CLIMATE VARIABILITY AND INCREASE IN INTENSITY AND MAGNITUDE OF DENGUE INCIDENCE IN SINGAPORE

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ABSTRACT

Introduction
Dengue is currently a major public health burden in Singapore. This study aims to establish association between dengue incidence, weekly mean temperature, and precipitation; and further discusses how these weather predictors influence the increase in intensity and magnitude of dengue incidence in Singapore during the years 2000-2007.

Materials and Methods
This study adopted a retrospective ecological design using time series Poisson regression model including time factors such as time trends, lagged terms of weather predictors, considered autocorrelation of dengue cases, and accounted for changes in population size by offsetting. Two-piece linear spline with breakpoint at the median of each predictor was used to enhance a more flexible analysis of the association between dengue and predictors below or above median breakpoints.

Results
Dengue incidence was positively associated with weekly mean temperature and cumulative precipitation at lag week 1-16 and 5-20, respectively. The strength of the association and lag time depended on the intensity of each of the weather predictors and their combined forces. Cumulative effects of relative risks indicated highest threat when weekly mean temperature above median breakpoint co-existed with weekly cumulative precipitation below median breakpoint.

Conclusion
As Singapore experienced higher average weekly mean temperature and cumulative precipitation in the years 2004-2007, the results signified positive impact of climate factors on the increase in intensity and magnitude of dengue cases; since the relative risk of dengue was higher in these years according to the exposure response relationship estimated.

Keywords: dengue, weather, mean temperature, precipitation, climate variability
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INTRODUCTION

Global burden of dengue incidence

Dengue fever (DF) and Dengue haemorrhagic fever (DHF) have re-emerged since 1980s and rapidly become a major epidemiological threat worldwide; especially in South East Asia and Western Pacific Region. According to World Health Organization, dengue fever is endemic in more than 100 countries with estimated 2.5 billions populations at risk and annual dengue infection of 50 million cases. [1] Of this, Asia Pacific Region shares the greatest burden of dengue with estimated above 70% of the 2.5 billions populations at risk living in the region. [2] To date, exact reasons for the re-emergence are not fully comprehended. However, the U.S. Centers for Disease Control and Prevention has identified factors such as accelerated urbanization, poor public health infrastructure, increased international travel, and lack of effective vector control system as some of the main determinants that have contributed global emergence of DF/DHF as a major public health burden. [3]

Fig. 1: World dengue distribution, 2007: Source: World Health Organization [4]
Besides burden on healthcare system, programs for dengue prevention and treatments have been consuming large amount of financial resources and casting burden on national economic system. In an economic evaluation of dengue in Puerto Rico, Meltzer et al. concluded that mean disability adjusted life year (DALY) lost to dengue incidence was estimated average 658 DALYs per year per million populations in the period 1984-1994; [5] while another economic study in Thailand estimated 427 DALYs per year per million population lost as a result of dengue incidence in Thailand, 2001. [6]

**Dengue Fever**

Dengue fever and dengue haemorrhagic fever are caused by dengue viruses transmitted by female mosquitoes, namely Aedes aegypti (principal vector) and Aedes albopictus. Aedes aegypti are mainly domestic vectors that feed in the day and lay eggs in artificial containers around residential areas. Due to the feeding characteristic of female Aedes, it can feed on several individuals in order to complete a single blood meal; thus, increase number of infected hosts in a short period. The transmission cycle of dengue fever involves host-vector-pathogen. Upon bitten by an infective mosquito, a host can be infected after 3-14 days of intrinsic incubation period. The host then goes through 2-10 days of viraemic period, during which a female mosquito may become infected by feeding blood meal on the infective host. The transmission cycle continues after extrinsic incubation period (8-12 days) takes place in the female mosquito and dengue virus is transmitted to other uninfected hosts through the bite of an infective mosquito. [7]

Currently there are four serotypes of dengue virus, namely DEN-1, DEN-2, DEN-3, and DEN-4, being detected and circulating in most of the dengue endemic countries. A patient infected with one serotype of dengue virus will be immune for that serotype; however, the same individual can be infected again with any one of the other three serotypes. Symptoms of dengue fever include sudden onset of fever, severe headache, muscle ache, joints pain, rashes, leucopenia, and thrombocytopenia. A patient who suffers dengue hemorrhagic fever will have similar symptoms as dengue fever, but also accompany with manifestation of hemorrhage such as skin hemorrhages, gum bleeding, and gastrointestinal hemorrhage. Severe dengue hemorrhagic fever can lead to
dengue shock syndrome (DSS) or systemic failure which might lead to subsequent death. On the other hand, some dengue cases can be asymptomatic and thus not being diagnosed. [1, 7] To date, there is no tetravalent vaccine available to prevent dengue infection. Thus, active dengue surveillance system completes with effective vector control, source reduction operations, and high community participation in elimination of mosquito breeding sources are thus far considered some of the proven strategies to disrupt transmission of dengue diseases. [1, 3, 7]

