ECONOMIC IMPACT OF DENGUE FEVER/DENGUE HEMORRHAGIC FEVER IN THAILAND AT THE FAMILY AND POPULATION LEVELS

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Abstract. Dengue fever and dengue hemorrhagic fever constitute a substantial health burden on the population in Thailand. In this study, the impact of symptomatic dengue virus infection on the families of patients hospitalized at the Kamphaeng Phet Provincial Hospital with laboratory-confirmed dengue in 2001 was assessed, and the disability-adjusted life years (DALYs) lost for fatal and non-fatal cases of dengue were calculated using population level data for Thailand. When we accounted for the direct cost of hospitalization, indirect costs due to loss of productivity, and the average number of persons infected per family, we observed a financial loss of approximately US$61 per family, which is more than the average monthly income in Thailand. The DALYs were calculated using select results from a family level survey, and resulted in an estimated 427 DALYs/million population in 2001. This figure is of the same order of magnitude as the impact of several diseases currently given priority in southeast Asia, such as the tropical cluster (trypanosomiasis, Chagas disease, schistosomiasis, leishmaniasis, lymphatic filariasis, and onchocerciasis), malaria, meningitis, and hepatitis. These results indicate that dengue prevention, control, and research should be considered equally important as that of diseases currently given priority.

INTRODUCTION

Dengue fever/dengue hemorrhagic fever (DF/DHF) constitute one of the leading causes of hospitalization of children in southeast Asia, and is the cause of approximately 20 million infections globally and thousands of deaths.1 In Thailand, dengue poses a substantial health burden on both the health care system and individual households. DF/DHF is a mosquito-borne viral infection caused by any of four serotypes of dengue virus, and infection with any serotype does not necessarily confer cross-protective immunity. Therefore, a person can potentially experience four separate dengue virus infections in a lifetime. Furthermore, the antibodies developed during infection with one serotype are thought to potentially enhance the symptom severity of subsequent infections with heterologous serotypes (antibody-dependent enhancement).2 The clinical presentation ranges from mild fever to high fever with hemorrhage and/or shock. Management consists of fluid replacement, and prevention efforts focus on vector control and larval-source reduction. Currently, there is no available vaccine, and development of a vaccine may or may not immediately translate into widespread use due to the high costs of introducing a new vaccine in a population. The time and costs involved in the development of new vaccines has been estimated to be 10–15 years from proof of principle to wide-scale availability, costing between US$100 and $300 million.3 However, these figures do not address the time and financial costs for developing countries, which may take an additional 10–15 years and a substantial portion of the country’s economic resources.3 Quantitation of the disease burden has been identified as one of five elements essential for accelerating the introduction of newly developed vaccines in a population.5 Disease burden data allows for rational decisions to be made as to allocation of resources, both with respect to regions of greatest need for a specific disease and relative burden of various diseases within a region.

Disability-adjusted life years (DALYs) have been used to quantify disease burden for a wide range of afflictions and countries globally, including the Global Burden of Disease (GBD) studies sponsored by the World Bank.4–7 DALYs offer a standardized, non-monetary measure of morbidity and mortality that is comparable across various conditions and geographic regions, serves as a useful tool for resource allocation, cost-effectiveness analyses, as well as burden of disease assessments. Calculation of DALYs involves summing the years of life lost due to premature mortality and the years of a healthy life lost due to the disability caused by the infection in a specific population, accounting for the degree of incapacity resulting from various conditions (disability weights) and the relative importance of a healthy life at different ages (age-weights). Extended explanation of the parameters comprising the DALY equation have been reported by Murray.5

Few studies have assessed the economic burden of dengue, and even fewer have used DALYs to do so. In Cuba, the 1981 dengue epidemic was estimated to cost approximately US$103 million including the cost of control measures (US$43 million), medical care (hospitalization, emergency rooms, outpatient clinics, and intensive care units, US$41 million), the costs of lost productivity (US$14 million), and loss of salaries of adult patients (US$5 million) for 344,203 reported cases.8 In Thailand in 1994, the overall patient costs of DHF were estimated at US$5.7 million, and provider costs were estimated to be US$6.9 million for 51,688 reported cases.1 DALYs were used to assess the burden of dengue in Myanmar, resulting in an estimated 83.8 DALYs lost due to dengue per year per million population from 1970 to 1997.9 In Puerto Rico from 1984 to 1994, the economic burden due to dengue, estimated to be 658 DALYs per year per million population, was found to be as important as that of tuberculosis, sexually transmitted diseases (excluding infection with human immunodeficiency virus), the tropical cluster of diseases, or intestinal helminths.10

