

Burden of Dengue in Malaysia. Report from a Collaboration between Universities and the Ministry of Health of Malaysia *

Donald S. Shepard, PhD ; Rosemary Lees, PhD; Chiu Wan Ng, MBBS, MPH; Eduardo A. Undurraga, MA; Yara Halasa, DDS, MS; Lucy Lum, MD

In collaboration with Laurent Coudeville, PhD

Brandeis University, Schneider Institutes for Health Policy, Heller School for Social Policy and Management, Waltham, MA 02454-9110 USA; University of Malaya, Kuala Lumpur, Malaysia

Version 50 –March 18th, 2013

ABSTRACT

Dengue represents a substantial burden in many tropical and sub-tropical regions of the world. Here we estimate the economic burden of dengue illness in Malaysia. Information about economic burden is needed for setting health policy priorities, but accurate estimation is difficult due to incomplete data. We overcame this limitation by merging multiple data sources to refine our estimates, including an extensive literature review, discussion with experts and review of data from both health and surveillance systems, and the implementation of a Delphi process. Because Malaysia has a passive surveillance system, the total number of dengue cases is underreported. Using an adjusted estimate of total dengue cases, we estimate an economic burden of dengue illness of US\$102.25 (95%CI: 77.94 – 310.66) million per year--approximately US\$3.72 (95%CI: 2.83-11.30) per capita. The overall economic burden of dengue would be even higher if we included costs associated with dengue prevention and control, dengue surveillance, and long-term sequelae of dengue.

Keywords: cost-effectiveness | health economics | public health | underreporting | vector-borne disease

* In the course of related research,¹ we uncovered a labeling error in our recent article on dengue costs in Malaysia based on this report² and on previous versions of this report. Appendix H explains the error and the resulting correction. In this updated version of the report we also present the corrected calculations in Tables 24 and 25 in this report.

Table of Contents

ABSTRACT.....	i
Executive Summary.....	1
Introduction: Dengue illness in Malaysia.....	4
Estimating the incidence of dengue: use of expansion factors (EFs):	6
Initial consideration of the official reported cases from the Ministry of Health (MoH)	6
Theory and literature of EFs.....	6
Estimation of dengue in Malaysia	7
Is there a difference between the EFs applicable to children and adults?.....	12
What is meant by a ‘hospital case’ in the reported dengue statistics?	14
How under-reporting impacts EFs	15
Foreign Worker Medical Examination Monitoring Agency (FOMEMA).....	16
Dengue illness in the private sector.....	22
Laboratory testing as a mean to estimate the under reporting of dengue cases	23
Differences between the public and private healthcare sectors.....	28
Reaching a consensus on appropriate EFs.....	29
Overall cost of dengue in Malaysia	34
Estimation of public and private sector medical costs	34
Economic burden of dengue: Introduction.....	34
Costs of service provision in public hospitals.....	34
Costs of service provision in public clinics	39
Costs of service provision in private hospitals.....	41
Summary: preliminary estimates of the cost of dengue	42
Sensitivity analysis of the cost estimates.....	48

Limitations of the cost estimates.....	49
Estimating the costs of dengue vector control activities: study design	49
Objectives of a study of vector control.....	49
Methodology.....	50
Burden of dengue in DALYs	52
Introduction to DALY calculations.....	52
Major causes of mortality and morbidity in Malaysia	53
DALY calculations for Malaysia	56
Dengue infection and Quality of Life	58
Discussion.....	59
References.....	61
Appendices.....	68
Appendix A: Countries or areas at risk of dengue fever in the world, 2010.....	69
Appendix B: Workshop participants	70
Appendix C: Workshop photographs.....	71
Appendix D: Use of EFs to estimate the incidence of dengue illness in Malaysia.....	73
Appendix E: Literature review procedure.....	76
Appendix F: First round of Delphi estimates of EFs.....	77
Appendix G: Reaching a consensus on proportion of dengue cases which are hospitalized and the proportion of cases treated in the private sector.....	80
Appendix H: Correction of labeling error.....	81