Dengue in Singapore

Dengue is currently a major public health concern in Singapore where dengue fever is hyperendemic all year round with detection of all four serotypes of dengue virus. [8, 9] Dengue invaded Singapore in the early 1960’s, but was curbed through aggressive and intensive vector control programs, public education, and law enforcement since 1970s. Nevertheless, dengue re-emerged in the late ‘80s with increasing incidence rate though overall percentage of houses detected with Aedes mosquito breeding was less than 2% in recent years. [10, 11, 12] The incidence of dengue in 2003 increased more than tenfold with 108.5 cases per 100,000 populations as compare to 9.3 cases per 100,000 populations in 1988. In the year 2005 Singapore experienced worst historical outbreak of dengue incidence with 326.5 cases per 100,000 populations. Dengue cases peaked every six years since late 1980s; however, this cycle seemed to be disrupted when cases surged to highest point in 2005, which was the 7th year of the cycle (Fig.2). As compare to past years, the intensity and magnitude of dengue cases had increased in year 2004 and 2005, lowered in 2006 but resurged in 2007. Almost all dengue infections were contracted locally with only 1% imported cases. Besides marked increased in cases, geographical expansion of dengue incidence from the east and southeast zones to west and north zones was also noted since 2004. [9, 12] A recent study revealed that increasing outdoor dengue transmission, lower herd immunity, and shift of vector control emphasis were some reasons for the upsurge of dengue. [11]
Vector Control in Singapore

As a world leader, Singapore has implemented aggressive vector control programs since early 70s. However, there was a change in emphasis from vector surveillance to case detection in the ‘90s. [11] Upon case detection, the National Environment Agency (NEA) immediately deploys dengue control team(s) to perform source reduction, adulticidal fogging, and activate various prevention activities according to the standard operation procedure. Since 2003, Geographical Information System was added to enhance analysis of distribution of dengue cases, Aedes mosquitoes, and weather data. In late 2005, NEA rolled out nationwide program for daily breeding source reduction in homes, initiated ‘carpet combing’ operations to eliminate breeding sources in all constituencies, and established task force to enhance communication and cooperation between government agencies and private organizations. National vector surveillance and control system were further strengthened in December to combat upsurge dengue incidence. [14, 15]
Climate in Singapore

As a tropical country, Singapore experiences slight variation of temperature, abundant rainfall, and high humidity throughout the year. Daily minimum temperature in Singapore ranges from minimum 73.4 °F to 78.8 °F (23-26 °C) and maximum temperature from 87.8 °F to 93.2 °F (31-34 °C); while the mean temperature is above 77 °F (25 °C). However, temperature can drop to 66.92°F (19.4°C) or rise to 96.44 °F (35.8 °C) in extreme cold or hot days. Average annual cumulative rainfall in the island is around 93 inches. As annual events, northeast monsoon brings heavier rainfall, thunderstorms and strong wind from December to March; whereas southeast monsoon causes dry months from June to September. The island also experiences slightly less rainfall in the east as compares to the west. Intermittent flood is a natural hazard that Singapore experiences during rainy period when heavy downpour coincides with high tide. [16, 17]

Studies had concluded that ambient temperature had significant impact on population size, maturation period, feeding characteristics, and survival rate of Aedes mosquitoes. [18, 19] In their studies, Ebi et al. suggested that small island states such as Singapore was more incline to experience higher temperature and changes in rainfall which in turn had significant impact on increase of infectious diseases. [20] According to Intergovernmental Panel on Climate Change (IPCC), the global mean surface temperature is rising approximately by 1.4 to 5.8 degree Celsius in current century. [21] Also, it was estimated that temperature for Asia Pacific region was to increase around 0.5-2 °C by 2030 and 1-7 °C by 2070. [22] In line with global climate change, mean temperature in Singapore had risen by 1.0-1.5 °C in the past 5 decades. [23]

Objectives

Several studies on relationship between weather variables and dengue incidence in Singapore have been documented in the past two decades; however, the extent of how these weather predictors influence increasing dengue incidence in especially year 2004-2007 is yet to be established. The aims of this study are to: 1) establish association between dengue incidence, weekly mean temperature and weekly cumulative precipitation with delayed effect of exposure to
these weather predictors; and 2) analyze how the association between dengue and weather
predictors affects the increase in intensity and magnitude of dengue incidence during the study
MATERIALS AND METHODS:

This research is an ecological study, a retrospective analysis of how the extend of dengue cases depend on levels of mean temperature and precipitation in Singapore.