In this study, the burden of DF in Thailand was assessed at both the family and population levels. A survey was conducted to determine the impact of patients hospitalized with a laboratory-confirmed dengue virus infection in 2001 on their families. Impact was measured in terms of the financial costs of hospitalization (direct costs), the number of school
days missed by the child and the number of work days missed by the caretakers (opportunity costs), the duration of illness (pre-, post-, and actual hospitalization costs), and the number of family members that were diagnosed with dengue in 2001. The combination of family and population level data provide a composite picture as to the impact of DF in Thailand, and results from the family level study were used in the DALY calculations.

**METHODS**

The participants in this study were enrolled in protocols reviewed and approved by the appropriate institutional review boards. Informed consent was not obtained for participation in this study. However, the identity of all participants was kept confidential.

**Geographic location.** This study was conducted in the city of Kamphaeng Phet located in Kamphaeng Phet Province in Thailand. Kamphaeng Phet is approximately 358 km northwest of Bangkok. Kamphaeng Phet city is the provincial capital and has a 332-bed public health hospital that is the major source of care for the province.

**Family level.** A survey was conducted in the Kamphaeng Phet province to determine the impact of dengue at the family level. The study population consisted of persons in Kamphaeng Phet hospitalized with laboratory-confirmed dengue virus infection in 2001. A cluster sampling design was used to select participants from the study population. One case was randomly selected from the records of laboratory-confirmed cases, and all surrounding cases were then selected (by location). The majority of respondents were from the Muang district (where the Kamphaeng Phet Provincial Hospital is located), with 6 of 10 additional districts represented. Surveys were administered primarily via home visits, but the telephone was used when available. In both cases, local nurses read all survey questions to the respondents in Thai. Because DF/DHF primarily affects children, surveys were administered to a family member of the hospitalized child. When possible, surveys were administered to the mother of the child with dengue, or to the patient if >15 years old. A total of 204 surveys were administered (~10% of the study population).

Information was collected on the self-reported direct economic costs of hospitalization, including transportation costs, costs associated with staying at the hospital for extended periods (any food and lodging expenses), and the hospitalization costs incurred by the family. Respondents were also asked to recall the number of workdays missed while taking care of the child, and the number of days of school that the child missed. The duration of illness was assessed in terms of the number of days the child was ill pre-hospitalization, the number of days the child was ill in the hospital, and the days post-hospitalization. The reported number of days the child spent in the hospital was compared with hospital records to assess the accuracy of the self-reported responses. The duration of illness responses were also plotted over time (based on the hospital admittance date) to assess potential recall bias. The study children were cross-referenced with the records of laboratory-confirmed dengue cases to assess the number of cases within families. Respondents were also asked if any family members had been diagnosed with dengue without laboratory confirmation.

**Population level DALYs.** The DALYs were calculated using the methodology described by Murray\(^5\) and used by the GBD studies.\(^6,7\) Calculations were based on five-year age groups (0–4, 5–9, 10–14, 15–20, and > 20 years old) and a standard life expectancy of 82.5 years for females and 80.0 years for males. The age weighting and discounting functions were also kept constant with those used in the GBD studies for ease of comparison (Table 1).

There were 124,409 cases and 209 deaths due to dengue reported to the Ministry of Health, Royal Thai Government in 2001.\(^8\) However, data on the number of unreported cases, the age/sex distribution of the cases, and the average age of death for fatal cases of dengue were unavailable. As a result, several estimations were made based on the available epidemiologic data and are detailed below. A sensitivity analysis was performed to assess the degree to which the various estimates affected the results.