Figures

Figure 1. Reported cases of dengue in Malaysia, 1988 - 2005	5
Figure 2. Reported cases of dengue illness and estimated cases using EFs in Malaysia, 1988 – 2005	10
Figure 3. Age distribution of reported dengue illness cases by age group in Malaysia, 1988 – 2005.....	11
Figure 4. Reported and estimated cases of dengue illness in Malaysia using alternative EFs, 1988 – 2005.	12
Figure 5. Total immigrants in Malaysia in March 2006, by country of origin	16
Figure 6. Resident international population in Malaysia, 1995-2002.....	17
Figure 7. Medical Screening Process, FOMEMA System.....	18
Figure 8. Pantai Laboratory Workflow	23
Figure 9. Number of laboratory positive dengue illness cases (serology + NS1) by month, year 2010 (totals and breakdown by location)	25
Figure 10. Distribution of positive dengue illness cases (serology + NS1), years 2009-2010.....	26
Figure 11. Total number of dengue tests requested by location, 2010	27
Figure 12. Projected total private sector dengue tests requests for year 2010.....	28
Figure 13. Comparison between the total reported dengue cases in 2009 and the total projected cases using an adjusted EF (50% share of ambulatory cases).....	32
Figure 14. Unit cost per clinic visit at 11 public health clinics in Kedah, 1995.....	40
Figure 15. Proportion of costs associated to dengue by facility, treatment, and type of cost based on adjusted factor (58% share of ambulatory cases)	45
Figure 16. Gantt chart plotting the projected progress of the study	50
Figure 17. Sampling Strategy for Malaysian Ministry of Health Districts	51
Figure 18. Vector control functions and associated costs to be considered for the Economic analysis.....	52
Figure 19. DALY by sex and age group, Malaysia, 2008.....	56
Figure 20. Quality of life measured daily in children (1a) and adults (1b) suffering from dengue.....	58
Figure 21-A. Countries or areas at risk of dengue fever in the world, 2010.....	69

Figure 22-C. Left to right: Ahmed Faudzi; Laurent Coudeville; Shree Jacob; Jeremy Brett; Shanaliza Sulaiman; Sharon Chiang; Rosemary Lees 71

Figure 23-C. Left to right: Ahamad Jusoh; Satwant Singh; Chiu Wan Ng; Jameela Zainudeen; BK Ho; Lucy Lum; CK Chong; A Faudzi; Jeremy Brett; Shanaliza Sulaiman; Rosemary Lees..... 71

Figure 24-C. Left to right: Shree Jacob, Jeremy Brett, Laurent Coudeville, Donald Shepard 72

Figure 25-F. Comparison between the total reported dengue cases in 2009 and the total projected cases using an adjusted EF (50% share of ambulatory cases) based on estimates during the workshop 78

Tables

Table 1. Reported Dengue Cases in Malaysia, 2009	6
Table 2. Key demographic and health statistics for Malaysia and Thailand.....	8
Table 3. Deriving a differential EF for cases in children from available information, 2009.....	14
Table 4. FOMEMA panel doctor case register and notification data (2009) in ENOTIS by state.....	20
Table 5. FOMEMA panel doctor notification data (2009) by state.....	21
Table 6. Malaysia hospital statistics, 2008-2009	22
Table 7. Total suspected dengue illness cases and diagnosis tests performed, by location of the laboratory	24
Table 8. Distribution of acute care hospital beds by sector, 2005	29
Table 9. Participants' final estimates of EFs for hospitalized cases in the public and private sector and the total share of total dengue cases that are ambulatory	30
Table 10. Expansion factors for each of the four categories of dengue patients reported in Malaysia, 2009, calculated from the Delphi estimates made by workshop participants.....	31
Table 11. Reported number of dengue cases in Malaysia, 2009, in each of four categories, and projected values calculated using the four estimated EFs.....	32
Table 12. Method of estimation of unit costs at the University of Malaya Medical Centre, 2005 and 2009	35
Table 13. Estimates of unit costs for services in 11 district hospitals in Malaysia, 2009	35
Table 14. Definition of facility types as used in the WHO-CHOICE project	37
Table 15. Predicted estimates of unit costs of public hospitals services for Malaysia, 2005.....	37
Table 16. Estimation of average unit costs per bed-day in a public hospital, 2009	38
Table 17. Estimation of average unit costs per outpatient visit in a public hospital, 2009.....	38
Table 18. Revised estimation of average unit costs per bed-day in a public hospital, 2009.....	39
Table 19. Revised estimation of average unit costs per outpatient visit in a public hospital, 2009	39
Table 20. Estimates of unit costs per health centre visit for Malaysia, 2005	40
Table 21. Out of pocket expenditure (OOP) estimates for private health facilities	41