Study Area

Singapore is a small island state nation situated 1.5° North of the Equator and links with the southern state of Malaysia Peninsula with a causeway. [16] The total land size of Singapore is approximately 710.2 square kilometer (inclusive of reclamation land) with less than 3% forest as a result of heavy urbanization in the past three decades. The small island has population size of about 4.8394 millions and population density of 6,814 persons per Square Kilometer. [24] Majority of the population lives in high rise buildings which comprise of private apartments and government flats.

Data

Weekly dengue data was collected from Ministry of Health and their weekly epidemiological publications. Dengue fever or dengue haemorrhagic fever is defined as cases confirmed with laboratory tests of dengue viral infection through detection of any one of the four serotypes of dengue virus in blood tests. Under the Infectious Diseases Act in Singapore, it is mandatory for all medical practitioners to notify all suspected, diagnosed, and confirmed dengue cases to the Ministry of Health within 24 hours. Also, all laboratories are required to notify Ministry of Health of all patients whose blood samples tested positive for dengue viral infection.

Weather data was collected by searching climate data online by country on the database of World Data Center for Meteorology, Asheville webpage. [25] Data of daily mean temperature (degree Fahrenheit) and precipitation (inch) from Changi station was obtained from World Meteorological Organization website. The meteorological data from the World Meteorological
Organization was provided by Meteorological Services Division of National Environmental Agency of Singapore through Exchange of Regional Weather Data by the use of Global Telecommunication System (GTS) of the World Meteorological Organization (WMO). According to the guideline from World Health Organization and Intergovernmental Panel on Climate Change, temperature could be considered as homogeneous within radius of 300km for using daily data and 1200km for monthly data. [21] Weekly mean temperature (degree Fahrenheit) and cumulative precipitation (inches) were computed from daily temperature and precipitation.

Mid year population for each year for the period 2000-2007 was obtained as descriptive statistics of the population from the website of Statistics Singapore. [26]

**Statistical Analysis**

This study established a time series Poisson multiple regression model (*) which included time factors such as trend and season; comprised lagged terms of weather predictors; accounted for changes in population size by offsetting; and included lag strata of dengue cases as auto regressive terms of the dependent variable in the analysis.

\[
Y(t) \sim \text{Poisson} \left( \mu(t) \right)
\]

\[
\log(\mu(t)) = \beta_0 + \log(\text{pop}_t) + \beta_1 \text{AR(den)}_t + \sum [\beta_i X(\text{temp})_{ti} + \beta_j X(\text{prept})_{lj}] + \text{st}(t, df)
\]

While \( t = \text{time}; \ AR(\text{den}) = \text{auto regressive term of dengue cases}; \ \log(\text{pop}) = \text{offset mid year population}; \ \text{st}(t, df) = \text{cubic spline smoothing of trend with 7 cubic knots}; \ X(\text{temp})_{ti} = \text{weekly mean temperature at specific lag strata, } li; \ X(\text{prept})_{lj} = \text{weekly cumulative precipitation at specific lag strata, } lj; \ \beta_i \text{ & } \beta_j = \text{Parameter estimates}; \text{ where } i \text{ and } j \text{ correspond to lag strata.}
As data for dengue cases and weather predictors was collected continuously year round, trend and seasonality pattern in collected data needed to be identified in order to control for un-measured confounders which might drive some parts of the seasonal and long term time trend variations in dengue cases. The plot of time series of dengue cases (fig.3) for the study period showed increasing trend in dengue cases; however, the plots of yearly dengue cases (Appendix i) did not reveal consistently distinctive seasonal pattern during the study period from 2000-2007. Thus, cubic spline smoothing function with 7 knots was used to adjust for variations of dengue cases over time.

The examination of auto correlation function (ACF) graph (appendix iv) indicated auto regressive or serial correlation for consecutive lags of dengue cases in the lag period of 40 weeks; whereas the partial autocorrelation function (PACF) showed most spikes were within confidence limits after 4th spike. Series of dengue lag terms ranging from 1 to 8 weeks were used as auto regressive term in the model. The range of auto regressive terms in lagged number of weeks were estimated by summing average duration of incubation period in infected person (3–14 days), infectious period of host (2-10 days from onset of fever), [7] and survival period of female Aedes mosquitoes (1-76 days) according to laboratory study in French Guiana, a tropical country, in 2006. [27]

The model included population in order to adjust for population growth or decay in the modeled cumulative effects of incidence (relative risk). Thus, mid year population of each year was included as an offset to account for population variations of dengue cases during the study period.

