) is assumed to be 1, due to the lack of available mosquito population data and to enable comparison with previous studies (Lindsay and Birley, 1996; Lindsay and Thomas, 2001). The feeding rate is calculated by using the following equation:

\[
a = \frac{h}{u} \tag{2}
\]

In this equation, \( h \) represents the proportion of female mosquito feeding incidences (blood meal) that are taken from humans. An accepted constant value for this is 0.42 (Lindsay et al., 2010). \( u \) is the length of time in days that it takes for a mosquito to complete the gonotrophic cycle (time between taking a blood meal, laying eggs and taking the next blood meal (Lindsay and Birley, 1996)). The gonotrophic cycle length is calculated by using the following formula:

\[
u = \frac{f_1}{T-g_1} \tag{3}
\]

Here, \( f_1 \) is a thermal sum, measured in degree days, representing the accumulation of temperature units over time that is required for the gonotrophic cycle to be completed (36.5°C) (Lindsay and Thomas, 2001). \( T \) represents the ambient temperature and \( g_1 \) is a temperature threshold below which development ceases (9.9°C; Lindsay et al., 2010). In the \( R_0 \) formula, \( b \) is the proportion of female mosquitoes that develop parasites after taking an infective blood meal (0.19). \( p \) is the daily survival probability for adult mosquitoes which, for this model, is calculated by a formula using the ambient temperature as a factor (Lindsay and Birley, 1996):

\[
p = \exp\left(\frac{-1}{4.4+1.31T-0.03T^2}\right) \tag{4}
\]

In the initial equation, \( n \) represents the sporogonic cycle (the length, in days, of the period of parasite development in adult mosquitoes) and is given by:

\[
n = \frac{f_2}{T-g_2} \tag{5}
\]

Where \( f_2 \) is a thermal sum representing the accumulation of temperature units over time to complete the sporogonic cycle (105 degree days; Lindsay et al., 2010), \( T \) is the ambient temperature and \( g_2 \) is a temperature threshold below which the cycle cannot be completed (14.5°C). \( r \) is the average recovery rate of humans once they have been infected with malaria (0.0167 recovery per day).

For the risk map projections, climate model outputs (monthly average temperature) from the Korean Meteorological Agency (MM5 RCM; Koo et al., 2009), for South Korea, and the CMIP5 CCSM4 model run for RCP8.5 (for the comparative maps of Japan and Korea) were incorporated into the temperature dependent parameters in the formulae to represent the temperature components of the model. Once run, time-slices of malaria risk were generated.
The measure of risk was designated as the number of months that malaria transmission could be supported ($R_0 > 1$), if a case of malaria was imported into the study area.

3. Results

3.1 Direct comparison

Annual reported cases of malaria in Japan and South Korea differ greatly, with Japan averaging 99 cases per year and South Korea averaging 1,575 cases per year (Figure 1). In addition to this, the annual variation between cases in South Korea is much greater than in Japan (Standard deviation 1239.5 and 23.4, respectively). Further analysis was undertaken to understand the nature of malaria cases in both countries. This revealed that 100% of the cases of malaria reported in Japan since 1990 were imported cases. When compared to imported cases in South Korea, it becomes clear that a vast majority of cases reported in South Korea are indigenous cases (Figure 2). Only 2.9% of cases reported in South Korea in 2010 were recorded as imported cases. Previous studies (Yeom et al., 2012; Jun et al. 2009) propose that the initial re-emergence of malaria in South Korea was caused by transmission from the Democratic People's Republic of Korea (North Korea). The cause of the outbreak in North Korea, which triggered the re-emergence in South Korea cannot be quantitatively attributed to a single cause due to the lack of data, though it has been proposed that it was a combination of a collapse of the medical care system, poor sanitation and a number of floods 1993–1996 (Feighner et al., 1998). These events produced more breeding sites for mosquito vectors in the vicinity of the border, which enabled the transfer of infected vectors into South Korea (Feighner et al., 1998). In order to understand the difference in malaria transmission patterns between Japan and South Korea, comparisons of other known malaria transmission parameters were made between both countries. This revealed that the land-use in both countries is distributed similarly, with the only significant difference being the percentage of the population living in urban areas—a poor land-use classification for malaria transmission. (92% in Japan, compared to 83% in South Korea (CIA World Factbook, 2014)).