Table 22. Average indirect cost of dengue per day	42
Table 23. Impact per dengue cases in days lost (ambulatory and hospitalized)	43
Table 24. Summary of total costs per dengue case [RM]	44
Table 25. Summary of estimated total costs [RM 1000s]	44
Table 26. Dengue cases in 2009 by geographical region	47
Table 27. Estimated costs of dengue by region (RM 1000)	47
Table 28. Top ten communicable diseases causing YLL Burdens, Malaysian Population, 2008 (total, and subdivided by sex).....	54
Table 29. Top ten communicable diseases causing YLD Burdens, Malaysia, 2008 (total, and subdivided by sex).....	55
Table 30. Top twelve communicable diseases causing a DALY Burden, Malaysia, 2008 (total, and subdivided by sex).....	57
Table 31-B. List of workshop participants.....	70
Table 32-D. Sensitivity of dengue surveillance systems in American countries and corresponding EFs	73
Table 33-D Other studies of EFs in South East Asia.	74
Table 34-F. Participants' estimates of EFs suitable to apply to four subdivisions of dengue cases reported in Malaysia based on evidence discussed during the workshop	77
Table 35-F. EFs for each of the four categories of dengue patient reported in Malaysia, 2009, calculated from the estimates made by workshop participants.....	78
Table 36-F. Reported number of dengue cases in Malaysia, 2009, in each of four categories, and projected values calculated using the four estimated EFs.....	79
Table 37-G. Reaching a consensus on proportion of dengue cases which are hospitalized	80
Table 38 G. Reaching a consensus on proportion of dengue cases which are treated in the private sector	80

Equations

Equation 1. Estimating an EF from the best estimate and number of reported dengue cases.....	7
Equation 2. Calculation of an EF for children aged 5-15 in the Kamphaeng Phet province of Thailand	9

Executive Summary

Introduction: On Dec. 6, 2010, the Malaysian Ministry of Health facilitated a one-day workshop in Putrajaya to review current knowledge and to fill the gaps related to the burden of dengue illness and its economic cost in Malaysia. Information about economic burden is needed for setting health policy priorities, but accurate estimation is difficult due to incomplete data. During the workshop and in subsequent stages of research and consultation, we believe we overcame this limitation by merging multiple data sources – extensive literature review, discussion with experts and review of data from both the health and surveillance systems, and implementation of a Delphi process--to refine our estimates.

Methods: (A) Workshop in Malaysia. The workshop was conducted in cooperation with Brandeis University and the University of Malaya and funded by Sanofi Pasteur. Conceptually, the economic cost of dengue can be calculated as (1) the number of cases that occur in a year multiplied by (2) the cost per case. Much of the workshop related to quantifying each of those two factors.

(1) Total number of dengue cases: As dengue is a reportable illness, it is easy to obtain a rough approximation of the number of dengue cases – simply the number of dengue cases officially reported to the Ministry of Health. In 2009, the latest year available at the time of the workshop, that number was 41,454. The challenge is that Malaysia’s passive reporting system is good for monitoring general trends, but inadequate to obtain a precise number because some dengue cases are not reported. To address the underreporting of dengue fever, we conducted a two-round Delphi process to obtain the best estimates of an expansion factor (EF) for reported dengue cases. An EF is the number by which reported cases need to be multiplied to obtain a realistic number of dengue cases. While reporting is considered relatively accurate for public hospitals, it is less complete for private hospitals and for public and private ambulatory settings.

To quantify under reporting, the workshop first examined experience from private hospitals. The workshop reviewed the experience of the system of medical examinations of foreign workers (FOMEMA). By comparing rates of key diseases found through FOMEMA examinations against the MOH reporting, we derived an EF of 52 for the private general sector (i.e. for every case reported through the MOH there are 52 cases in the private hospitals). The workshop then examined private laboratory data. Pantai Holdings laboratory generously shared their internal data and an indication of their market share. It was estimated that about 125,000 cases of suspected dengue cases were tested nationally in all private hospitals, and of these 25,000 were positive dengue cases. Using these figures we generated a preliminary estimate of the number of dengue cases in the private sector.

The workshop also discussed international literature and research on expansion factors, and examined the surveillance system and data from the Malaysian Ministry of Health (MOH). The workshop next addressed participants’ estimates of EFs in the first round of a Delphi process. The overall EF mean from the first round was about 2.0. For most items, 7 persons invited responded in the first round.