In order to analyze relative association and risks between weather predictors and dengue with effect of different time lags, lag terms ranging from 1 to 20 weeks were created for each weather predictor. Cross correlation coefficients of each weather variable and dengue cases as well as literature reports were examined to estimate maximum lag term. Each lag term was further divided into two sub-terms by using piece wise linearity or 2-piece linear spline with breakpoint
at the median of the predictor. The piece wise linear predictor was then used to generate below median and above median relative risks within each lag term. The 2-piece linear spline allowed interpretation and comparison of relative risks of dengue cases between weather predictors below or above 50 percentile breakpoint of each lag term. Cumulative effects of relative risks of all lags for weather predictors were also computed by summing the coefficient estimated at each lag term, and were interpreted as the cumulative effect of every one unit increase of each weather predictor below or above the median breakpoint. Combined cumulative effects of relative risks of both mean temperature and precipitation were also computed by summing the relative risks of both variables and were valid according to combinations. The combined cumulative relative risk was interpreted as for each unit increase in both predictors simultaneously over the full period of lag time included in the cumulative estimate.

Model selection was determined by using lowest value of Akaike’s Information Criterion (AIC), and it was then validated by examining post estimation residuals of the time series Poisson regression model. The post estimation was performed by plotting predicted residuals against observed data as well as by using sequence plot and normality tests or histogram of the residuals. Autocorrelation (ACF) and partial autocorrelation function (PACF) of the fitted model was also used to further validate good fit of the model. Statistical analyses were conducted by using a 95% confident interval in STATA 10 (StataCorp, College Station, Texas, USA).

Finally, this study analyzed the dependency between dengue cumulative incidence and weather predictors such as weekly mean temperature and cumulative precipitation as well as how these predictors associated with increasing dengue incidence in the study period; particularly in year 2004 – 2007 by using combined cumulative effects of relative risks.
RESULT

Dengue cases and weather predictors

Dengue incidence in Singapore increased massively in the study period, especially in 2004-2007, and reached historical record in year 2005. During the study period, recorded dengue incidence increased from 673 cases in year 2000 to 4788 cases in 2003, after which, annual dengue cases increased with greater magnitude and intensity with record of 9459 cases in year 2004 and peaked in year 2005 with 14209 cases. The incidence then decreased to 3127 cases in 2006, but again surged in 2007 with 8826 cases. The highest dengue cases in the study period were reported in week 38 of year 2005 with 714 cases being recorded. (Refer to Appendix i)
Table 1: Average weekly mean temperature and cumulative precipitation for period 2000-2003 & 2004-2007

<table>
<thead>
<tr>
<th>Variable</th>
<th>Year</th>
<th>Mean</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly Mean Temperature (°F)</td>
<td>2000-2003</td>
<td>81.99</td>
<td>78.27</td>
<td>86.47</td>
</tr>
<tr>
<td></td>
<td>2004-2007</td>
<td>82.11</td>
<td>77.91</td>
<td>86.71</td>
</tr>
<tr>
<td>Weekly Cumulative Precipitation</td>
<td>2000-2003</td>
<td>1.68</td>
<td>0</td>
<td>10.39</td>
</tr>
<tr>
<td></td>
<td>2004-2007</td>
<td>1.78</td>
<td>0</td>
<td>15.52</td>
</tr>
</tbody>
</table>

As shown in Fig.4, Singapore experienced highest average weekly mean temperature and lowest cumulative precipitation in year 2002 (82.63 °F & 1.36 inches) followed by 2005 (82.52 °F & 1.45 inches) and 2004 (82.23 °F & 1.62 inches). However, weekly mean temperature and cumulative precipitation in each year (Fig.5, 6, Appendix ii & iii) revealed that year 2002 experienced lower maximum weekly mean temperature of 86.47 °F and higher weekly precipitation of 8.38 inches as compare to year 2005 with 86.71 °F and 6.43 inches respectively. The highest maximum weekly mean temperature in the study period was recorded as 86.71 °F in week 17 of year 2005 coinciding with weekly cumulative precipitation of zero. The weekly mean temperature in 2005 remained above median breakpoint till week 27. Highest weekly cumulative precipitation was found in year 2006 with 15.52 inches.

The average weekly mean temperature (table 1) for the period 2000-2003 was below median breakpoint of 82.07 °F (27.8 °C); while it was above the median breakpoint for period 2004-2007. On the other hand, average weekly cumulative precipitation was above median breakpoint of 1.165 inches (360mm) throughout the study period.
Model diagnostic and estimation

Fig. 7: Predicted cases vs. observed dengue cases in 2000-2007

Fig. 8: Predicted cases vs. observed dengue cases in 2006-2007

Fig 9: Post estimation sequence plot of residuals

Fig. 10: Post estimation histogram of residuals

Fig. 11: Post estimation autocorrelation of residuals

Fig. 12: Post estimation partial autocorrelation of residuals
Post estimation plots indicated good fit of Poisson regression model for the analysis. The model was able to explain 86% of the variance in weekly dengue cases and it produced good fit of predicted cases when plotted against observed data in the study period (Fig.7 & 8). The sequence plot (Fig.9) showed that most of the residuals were in range of -100 and 100 and indicated constant location and scale between observed and predicted values; while the histogram of residuals (Fig.10) showed approximately normal distribution. At the same time, auto correlation function (ACF) and partial autocorrelation function (PACF) as shown in Fig.11 & 12 indicated independent residuals as majority of spikes were within confidence limits. Thus the graphs indicated appropriate choice of model.