**Parameter estimates.** As with many conditions, the number of reported cases of DF/DHF constitutes only a fraction of the actual cases. Estimated ratios of actual to reported cases have varied from 17:1 to 60:1,\(^10\) indicating that for every reported case of DF/DHF there are as few as 17 and as many as 60 unreported cases. To account for unreported cases, the number of reported cases is often multiplied by a set factor. In a study by Meltzer and others, multiplication factors of 10 and 27 were assigned to the 0–15- and > 15-year-old age groups, respectively, to estimate the number of unreported dengue cases in Puerto Rico.\(^10\) The different multiplication factors were designed to reflect the increase in under-reporting observed with age. For this work, a higher multiplication factor was not used for the adult age group primarily because in highly epidemic areas such as Thailand, where all four serotypes of the dengue virus circulate, the majority of the adult population is immune to the disease. A multiplication factor of 10 was assigned to all age groups to estimate the number of unreported DF/DHF cases in Thailand for 2001. However, since the unreported cases were most likely less severe than the reported cases, a shorter duration of illness (four days) was assigned to the unreported cases.\(^10,12\) A disability weight of 0.81 was used for both reported and unreported cases, implying that even mild cases of dengue will impede an individual from conducting most of their normal daily activities for a period of time.\(^10\)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Range*</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiplication factor</td>
<td>10</td>
<td>5–15</td>
<td>Meltzer and others(^10)</td>
</tr>
<tr>
<td>Age correction constant</td>
<td>0.1624</td>
<td>†</td>
<td>Murray(^5)</td>
</tr>
<tr>
<td>Age-weight factor</td>
<td>0.04</td>
<td>†</td>
<td>Murray(^5)</td>
</tr>
<tr>
<td>Discount rate</td>
<td>0.03</td>
<td>†</td>
<td>Murray(^5)</td>
</tr>
<tr>
<td>Average age of death (years)</td>
<td>10</td>
<td>5–24</td>
<td>Meltzer and others(^10)</td>
</tr>
<tr>
<td>Disability weight</td>
<td>0.81</td>
<td>0.6–0.92</td>
<td>Meltzer and others(^10)</td>
</tr>
<tr>
<td>Duration of disability, reported cases (days)</td>
<td>9.1</td>
<td>4–14</td>
<td>Kamphaeng Phet study(^9)</td>
</tr>
<tr>
<td>Duration of disability, unreported cases (days)</td>
<td>4</td>
<td>4–14</td>
<td>Meltzer and others(^10)</td>
</tr>
</tbody>
</table>

* Ranges were used in sensitivity analysis.
† Values used in the Global Burden of Disease studies, kept constant for direct comparison.
‡ Result obtained in the family survey conducted in Kamphaeng Phet presented in this report.
The age/sex distribution of cases in 2001 was estimated by applying the distribution observed in the Kamphaeng Phet study population (n = 2,000) to the estimated number of actual cases of DF/DHF in 2001. The distribution used (Figure 1) is representative of the age-related trends typically observed in dengue epidemics; 1998 Thai hospital records indicate that 70–75% of patients with dengue are between 5 and 14 years of age. The average age at death due to dengue was assumed to be 10 years.

A sensitivity analysis was conducted to determine the sensitivity of the results to the parameter estimates used in this study. These values, as well as the ranges assessed in the sensitivity analysis, can be found in Table 1.

RESULTS

**Family level costs.** The total costs to the family consisted of direct economic costs incurred by hospitalization, and the opportunity costs due to loss in productivity. Food, transportation, and hospital bills constituted a total average cost of 1,026 Baht (approximately US$24). This figure seems high considering that hospitalization for children < 12 years old is free in Thailand. However, several of the families indicated that they first went to a private clinic, which is not free, before going to the hospital. The opportunity costs resulting from hospitalized dengue patients was assessed in terms of the average number of school or work days missed by the patient and work days missed by the family members, which was reported as an average of 4.8 and 4.2 days, respectively. Each of these numbers account for only half of the average duration of illness (9.1 days), which is a result of weekends and school holidays for those still attending school, and the availability of a non-working caretaker or an occupation such as farming, where the parents often reported alternating between caring for the child and working.

**Number of family members with DF/DHF.** Of 204 cases sampled, 34 had a sibling with laboratory-confirmed DF/DHF in 2001 (17 families had two children contract dengue in the same year). However, several families reported family members diagnosed with DF/DHF from a hospital or clinic that were not confirmed by blood testing. Twenty-three percent of the families sampled had one additional person diagnosed with DF/DHF, 4% had two people diagnosed, and 1% had three people diagnosed. On average, 1.4 family members were diagnosed with DF/DHF (0.4 additional members other than the selected case). These numbers only account for diagnosed cases of DF/DHF, and respondents often indicated that other family members who were not included in the results had similar symptoms to those of the hospitalized person.

**Duration of illness.** The duration of illness due to DF/DHF was recorded as the reported number of days ill before, during, and after hospitalization. The average number of days in the hospital and pre-hospitalization were both 3.5 (range = 1–16 and 0–10, respectively) and post-hospitalization illness averaged 2.1 days (range = 0–30 days). The average total duration of illness was 9.1 days (Table 2).