(2) *Cost of dengue*: The workshop proceeded to discuss the work done to estimate the unit costs of medical treatment in Malaysia to date. A series of studies has been done with generally consistent results. The workshop also examined existing literature and research on the cost of dengue elsewhere. Finally, the workshop also reviewed preliminary estimates of disease burden by Dr Faudzi Yusoff and plans by Dr P Ravi Raviwharmman for a study of dengue vector control.

(B) Further work and analysis: As expected, the initial analysis showed some inconsistencies among workshop estimates. The mean EFs suggested that the majority of dengue cases would be hospitalized, which was probably not realistic. After the workshop, some alternative multiplicative factors were explored that adjusted by the total share of total ambulatory cases, so that the share of ambulatory cases would rise to the target levels of 50% or 60% considered by workshop participants as the correct proportion (Table 34-F and Table 35-F in Appendix F).

We then directed our efforts towards further refining our estimates of EFs for the different types of facilities and kind of treatment that the patients receive. We carried out the second round of the Delphi process by sending to the expert committee a report and a power point presentation (with audio) highlighting the main results of the workshop. We then requested the experts committee to provide new estimates for the expansion factors and total share of ambulatory dengue cases from overall dengue cases. In the second round 10 experts provided Delphi estimates. Experts in both rounds reflected a mixture of government, academic, and private sectors.

Results: The second round of the Delphi process led to an EF of 3.79, adjusted using the mean value of 58% share of ambulatory cases, and a total number of 157,140 dengue cases. Using only the mean EFs from the workshop, without considering 58% of ambulatory cases, gave a more conservative number of 99,163 cases. In addition, we refined estimates of unit costs of medical services in Malaysia.

In this report, we have used an adjusted estimate of the total number of dengue cases, following the Delphi process estimates of the distribution of dengue illness between hospitalized and ambulatory patients at 58%, and estimated the cost per case to generate the total cost of dengue for Malaysia. The estimated total cost was 359.79 (95%CI: 274.25-1,093.09) million Malaysian Ringgits per year. This can be broken down along several dimensions. In terms of types of costs, 69% is direct medical costs and 31% indirect costs. In terms of sector where cases are primarily managed, 66% of costs occur in public sector cases and 34% in private sector cases. In terms of type of facility where the patient receives the most intensive treatment, 60% of costs relate to cases that are hospitalized compared to 40% of cases that are entirely ambulatory cases.

We report our results in US\$ using the exchange rate of July 1st, 2009 (1 Ringgit = US\$0.284) ³, The economic burden is for dengue illness is about US\$102.3 (95%CI: 77.94-310.66) million per year. With a 2010 population of 27.5 million residents, Malaysia's per capita cost of dengue illness was

US\$3.72 (95%CI: 2.83-11.30). Expenditures on vector control would be an additional expenditure not included in this estimate.

Conclusion: The results of the workshop and subsequent consultations suggest that there is substantial underreporting of symptomatic dengue fever in Malaysia, and that the economic burden of dengue fever in Malaysia is considerable. Combining multiple sources of data is critical to achieve reliable estimates of the total cases and economic burden of dengue fever. Implementing a technology which would control dengue efficiently would most likely be economically valuable.