Relative risks of dengue incidence

The results of this study indicated positive association between dengue incidence, weekly mean temperature, and cumulative precipitation. The strength of relative risks between dengue and weather predictors varied according to lag time and corresponding breakpoint level.

Fig.13: Relative risks of dengue incidence with weekly mean temperature at various lag time
As shown in Fig.13 and Table 2, relative risk of dengue incidence peaked at lag week 9-16 and 13-16 with weekly mean temperature below and above median breakpoint of 82.07°F (27.8°C), respectively. When weekly mean temperature was below median breakpoint, the relative risk of dengue incidence was 12% at lag week 9-16 for every one degree Fahrenheit increase of weekly mean temperature. However, the association between dengue and weekly mean temperature became negative (RR = 0.82) after lag time of 16 weeks; this indicated that every 1 degree Fahrenheit decrease in weekly mean temperature below median breakpoint corresponded to an increase in relative risk of dengue incidence at lag week 17-20. On the other hand, as weekly mean temperature elevated above median breakpoint, the relative risk increased gradually from 1.02 to 1.07 with every degree increase in mean temperature at lag time of 1-16 weeks.
The results in fig.14 and table 3 indicated high positive relative risk (RR = 1.22-1.26) for dengue incidence at lag terms 5-16 weeks when precipitation was below median breakpoint. The results also revealed opposite effect at lag weeks 17-20 by increasing relative risk of dengue incidence.
with every one unit decrease in weekly cumulative precipitation below 1.165 inches. On the whole, the highest relative risk (RR=1.26) of dengue incidence occurred at lag week 9-12 as precipitation was below median breakpoint of 1.165 inches (360mm); whilst highest relative risk (RR = 1.07) occurred at lag week 13-16 when cumulative precipitation was above median breakpoint. When weekly cumulative precipitation was high, the result also showed negative association between dengue incidence and precipitation at lag week 1-8, but remained positively associated at lag week 17-20.

Table 4: Cumulative effects of relative risks for dengue incidence with individual or combined weather predictors at lag week 1-20

<table>
<thead>
<tr>
<th>Weekly weather Predictor</th>
<th>Cumulative RR</th>
<th>z</th>
<th>p-value</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Temperature &lt; 82.07°F</td>
<td>1.02*</td>
<td>1.13</td>
<td>0.25</td>
<td>0.98-1.07</td>
</tr>
<tr>
<td>Mean Temperature &gt; 82.07°F</td>
<td>1.19</td>
<td>9.19</td>
<td>0.00</td>
<td>1.14-1.23</td>
</tr>
<tr>
<td>Cumulative precipitation &lt; 1.165 inches</td>
<td>1.51</td>
<td>7.88</td>
<td>0.00</td>
<td>1.36-1.67</td>
</tr>
<tr>
<td>Cumulative precipitation &gt; 1.165 inches</td>
<td>1.09</td>
<td>4.90</td>
<td>0.00</td>
<td>1.05-1.12</td>
</tr>
<tr>
<td>Mean Temp &lt; 82.07 °F + precipitation &lt; 1.165</td>
<td>1.55</td>
<td>8.48</td>
<td>0.00</td>
<td>1.40-1.72</td>
</tr>
<tr>
<td>Mean Temp &lt; 82.07 °F + precipitation &gt; 1.165</td>
<td>1.11</td>
<td>3.14</td>
<td>0.00</td>
<td>1.04-1.19</td>
</tr>
<tr>
<td>Mean Temp &gt; 82.07 °F + precipitation &lt; 1.165</td>
<td>1.80</td>
<td>9.55</td>
<td>0.00</td>
<td>1.59-2.03</td>
</tr>
<tr>
<td>Mean Temp &gt; 82.07 °F + precipitation &gt; 1.165</td>
<td>1.29</td>
<td>11.08</td>
<td>0.00</td>
<td>1.23-1.35</td>
</tr>
</tbody>
</table>

* Insignificant

Cumulative effects of relative risks with individual weather predictor at lag week 1-20 in Table 4 indicated high risk of dengue incidence when either weekly mean temperature was above median breakpoint of 82.07 °F or weekly cumulative precipitation was below median breakpoint of 1.165 inches. The association between dengue and mean temperature was strongly positive when weekly mean temperature was above 82.07 °F. Relative risk of dengue incidence increased by 19% for every one degree Fahrenheit increased when weekly mean temperature was above median breakpoint. At the same time, independent cumulative risk for dengue incidence was 51% for every inch increase of weekly cumulative precipitation when below median level, but reduced to 9% when it was above median breakpoint.
The cumulative effects of relative risks for combined weather predictors revealed greater strength in association between dengue incidence and weather predictors. The combined risk was lowest when weekly mean temperature below breakpoint co-existed with precipitation above breakpoint (RR = 1.11), followed by high weekly mean temperature combined with high precipitation (RR = 1.29). As weekly cumulative precipitation remained below median breakpoint, relative risk of dengue incidence increased to 1.55 when weekly mean temperature was below breakpoint and 1.80 as mean temperature was above breakpoint. Thus, risk of dengue outbreak was greatest when elevated weekly mean temperature and low cumulative precipitation co-existed in the same period.
DISCUSSION