To control for the impact of memory on the reported results, hospital records were referenced for onset of illness and hospital admittance dates recorded at the time of illness and compared with the reported number of days ill prior to hospitalization. On average, the respondents under-reported the number of days ill pre-hospitalization by approximately one day. There was no trend observed in the reported duration of illness over time, implying that any recall bias was not influenced by the passage of time.
Table 2  
**Average duration of illness due to dengue in Thailand in 2001**

<table>
<thead>
<tr>
<th>Reference period</th>
<th>Average no. of days</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-hospital (recorded)*</td>
<td>4.3</td>
<td>0–10</td>
</tr>
<tr>
<td>Pre-hospital</td>
<td>3.5</td>
<td>0–10</td>
</tr>
<tr>
<td>Hospital</td>
<td>3.5</td>
<td>1–16</td>
</tr>
<tr>
<td>Post-hospital</td>
<td>2.1</td>
<td>0–30</td>
</tr>
<tr>
<td>Total duration†</td>
<td>9.1</td>
<td>3–39</td>
</tr>
</tbody>
</table>

* Average number of recorded ill days were drawn from hospital records of the sampled cases.
† Total duration was calculated using reported numbers.

**DALYs lost due to dengue.** Using the baseline values outlined in the Methods section, there were 427 DALYs lost per million population due to dengue in Thailand in 2001. The sensitivity analysis indicated that the parameter with the greatest influence on the results was duration of illness, resulting in a minimum of 393 DALYs/million population (duration = 4 days), and a maximum of 1,046 DALYs/million population (duration = 14 days). The DALYs have been calculated for various regions of the world, as well as for a myriad of diseases and disabilities. In Table 3, the burden of dengue in Thailand calculated in this study is compared with other infectious and parasitic diseases in southeast Asia. Table 4 shows the burden of dengue compared across geographic regions. Both tables use data from the World Health Report, 2001 (estimates for 2000).  

**DISCUSSION**

The results obtained in the family-based survey provide information specific to the burden of dengue in Thailand at the family level. In economic terms, the direct patient costs per hospitalization are minimal for dengue patients in Kamphaeng Phet (average = 1,026 Baht or US$24), although costs are higher if treatment is sought from a clinic as opposed to a public hospital, or if the patient was an uninsured adult. A study on treatment-seeking behavior of DHF patients in Thailand found that most patients had attended a clinic as the first step in treatment. Other studies have reported direct patient costs ranging from US$23 to US$61 for dengue patients in rural areas of Thailand, and US$67 in Bangkok (1997 estimates). When the opportunity costs of missed days of school and work (4.8 and 4.2 days, respectively) are taken into account, the financial burden of dengue is even greater than these numbers suggest. In a survey by the National Statistics Office, the average monthly income per household in Thailand in 2000 was 12,150 Baht (~US$283), with an average monthly expenditure of 9,848 Baht (~US$229). Since dengue incidence is not generally associated with income level, the average monthly income in Thailand is most likely representative of the average monthly income for families with dengue cases. If one assumes equal income for two persons per household and unpaid leaves of absence, missing 4.2 days of work for one person would result in an approximate loss of 850 Baht (~US$20), or approximately 37% of the net household income for that month. Combining the direct and indirect costs results in a loss of 1,876 Baht (~US$44) or approximately 81.5% of the net household income for that month per hospitalized family member, assuming only one person in the family goes to the hospital. However, dengue virus transmission by mosquitoes among family members is fairly common; results from the family survey indicated an average of 1.4 persons infected for families with one infection. Taking this into account, an average cost of 2,627 Baht would be incurred per family (~US$61), which is more than the average monthly income in Thailand. Since the estimated lifetime number of dengue virus infections for persons living in southeast Asia is 3.3, families in Thailand could be repeatedly faced with this economic burden.

This work did not address the cost of dengue carried by the hospitals and the Thai government; however, other studies estimate the net hospital cost as being between US$38.65 and US$54.60 per DHF patient (1997 estimate), and the total cost of dengue prevention and control to the Thai government as US$4.87 million (1994).  