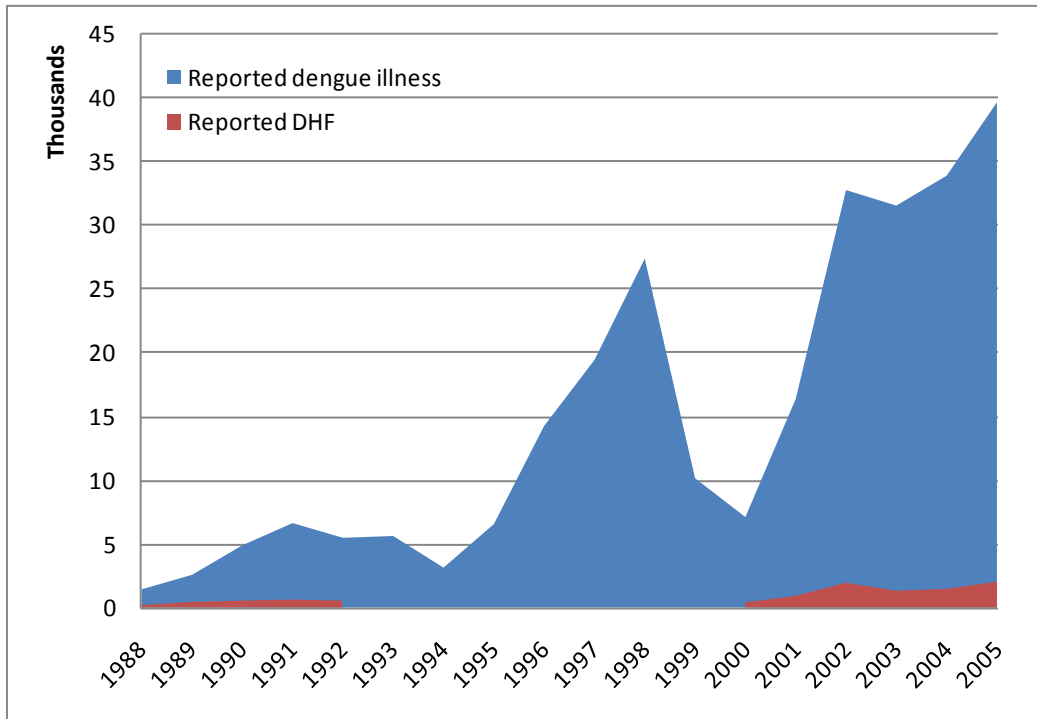
Introduction: Dengue illness in Malaysia

Dengue virus infection is a major health problem and represents a large economic burden to communities and health services in developing countries, with a fourfold increase in the number of cases in the last thirty years⁴⁻⁸. Dengue fever has become a major public health problem in many tropical and subtropical regions, with an estimate of 50 million dengue infections occurring each year and approximately 24,000 resulting in death⁷⁻¹¹. Appendix A shows the regions of the world at risk of dengue fever. Controlling dengue illness is a major health, political, and socio-economic challenge that requires local, national, regional, and global response^{12,13}. To better understand dengue burden and its cost, especially the under-reporting of dengue, the Malaysian Ministry of Health convened a workshop on 6 December 2010 at the Shangri-La Hotel, Putrajaya, Malaysia in cooperation with Brandeis and Malaya Universities and with support from Sanofi Pasteur. Appendix B lists and participants and Appendix C provides some photographs.

The transmission of dengue illness is associated with the geographic expansion and distribution of mosquito vectors and viruses.^{14,15} There are many factors that have created the ideal conditions for this expansion, especially in low- and middle-income countries, including Malaysia. The propagation of the virus is associated with high rates of population growth, unorganized urbanization and the proliferation of slums, crowding, poor water, sewer, and waste management systems, global warming, rise in global commerce and tourism, changes in public health policy, decreasing resources for vector prevention and control, and the development of hyperendemicity among other factors^{13,14,16,17}. World War II led to a significant expansion in the distribution and population of dengue fever vector *Aedes Aegypti* in Southeast Asia, associated with the movement of equipment and troops^{8,13,18}.

Southeast Asia has the highest dengue incidence of all regions of the world, and cycles of epidemics have affected the region since the 1950s, with increasing magnitude^{13,19}. Dengue illness is among the most relevant public health problems in Malaysia^{19,20}. The first reported dengue episode in Malaysia was in 1901, and ever since it has spread throughout the whole country¹⁹. Dengue episodes have been tabulated in Malaysia since 1974, and there has been an increasing trend of reported dengue in the last decade (Figure 1). Since the 1980s there has been a shift in the peak age incidence of dengue from children to young adults. A recent study in Malaysia showed that dengue has a considerable impact on social function, vitality, and well being, and represents a 60% lost in quality of life (QoL) at its worst symptoms²¹.

Figure 1. Reported cases of dengue in Malaysia, 1988 - 2005



Source: Ministry of Health Malaysia²²; WHO, Regional Office for the Western Pacific²³

The total incidence of symptomatic dengue illness is not fully captured by surveillance systems, which usually underreport the total number of cases²⁴⁻²⁹. Malaysia, like most countries, uses a passive surveillance system to capture the incidence of dengue illness³⁰. While this approach is very helpful for identifying outbreaks and examining trends, passive surveillance has several limitations due to the variety of manifestations of dengue illness that make the clinical diagnosis difficult, the reliance on health-care professionals for disease notification, differences in clinical diagnosis between epidemic/non-epidemic periods, and variations in the definitions of dengue illness reported³⁰⁻³².