3.2 Quantitative assessment of climatic factors

A strong seasonal trend in the number of reported cases of malaria was found in all provinces. July and August were found to be the most prevalent months for malaria, with an average of 390.8 and 404.5 cases respectively (Figure 3). Multiple regression analysis was undertaken to determine the relationships between monthly reported malaria cases and the corresponding monthly average values of four climatic variables: Minimum and maximum temperature; precipitation; relative humidity. The variables statistically significantly predicted 11.1% ($R^2$) of the variation in malaria cases. The low $R^2$ values can be explained by the vast regional differences in the number of cases recorded each month. Multiple regression analysis was re-run with the regions selected as nominal value variables. The statistically significant regression ($R^2 = 13.1\%$) identified the region variable as the most significantly significant predictor of cases ($\beta=$
To investigate the climatic impact at a regional level, multiple regression analysis was performed for each region. This identified a stronger relationship between the four climate variables and malaria prevalence (Table 1). A strong relationship was found between average monthly minimum and maximum temperature and malaria prevalence, particularly in Gyeonggi province ($R^2$ 68.7% and 61.2%, respectively; Figure 4). Other provinces showed similar trends, though with lower $R^2$ values. Regression analysis of precipitation and relative humidity and malaria prevalence showed that a significant relationship existed, although it was weaker than the relationship with temperature variables. This provided the foundation for producing a prediction model based upon temperature.

3.3 Base reproduction rate model risk projections

The projections show the number of months per year that malaria transmission can be sustained based upon monthly average temperature. The projections were initially computed for South Korea for the time slice 2001–2010 by combining the base-reproduction rate model with a Regional Climate Model output, MM5 (Koo et al., 2009). When 2001–2010 projections are compared with observations of malaria cases it can be seen that temperature is not currently the limiting factor for malaria prevalence in South Korea. The projection indicates that there is more malaria transmission potential in the South and West, whereas observations show that most cases occur in the North and North-west. However, when analysing the most prevalent areas (37–38° North), the trend is represented well in the projections (Figure 5).

The number of months that the $R_0$ value is greater than 1 was computed as an average for ten year time slices 2001–2010 to 2091–2100 (Figure 6). The projections indicate that South Korea will become more suitable for supporting malaria transmission in the future. Areas that are most suitable for transmission appear to be located more towards the South and West of the country and in low-lying regions.

### Table 1: Multiple regression analysis of climatic variables and regional malaria prevalence (2001–2010)

<table>
<thead>
<tr>
<th>Region</th>
<th>$R^2$%</th>
<th>Total malaria cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gyeonggi</td>
<td>76.2</td>
<td>7423</td>
</tr>
<tr>
<td>Inchon</td>
<td>56.4</td>
<td>2693</td>
</tr>
<tr>
<td>Seoul</td>
<td>66.5</td>
<td>2444</td>
</tr>
<tr>
<td>Gangwon</td>
<td>36.9</td>
<td>1827</td>
</tr>
<tr>
<td>Busan</td>
<td>51.6</td>
<td>420</td>
</tr>
<tr>
<td>South Gyeongsang</td>
<td>41.7</td>
<td>304</td>
</tr>
<tr>
<td>North Gyeongsang</td>
<td>17.6</td>
<td>285</td>
</tr>
<tr>
<td>North Jeolla</td>
<td>53.3</td>
<td>240</td>
</tr>
<tr>
<td>Daegu</td>
<td>57.3</td>
<td>232</td>
</tr>
<tr>
<td>South Chungcheong</td>
<td>51.7</td>
<td>221</td>
</tr>
<tr>
<td>South Jeolla</td>
<td>51.1</td>
<td>210</td>
</tr>
<tr>
<td>North Chungcheong</td>
<td>47.7</td>
<td>196</td>
</tr>
<tr>
<td>Daejon</td>
<td>47.2</td>
<td>175</td>
</tr>
<tr>
<td>Ulsan</td>
<td>39.7</td>
<td>163</td>
</tr>
<tr>
<td>Gwangju</td>
<td>35.5</td>
<td>145</td>
</tr>
</tbody>
</table>
To further compare the risk of an outbreak of malaria arising from an imported case, projections of Japan and South Korea as a whole were made at a larger scale from the CMIP5 CCSM4 model. The resulting projections show similar trends of a lengthening transmission season based on the climate in both countries, with a greater extension of the season being projected in Southern and Western Japan (Figure 7).

4. Discussion

4.1 Direct comparison

South Korea has substantially more cases of malaria reported each year. Almost all of these are indigenous cases of malaria (Park, 2011). Due to the similar environmental, climatic and demographic conditions between Japan and South Korea, South Korea’s proximity to North Korea can be identified as the main cause of the variation between Japan and South Korea.
Due to the similar climatic and environmental conditions in Japan and South Korea, Japan is potentially vulnerable to an outbreak of malaria from imported cases (Kano and Kimura, 2004). The distribution of mosquito vectors in has not been mapped, although evidence of mosquito vectors has been discovered in both countries (Kano and Kimura, 2004; Park, 2011; Rueda et al., 2006) and is evidenced in South Korea by the fact that 97.1% of reported cases were classified as internal transmission cases.