Assessing the burden of DF/DHF using DALYs allows comparisons to be made across geographic regions and between diseases within a region. When comparing DALYs lost for different diseases, significant differences are those of greater than one order of magnitude. To facilitate this comparison, Table 3, which displays the estimated DALYs for various diseases in southeast Asia (estimates for 2000), contains a column of the log base 10 (log_{10}) of the DALYs per million population. The data in this column show that the burden of dengue in Thailand in 2001 is on the same level as the burden of the tropical cluster, malaria, meningitis, and hepatitis in all of southeast Asia in 2000. The log_{10} of the

**Table 3  
Burden of infectious and parasitic diseases in southeast Asia, estimates for 2000**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Total DALYs</th>
<th>DALYs/million population</th>
<th>Log_{10} of DALYs/million</th>
<th>% Total infectious and parasitic diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infectious and parasitic</td>
<td>86,382,000</td>
<td>56,251.7</td>
<td>4.750</td>
<td>100</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>23,363,000</td>
<td>15,213.9</td>
<td>4.182</td>
<td>27.0</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>14,992,000</td>
<td>9,762.7</td>
<td>3.990</td>
<td>17.4</td>
</tr>
<tr>
<td>Childhood cluster</td>
<td>13,727,000</td>
<td>8,399.0</td>
<td>3.951</td>
<td>15.9</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>11,477,000</td>
<td>7,473.8</td>
<td>3.874</td>
<td>13.3</td>
</tr>
<tr>
<td>Tropical cluster</td>
<td>4,014,000</td>
<td>2,613.9</td>
<td>3.417</td>
<td>4.6</td>
</tr>
<tr>
<td>Malaria</td>
<td>1,874,000</td>
<td>1,220.3</td>
<td>3.086</td>
<td>2.2</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1,871,000</td>
<td>1,218.4</td>
<td>3.086</td>
<td>2.2</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>854,000</td>
<td>556.1</td>
<td>2.754</td>
<td>1.0</td>
</tr>
<tr>
<td>Dengue (Thailand 2001)†</td>
<td>26,381</td>
<td>426.9</td>
<td>2.63</td>
<td>0.76</td>
</tr>
<tr>
<td>Dengue (southeast Asia)</td>
<td>371,000</td>
<td>241.6</td>
<td>2.38</td>
<td>0.43</td>
</tr>
</tbody>
</table>

* DALYs = disability adjusted life years; HIV/AIDS = human immunodeficiency virus/immunodeficiency syndrome.
† Results calculated in this study.
minimum of 393.1 DALYs/million population found in the sensitivity analysis is 2.595, which is still on the same order of magnitude as those diseases previously mentioned. If ones uses the maximum DALYs/million for comparison (log_{10} = 3.02), the burden of dengue in Thailand is comparable to all of the infectious and parasitic diseases listed, with the only exception being diarrheal diseases. It is important to note that comparing diseases even in the same year is complicated; for example, 2001 was an epidemic year for dengue in Thailand, where the diseases being compared may or may not have been. This caveat also applies to Table 4, which illustrates the burden of dengue in 2000 in the World Health Organization member regions. The burden of dengue in Thailand in 2001 was greater than all of the regions in 2000, including southeast Asia, when comparing DALYs per million population. The DALYs reported in this study differ from the GBD estimates for southeast Asia for several reasons. First, Thailand has the highest reported incidence of dengue in the southeast Asia region, and therefore will have a higher DALYs per million population than the region. Second, different assessments of duration of illness and disability were used to calculate DALYs. The duration of illness used by the GBD study is derived using population estimates of incidence and prevalence, whereas in this study the duration observed in the family level survey was used. The disability weight assigned to dengue in the GBD study (0.172–0.211 depending on age) is also much lower than the disability weight used in this work (0.81).

Although many estimates were used in the DALY equation parameters and responses obtained from human subjects are rarely exact, all results presented here are conservative estimates. Even as such, this study indicates that dengue constitutes a larger burden than various diseases that currently receive more resources, and is a particular health burden on the Thai people. Therefore, governments and international funding agencies should consider giving equal priority to DF/DHF research, prevention, and control as diseases currently receiving more resources. In addition, cost-effective assessments using disease burden data, such as the results presented here, should be initiated. Clear representation of the costs of various interventions, as well as the expected alleviation of disease burden resulting from each intervention, further facilitate rational policy making. In particular, cost-effectiveness studies should be undertaken to accelerate the introduction of new tetravalent dengue vaccines into areas of highest need. A recent study by Shepard and others used DALYs to assess the cost-effectiveness of a pediatric dengue vaccine in southeast Asia, and found that vaccinating children at 15 months of age at US$0.50 per dose in the public sector and US$10 per dose in the private sector would be highly cost effective.

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