Since 1990 the number of dengue cases and subsequent deaths, have been increasing in many countries. In order to get the disease under control, novel technologies and approaches are required. Malaysia is at the forefront of developing such novel approaches, to control both dengue and the vector mosquito species. The current economic burden caused by the disease must be considered when making decisions about the introduction of new technologies or techniques. The economic burden of dengue is divided into two parts: spending on prevention and control activities and the direct and indirect economic costs associated with the illness itself, simply calculated as 'cost per case x number of cases'. Estimates exist for both elements of this equation, but neither is clearly defined. The purpose of this section of the workshop was to bring together estimated data and indirect evidence to enable an estimation of the total incidence of dengue illness in Malaysia using EFs. In this way we move closer to being able to estimate the total economic burden of illness caused by dengue.

Estimating the incidence of dengue: use of expansion factors (EFs):

Initial consideration of the official reported cases from the Ministry of Health (MoH)

The official reported cases of dengue by the Ministry of Health in Malaysia in 2009, were subdivided into ambulatory and hospitalized cases, and those, which were reported by the public and the private sector (Table 1).

Table 1. Reported Dengue Cases in Malaysia, 2009

	HOSPITAL CASES	AMBULATORY CASES	TOTAL
PUBLIC	27,955	1,165	29,120
PRIVATE	12,105	229	12,334
TOTAL	40,060	1,394	41,454

Source: Ministry of Health Malaysia

On initial discussion of these numbers, Dr. Zainuddin, from the Malaysian Ministry of Health, said she thought the total number of reported cases was too low, based on her knowledge that the dengue prevalence in Malaysia is 137 per 100,000 of the population. However, multiplying this figure by the estimated 27 million inhabitants of Malaysia gives a figure of 36,990, which is broadly close to the 41,454 cases reported. Similar estimated based on the prevalence of dengue hemorrhagic fever (DHF), yield an estimate of 2,700 DHF cases occurring in 2009.

Dr. Ho said that these figures were misleading, given that approximately 75% of cases were likely to be ambulatory. She reasoned that primary health care workers under-report cases, based on a common perception that there is no need to hospitalize dengue cases. The work of Dr. Lum suggests a higher figure, though this was conducted in a referral hospital, which likely deals with more severe cases than does the primary health care setting of which Dr. Ho has more experience.

Theory and literature of EFs

The total number of dengue illness cases may be more accurately estimated using an “expansion factor” (EF) which corrects for underreporting. A study by Shepard et al. (2011) of the economic impact of dengue illness in the Americas identifies five studies in four different countries to estimate EFs in the Americas²⁵. The EFs range from 1.6 cases of dengue illness for each hospitalized case in Brazil (1996-2002) to 28 cases of dengue illness for each clinically diagnosed case in Nicaragua (2005-2006). A summary table of the EFs for the Americas is shown in Table 32-D in Appendix D.

While there are considerable regional differences in the epidemiology of dengue illness between Southeast Asia and the Americas, in both regions dengue consists of the same four virus serotypes, is officially notifiable, and is considerably underreported¹⁸. The incidence of dengue hemorrhagic fever

(DHF) and dengue shock syndrome (DSS) in Southeast Asia is approximately 18 times that of the Americas, and affects mostly children.¹⁸

Some authors have used EFs obtained from studies in the Americas to estimate the burden of disease in Asian countries^{33,34}. However, we believe that given the differences in epidemiology and surveillance systems, it is preferable to rely on studies from the same region. We conducted a systematic literature review (1995-2011) and identified 10 published papers reporting original, empirically derived EFs or the necessary data to estimate the total incidence of dengue illness in four different Southeast Asian countries. Table 33-D in Appendix D shows a summary of EFs that we obtained from the literature review and some of the assumptions the authors make, and Appendix E provides further detail on how the literature review was done.