The nature of reported cases in South Korea has changed since it re-emerged (Park, 2011), with over 60% of cases in 2010 being civilian (compared to 100% of cases initially being in the military). This indicates that conditions in South Korea are suitable for sustaining malaria transmission. The pattern of malaria transmission in South Korea is heavily influenced by the conditions in North Korea; however, there is evidence of local transmission, as the pattern of cases in 2009 was different between the two countries (Yeom et al., 2012). Therefore, the occurrence of malaria in South Korea is influenced by both local transmission and the malaria situation in North Korea (Yeom et al., 2012). Two studies (Yeom et al., 2012; Park, 2011) reported that the transmission season in South Korea extended annually 1993–2010, meaning that the length of time that malaria transmission can be supported is extending as a result of climate change. Japan is also experiencing climate change, suggesting that it could become more at risk from malaria outbreaks in the future, as the mosquito vector species is widespread and abundant in both Japan and Korea (Rueda et al., 2006). However, vector population density needs to be fully analysed in order to comprehensively determine the risk of malaria re-emergence in Japan and transmission in South Korea.

An assessment of climatic suitability can be used as the first stage of analysis, to target areas for more detailed analysis of vector density, environmental conditions and medical care status.

4.2 Quantitative assessment of climatic factors

A statistically significant relationship between monthly minimum and maximum temperatures and the number of malaria cases exists at a regional level in South Korea. This is supported in the literature through statistical studies (Kleinschmidt et al., 2000) and biological studies (Rúa et al., 2005; Bayoh and Lindsay, 2004). The sensitivity of both the mosquito vector and the malaria parasite to temperature is strong, meaning that small temperature increases can extend the transmission season of the parasite (van Lieshout et al., 2004; Zhou et al., 2004). The climate of South Korea currently does not support year-round transmission of malaria, meaning that it is climatically vulnerable to an extended transmission season (Park et al., 2009). A significant relationship between temperature and the number of malaria cases found in this study also suggests that the distribution of malaria could spread to areas where it is currently limited by temperature (Kovats et al., 2001). There appears to be a significant trend between both relative humidity and malaria prevalence at a seasonal level (Table 1). This trend can be explained by the link between increased humidity and precipitation and the amount of standing water on the ground surface (Lindsay and Birley, 1996). The relationship between precipitation and malaria prevalence is less clear due to the uncertainty of the impact of heavy rain on transmission rates (Singh and Sharma, 2002). The transmission rate of malaria is dependent on a wide variety of factors, including the level of medical controls, vector density, and the environmental characteristics. Annual trends indicate that temperature is not the main factor in determining the prevalence of malaria in the studied region (Figure 1). However, the analysis of climatic factors and malaria in South Korea displayed that prevalence is linked to climate, particularly temperature at a monthly level. Therefore, it is possible to use the temperature dependent base reproduction rate model as an indicator of the climatic suitability of a region to malaria transmission, if separated from the other variables.

4.3 Base reproduction rate prediction model

The model identifies areas that are climatically vulnerable to malaria outbreaks if other conditions are met. Potential risk areas are identified easily, enabling a preliminary assessment of malaria transmission potential. The main practical use of the model is as the initial component of a vulnerability assessment of an area to a vector borne disease (van Lieshout et al., 2004). In this study, an assumption was made to...
calculate \( ma \), due to the lack of available data on the population distribution of the \textit{Anopheles} mosquito. The resulting map projections should be taken as a guide depicting relative climatic suitability (Figure 5). With this caveat taken into account, the model projections provide a useful overview and highlight the relative suitability of each location for malaria transmission based on temperature projections.

In order to address model uncertainty, a review of the biological components of the model was conducted (Rúa et al., 2005; Lindsay et al., 2004; Chitnis et al., 2008; Poncon et al., 2008). The human biting rate is the most sensitive parameter. This indicates that the suitability of the model is highly dependent on this calculation. Future improvements to this model would be to include human and mosquito population density data in order to more accurately depict \( ma \). This would greatly improve the ability of the model to predict malaria risk. This data would also enable projections of actual prevalence to be made, rather than transmission potential. Identifying the human biting rate as the most sensitive parameter also identifies this as a key parameter to target for potential countermeasures, such as those that limit human-mosquito contacts (Chitnis et al., 2008; Sharma et al., 2005).

Despite temperature not being identified as the principle controlling variable, it is important to analyse trends in potential transmissivity due to the risk of imported cases of malaria transmitting locally (Danis et al., 2011). There is evidence of independent transmission within South Korea and other temperate, developed countries, including Greece (Danis et al., 2011), France and Germany (Zoller et al., 2009). These factors highlight the importance of modelling malaria risk.

Future studies should focus on improving the robustness of this parameter and conducting site specific model sensitivity analyses. The model provides an important insight into impact of climate on malaria transmission. This is the first step towards assessing malaria risk, which can be followed up by collecting vector mosquito population and habitat data to investigate other controls on transmission.

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**References**


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