The contributing factors for re-emergence of dengue with increasing intensity and magnitude in countries with dengue endemic are complex. A wide spectrum of causal factors includes climate variability, distribution and infection rate of vectors, transmission rate, herd immunity, public health infrastructure and vector control capacity of dengue endemic countries, international travel, migration, and others. However, conclusive reasons for the increase in dengue incidence in recent years are yet to be established. This study attempts to analyze increasing dengue incidence in Singapore in the period 2000-2007 from a climatologic perspective.

Studies have shown that weather variables have strong impact on Aedes mosquitoes and dengue viruses. The mortality rate of larvae, pupae, and adult female mosquitoes as a function of temperature 50-104°F (10-40 °C) is represented by a wide-base ‘U’ graphical shape. At temperature range between 60.8–86 °F (15-30 °C) female mosquitoes experience lower mortality rate, while maximum temperature for survival for larvae and pupae is below 95 °F (35 °C). [18]

Under favourable environment conditions, Aedes mosquitoes may survive as long as 76 days. [27] Simultaneously, female Aedes may have shorter reproduction cycle at 89.6 °F (32 °C) and increase feeding frequency to more than twofold as compare to temperature below 78.8 °F (26 °C); pupae development period shorten from 4 at 71.6 °F (22 °C) to less than 1 day as temperature increases to 93.2 °F (34 °C); thus, population of mosquito increase swiftly as temperature elevates. [19] Moreover, the extrinsic incubation period of dengue virus may shorten from 12 at 86 °F (30 °C) to 7 days at temperature of 89.6-95 °F (32-35 °C). [28] Overall, high temperature has strong impact on dengue incidence by increasing exponential growth of mosquito population at shorter time as well as increasing vector biting and infective rate. Also, the fact that low temperature lengthens maturation period and increased survival rate of vector explains the risk of dengue incidence at long lag time of 17-20 weeks. On the other hand, though high precipitation destroys larvae and reduces survival rate of female Aedes in the short run, it increases abundant breeding sources which are conducive for the increase of vector population at longer lag time. [27, 29] Whereas lower precipitation induces higher ambient temperature with
prolonged dry spell, increases usage of water and air-coolers, and also increases household water storage which may serve as breeding habitats as well.

The findings in this study are in line with other studies that there is association between dengue incidence, mean temperature and precipitation. [30, 31] The long lag terms of 16-20 weeks is consistent with study by Koh et al. (2008) that dengue incidence in year 2005 was highly correlated with weekly mean temperature at lag time of 18 weeks as well as study by Heng et al. that dengue incidence occurred at lag time of 8-20 weeks following elevated temperature. [23, 32]

The results of this study indicates that strength of association between dengue incidence, weekly mean temperature and cumulative precipitation and the delayed effect of exposure varied according to the intensity of each weather predictor as well as their combined forces which corresponded to every one unit change below or above median breakpoint. As Singapore experienced higher average weekly mean temperature and precipitation in the years 2004-2007, the results signified positive impact of climate factors on the increase in dengue cases; since the relative risk of dengue was higher in these years according to the exposure response relationship estimated. As a tropical country, Singapore received average weekly cumulative precipitation above median breakpoint throughout the study period and this possibly explained a fraction of reasons as to dengue endemic in Singapore. Ooi et al. [11] in their study suggested virus transmission outside homes as one of the reasons for resurgence of dengue in Singapore; while Koh et al. (2008) also stated that 50% of all mosquito breeding habitats which included discarded receptacles, choked drains, water pump room were located outdoor. [23]

Climate variability between years could have impact on dengue incidence. [33, 34] Inter-annual climate variability could be influenced by both local climate variability and higher temperature caused by irregular warming of sea surface temperature (El Nino Southern Oscillation or ENSO). During the study period, average weekly mean temperature was higher in year 2002, 2004, and 2005 as compared to other years in the period. Simultaneously, ENSO (which caused higher temperature) was recorded in May 2002 – Mar 2003, June 2004 - Feb 2005, and Aug 2006 – Jan
These inter-annual climate variability or warm air episodes produced higher mean temperature and dry period which in turn increased relative risk of dengue incidence in Singapore as record showed larger dengue outbreak in year 2004, 2005, and 2007. According to World Health Organization, slight changes in climatic condition could lead to exponential dengue transmission as climate strongly influenced vector capacity and infection rate of vector. Thus, each unit change of weekly mean temperature and cumulative precipitation above or below median breakpoint in the study period, particularly year 2002-2005, coupled with inter-annual climate variations and ENSO could lead to explosive dengue incidence in each respective year as well as subsequent years. The reduction of dengue in year 2006 was partly due to the additional intensive vector control measured that took place since late 2005.