Estimation of dengue in Malaysia

Although dengue is a reportable disease in Malaysia, underreporting inevitably leads to a lower estimation of the real number of cases, as in the case of an iceberg which is much larger below the surface of the water than it first appears from the portion which is above water. Dr. Coudeville explained that passive (as opposed to active) surveillance is sufficient to monitor the trend of number of cases, but to understand the true economic burden of dengue and therefore to set strategies to control the disease, it is important to know the actual numbers of cases. This is one place where the use of EFs can be useful. In the iceberg metaphor, a constant proportion of an iceberg is hidden below water, relative to that part which is visible. If the proportion of the hidden iceberg was 90% then an EF of 10 (for example: if the true iceberg size is 100 then using the equation below the expansion factor will be $100 \text{ (true iceberg size)} / 10 \text{ (the visible size of the iceberg)} = 10$) could be used to estimate the total size of an iceberg: measuring the volume of ice above water and multiplying this by 10 would generate a reasonable estimate of the total volume of the iceberg. Equation 1 describes how EFs can be calculated from the best estimate and reported number of cases (an EF of 1 indicates perfect reporting of dengue and a figure greater than one represents the level of under-reporting).

Equation 1. Estimating an EF from the best estimate and number of reported dengue cases

$$\text{Expansion factor} = \frac{\text{Analyst's best estimate of the number of cases of dengue illness in a specified population in one year}}{\text{Number of reported cases considered dengue illness (whether or not they actually were lab. confirmed or real dengue illness) in that population in one year}}$$

To illustrate, consider the paper by Anderson et al.³⁵ for Thailand. This is one of only a few such examples of how to use this equation and calculate an EF for dengue in a real world scenario. The study by Anderson et al. provides a reliable estimate of underreporting of dengue illness in Thailand, as discussed below. Given that there are no known empirical data in Malaysia for EFs, and that both Thailand and Malaysia are nearby middle-income countries with relatively robust surveillance systems³⁰ and similarly strong health systems, both having an estimated 25% of their hospital beds in the private

sector, and a similar climate. Therefore, we might expect the underreporting to be generally similar in both countries (see Table 2 for a comparison of some demographic and health statistics for both countries).

A five year cohort of primary school children aged 5 to 15 years old was enrolled in a study at 12 local primary schools in the Kamphaeng Phet province of Thailand (N=2,114). Anderson et al. conducted active surveillance, following up on every school absence and hospitalization, confirming suspected cases with laboratory testing, and finding 328 confirmed cases in the cohort. The number of cases reported by local hospitals during the time period of the study, 96, was used as an assumed representative sample of the level of dengue reporting in the area.

Table 2. Key demographic and health statistics for Malaysia and Thailand

STATISTIC	YEAR	MALAYSIA	THAILAND
Population	2008	26,473,670	63,389,730
Gross Domestic Product (GDP) per capita (2008 PPP \$)**	2010	\$14,410	\$8,328
Human Development Index Rank (from 169 countries)	2010	57* (HDI=0.744)	92* (HDI=0.654)
% population living in urban areas	2008	70.5	33.2
Life expectancy at birth (years)	2010	74.7	69.3
Total expenditure on health per capita (PPP international \$)	2008	620	323
Government expenditure on health per capita (PPP international \$)	2008	273	242
Total expenditure on health as % of GDP	M 2007 T 2006	4.4	3.5
Total expenditure on public health as % of GDP	2007	1.9	2.7
Total hospital beds, private sector	2006	11,637	35,806
% hospital beds, private sector	2006	23.15%	25.56%

Sources: WHO³⁶; UNDP³⁷; Ministry of Health Malaysia^{38,39}; Ministry of Public Health Thailand⁴⁰, US Department of Commerce⁴¹

Notes:

* 169 countries are ranked from 1 (most developed) to 169 (least developed), therefore the higher the number the lower the Human Development of a country; HDI value is the absolute Human Development Index.

** PPP (purchasing power parity) takes into account the relative cost of living and inflation rates of the countries, rather than using just exchange rates to calculate relative GDP.

Anderson et al.'s study has at least two important strengths. First, it is a five year cohort study using a considerable sample size (n=2,114 children). Second, it uses active surveillance and all dengue cases are laboratory confirmed.

To adopt these estimates to Malaysia we need to depend on some assumptions. First, we must assume that all reported cases in the surveillance system come from hospitalized cases, and also that all hospitalized cases are reported. We know that Thailand essentially reports hospitalized cases, so this

assumption should be robust. Second, the estimate is representative of a population of children between 5 and 15 years old, so extrapolating the estimates to other age groups might under- or over-estimate the cases depending on the age distribution of dengue illness. Third, we need to assume that all children are hospitalized in public facilities. Most people at Kamphaeng Phet province visited private facilities when they suspected dengue illness, but were hospitalized at public facilities.³⁵ Finally, and most important, we need to assume that the EF for underreported symptomatic dengue illness in Thailand is similar to that of Malaysia.

