Reviewer’s report

Title: The Changing Epidemiology of Dengue in China, 1990-2014: a descriptive analysis of 25 years of Nationwide Surveillance Data

Version: 3 Date: 8 March 2015

Reviewer: Eng Eong Ooi

Reviewer’s report:

This manuscript by Lai and colleagues reports the trend of dengue incidence in China from 1990 to 2014. Using data obtained from passive surveillance through mandated notification of both clinically diagnosed and laboratory confirmed dengue, the authors show that the incidence of dengue is increasing in many parts of China, especially in the southern provinces. They also suggest that the indigenous transmission is fuelled by importation of virus through viremic travellers and pose the question of whether dengue has established endemicity in southern China. The findings in this manuscript is important as not only does China have the population in the world, southern China also has several cities with high human population density. Both factors may contribute to the overall increasing burden of dengue globally.

There are, however, a number of areas in the manuscript that needs to be clarified. These are:

Major compulsory revisions

1. The case definition of dengue needs to be carefully defined. The authors report here that clinically diagnosed cases using the WHO 2009 dengue classification scheme without laboratory confirmation were considered probable dengue. This is not plausible as the study period started in 1990. The authors should provide detailed case definition that was issued to medical practitioners to guide disease notification. It may well be likely that the case definition evolved over time, especially since WHO issued two dengue case classification schemes during the study period; one in 1997 and another in 2009. Perhaps the authors would consider describing the case definitions that were applied during the different periods between 1990 and 2014?

2. More details on the laboratory methods for diagnosis should also be described. Again, that this study covered a 24-year period presents challenges that the authors need to carefully consider. What methods were used to detect a four-fold or greater rise in antibody titer in paired serum samples? What methods were used to isolate dengue virus? When was RT-PCR introduced as a diagnostic test for dengue in China? These descriptions are important as the introduction of more sensitive tests could result in increased number of reported cases without increased transmission.

3. Following on from both comments #1 and #2, changes to the case definition
used for probable dengue surveillance and laboratory tests used to confirm dengue could result in major shifts in the incidence of dengue. The authors should provide a discussion on how changes in both case definition and introduction of new laboratory tests might have impacted the observed dengue incidence.

4. The definition of an imported case is problematic. To classify a dengue case as imported instead of indigenous, the authors applied three criteria: a recent travel history, recall of having been bitten by mosquitoes within the past 15 days and no recollection of being bitten by mosquitoes domestically. This case definition introduces major problems with recall bias. In fact, most people are unable to recall being bitten by day-biting Aedes mosquitoes and tend to remember nigh-biting mosquitoes as the latter would disrupt their sleep. Perhaps there may be some confusion when translated from Chinese but this case definition would provide very misleading results on the proportion of imported and indigenous cases.

Minor compulsory revisions
1. 1st paragraph of introduction: the authors attributed the observation that sequential dengue infection increases the risk of severe dengue to the work of Sabin reported in 1952. This is inaccurate. Please cite the relevant papers to support this statement.

2. The authors suggested that preventing exposure to mosquito bite is the most effective method to reducing dengue incidence, in the last sentence of the 1st paragraph of introduction. This is erroneous. The only instances where dengue incidence was successfully reduced for significant span of time were the Pan American Aedes eradication program and the vector control efforts in Cuba and Singapore. All of which relied on suppressing vector population. Furthermore, there is no evidence to show that methods that could reduce exposure to mosquito bites, such as the type of clothing or the use of mosquito repellants, were able to reduce significantly the incidence of dengue. Please correct this statement.

3. “Seasonal” on the 2nd y-axis has been misspelt.

Discretionary revisions
1. The description on the vector surveillance and control program in China is currently rather cursory and even vague. Given the increasing trend of dengue and the call made by the authors for better preventive measures, perhaps the authors would consider providing a more detailed description of the current vector control program and suggestions on the improvements that could be made.

2. The reported demographic of dengue cases show that a high proportion of cases are adults. This trend suggests a predominance of peri-domestic transmission, which would be consistent with the authors’ suggestion that virus transmission is driven mostly by Aedes albopictus. Perhaps the authors could
consider making this link in the discussion?

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I was a paid member of the Scientific Advisory Board on dengue vaccine in 2014 (Sanofi Pasteur). Apart from this, I have no other competing interests.