Though inter-annual climate variability could be served as important indicator for dengue incidence, weather data is dynamic with day to day or week to week variation. Therefore, it is also essential to interpret the findings of this study by analyzing both short term and long term weather or climate variations in the study period in order to draw more meaningful conclusion and avoid camouflaging of temporal variations of climate. For instance, the combined cumulative effects of weekly mean temperature and precipitation in the first quarter of year 2005 indicated combined relative risk of 1.80 for dengue incidence in subsequent quarters; while the average combined relative risk for the whole year is 1.29 (data not shown). The highest weekly dengue cases for the entire study period was reported in year 2005 and this coincided with highest weekly mean temperature and low cumulative precipitation recorded in the same year. The year 2005 began with low cumulative precipitation in the first 17 consecutive weeks with average weekly cumulative precipitation less than 0.78 inches and high weekly mean temperature above median breakpoint and peak in week 17 (appendix ii & iii). As such the combined relative risk for dengue incidence in 2nd and 3rd quarters of year 2005 was much higher than overall combined relative risk for the year (data not shown).

As weather condition of high weekly mean temperature and low cumulative precipitation persists in consecutive weeks or prolonged period, it is possible that combined cumulative relative risks might increase by compounded rate and thus create greater risk for exponential growth of dengue
incidence with effect lasting up to 20 weeks in succeeding period. This effect could be more severe for Singapore as a small tropical island nation with extremely high urbanization and little forest area. As a result, Singapore faces higher threat of urban heat island impacts [36] as well as extreme temperature and precipitation events. Urban heat island impacts due to heated pavement, roofs, concrete, and etc could increase ambient temperature and to certain extend increase dengue transmission during the period. Nevertheless, tailored research is required to analyze compounded cumulative risk secondary to heat island impacts before conclusion can be drawn.

A limitation in the study of dengue incidence is the issue of under reported dengue cases. In view of the fact that some dengue cases are asymptomatic and undiagnosed, it is highly possible that numerous dengue cases take place without notice; whereas some dengue cases might not be reported accordingly. This limitation restricts study result as actual dengue data could be multifold higher than recorded data. As reported by Ye et al. (2007) in their survey on seroprevalence in Singapore, asymptomatic cases were approximately 19 times higher than reported cases. [37] The under reported cases may possibly surge even higher during peak tourism period(s) as tourists from regional countries with asymptomatic dengue infection could infect mosquitoes in Singapore “silently” and thus causing great potential threat of dengue outbreak in near future.

Climate variability in dissimilar geographical areas may have diverse local effects on dengue outbreak as climate variables influencing dengue transmission may be unique in different locations. [38] For instant, a study in Southern Thailand showed relative importance of weather predictors varied with geographical areas. The study indicated mean temperature, rainfall, and relative humidity were associated with DHF in provinces along Andaman Sea border; while minimum temperature, number of rainy days, and relative humidity were associated with DHF in provinces along the Gulf of Thailand border. [31] On the other hand, non climate variables which include dengue surveillance emphasis and capacity of government, urbanization, socioeconomic, and herd immunity could also influence dengue distribution. Thus, spatial and transmission
heterogeneity secondary to unique local factors may limit generalizability of the study result from one city to another.

As risk of dengue is increasing rapidly in Asia Pacific and dengue viruses are spreading among countries in the region through international travel and trade, further studies concerning impact of climate factors on both regional and local dengue outbreaks are essentials for analysis of dengue transmission and distribution patterns in global and local contexts; thus enhance formulation of regional adaptation and prevention strategies accordingly.
CONCLUSION

Global warming is an inevitable trend in the coming decades and climate or weather attributed risks for dengue incidence remain high among countries with dengue endemic; especially in tropical countries where environment condition is more conducive for both vectors and pathogens. The finding of this study reveals potential exponential transmission of dengue disease as a result of both short and long term climate variability; thus, provides forewarning and enable relevant actions to prevent dengue attacks; particularly in periods following short or long term extreme high temperature and low precipitation. The result of this study also shows weekly mean temperature and cumulative precipitation as indicators for possible long dengue transmission period up to 20 weeks; therefore, additional mosquito breeding source reduction measures for up to 20 weeks might enhance effectiveness of current vector control.

One of the keys to eradicate dengue from community is participation and commitment from individual population. As such, to integrate climate change and adaptation into national dengue prevention or educational programs would not only create awareness but also enable individuals to gain knowledge as to how weather predictors could increase their risk to dengue fever and thus take necessary precaution.
APPENDIX

i. Weekly dengue cases in Singapore (Year 2000-2007)

Fig.1: Weekly dengue cases of each year in the period 2000-2007
ii. Mean temperature in Singapore (Year 2000-2007)

![Weekly mean temperature in year 2000-2003](image1)

![Weekly mean temperature in year 2004-2007](image2)

Fig.2: Weekly mean temperature for 2000-2003  
Fig.3: Weekly mean temperature for 2004-2007

Table1: Average weekly mean temperature for each year in the period 2000 - 2007

<table>
<thead>
<tr>
<th>Weekly Mean Temperature</th>
<th>Mean</th>
<th>Std. Dev.</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 2000 – 2003</td>
<td>81.99</td>
<td>1.55</td>
<td>78.27</td>
<td>86.47</td>
</tr>
<tr>
<td>Year 2004 – 2007</td>
<td>82.11</td>
<td>1.6</td>
<td>77.91</td>
<td>86.71</td>
</tr>
<tr>
<td>Year 2000</td>
<td>81.56</td>
<td>1.48</td>
<td>78.9</td>
<td>84.87</td>
</tr>
<tr>
<td>Year 2001</td>
<td>81.71</td>
<td>1.38</td>
<td>78.27</td>
<td>84.58</td>
</tr>
<tr>
<td>Year 2002</td>
<td>82.63</td>
<td>1.41</td>
<td>79.81</td>
<td>86.47</td>
</tr>
<tr>
<td>Year 2003</td>
<td>82.08</td>
<td>1.72</td>
<td>79</td>
<td>86.13</td>
</tr>
<tr>
<td>Year 2004</td>
<td>82.23</td>
<td>1.74</td>
<td>78.61</td>
<td>85.95</td>
</tr>
<tr>
<td>Year 2005</td>
<td>82.52</td>
<td>1.57</td>
<td>78.62</td>
<td>86.71</td>
</tr>
<tr>
<td>Year 2006</td>
<td>82.05</td>
<td>1.49</td>
<td>77.91</td>
<td>84.38</td>
</tr>
<tr>
<td>Year 2007</td>
<td>81.66</td>
<td>1.55</td>
<td>78.78</td>
<td>84.44</td>
</tr>
</tbody>
</table>
Fig. 4: Weekly mean temperature of each year in the period 2000-2007
iii. Precipitation in Singapore (Year 2000-2007)

Fig. 5: Weekly cumulative precipitation 2000-2003  
Fig. 6: Weekly cumulative precipitation 2004-2007

Table 2: Average Weekly cumulative precipitation for each year in the period 2000-2007

<table>
<thead>
<tr>
<th>Year Range</th>
<th>Mean</th>
<th>Std. Dev.</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 2000 – 2003</td>
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<td>1.66</td>
<td>0</td>
<td>10.39</td>
</tr>
<tr>
<td>Year 2004 – 2007</td>
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<td>2.33</td>
<td>0</td>
<td>15.52</td>
</tr>
<tr>
<td>Year 2000</td>
<td>1.7</td>
<td>1.46</td>
<td>0.04</td>
<td>5.7</td>
</tr>
<tr>
<td>Year 2001</td>
<td>1.82</td>
<td>1.84</td>
<td>0.03</td>
<td>10.39</td>
</tr>
<tr>
<td>Year 2002</td>
<td>1.36</td>
<td>1.73</td>
<td>0</td>
<td>8.45</td>
</tr>
<tr>
<td>Year 2003</td>
<td>1.85</td>
<td>1.59</td>
<td>0</td>
<td>8.38</td>
</tr>
<tr>
<td>Year 2004</td>
<td>1.62</td>
<td>2.34</td>
<td>0</td>
<td>12.53</td>
</tr>
<tr>
<td>Year 2005</td>
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<td>1.50</td>
<td>0</td>
<td>6.43</td>
</tr>
<tr>
<td>Year 2006</td>
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<td>3.09</td>
<td>0</td>
<td>15.52</td>
</tr>
<tr>
<td>Year 2007</td>
<td>1.95</td>
<td>2.13</td>
<td>0</td>
<td>12.42</td>
</tr>
</tbody>
</table>
Fig. 7: Weekly cumulative precipitation of each year in the period 2000-2007
iv. Autocorrelation function and partial autocorrelation function

![Autocorrelation of dengue cases](image8)

![Partial autocorrelation of dengue cases](image9)

v. Post estimation autocorrelation function and partial autocorrelation function

![Post estimation autocorrelation of cases](image10)

![Post estimation partial autocorrelation of cases](image11)
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World Meteorological Organization: for supplying online meteorological data (daily mean temperature and precipitation from Changi Station, Singapore) for research purposes.
References