Comparison of these numbers, Equation 2, gives an EF of 3.42, i.e. for every case that is reported in this area of Thailand the authors expect there to be 3.42 times as many cases actually occurring. Conversely, this figure also suggests that 32% of dengue cases in this area are hospitalized. Interestingly, this figure is close to the estimate made by Dr. Ho that 30% of dengue cases in Malaysia are hospitalized, which was based on her experience in the primary health sector, as was this study.

Equation 2. Calculation of an EF for children aged 5-15 in the Kamphaeng Phet province of Thailand

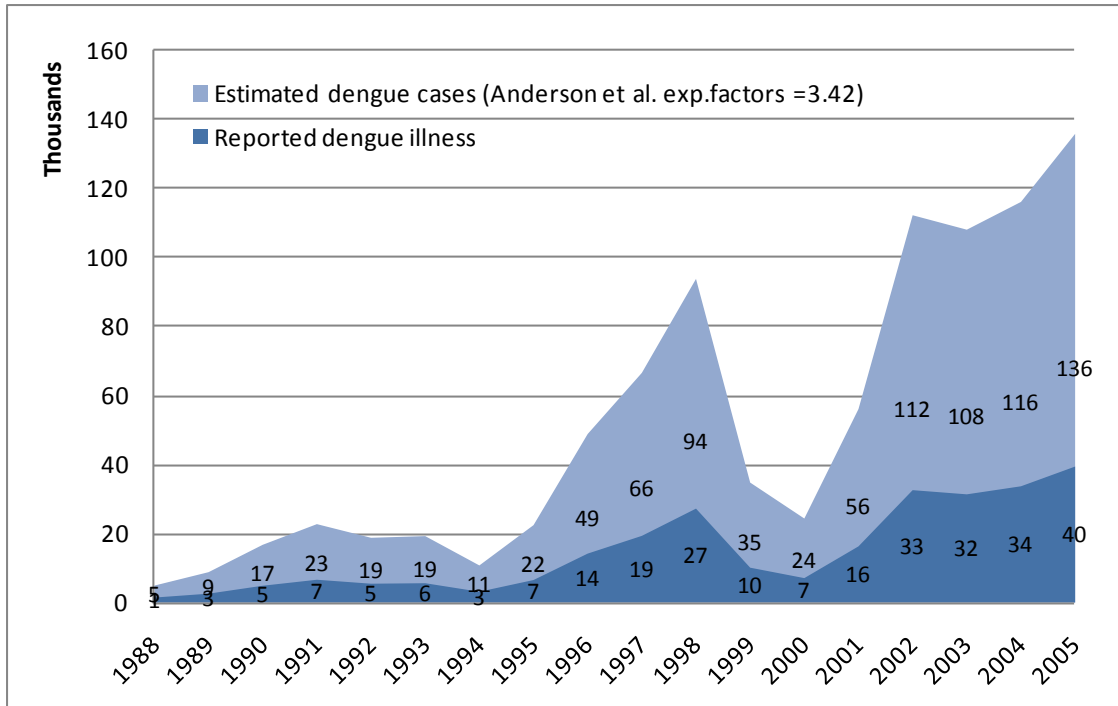
$$\text{Expansion factor} = \frac{328}{96} = 3.42 = \frac{[\textit{estimated total laboratory confirmed symptomatic dengue illness cases in children 5 – 15 years old}]}{[\textit{serologically confirmed symptomatic dengue illness cases hospitalized in public hospitals in children 5 – 15}]}$$

Application of EFs from the literature to reported dengue cases in Malaysia

In light of the similarities between the dengue situation in Thailand and Malaysia, it may be instructive to apply the EF of 3.42 to the reported number of cases over time in Malaysia (Figure 2) and then use other available evidence to consider whether this seems like a reasonable estimate of the actual number of cases in Malaysia in this period. The projected number of dengue cases in Malaysia using the EF derived from Anderson et al. (2007)³⁵ is 105,493. The study by Anderson et al. (2007) conducted active surveillance to quantify case numbers, and so gives us a good understanding of the actual dengue prevalence and relevant EF in children in Thailand. This study becomes less relevant if we note that most Malaysian dengue cases are in adults (Figure 3).

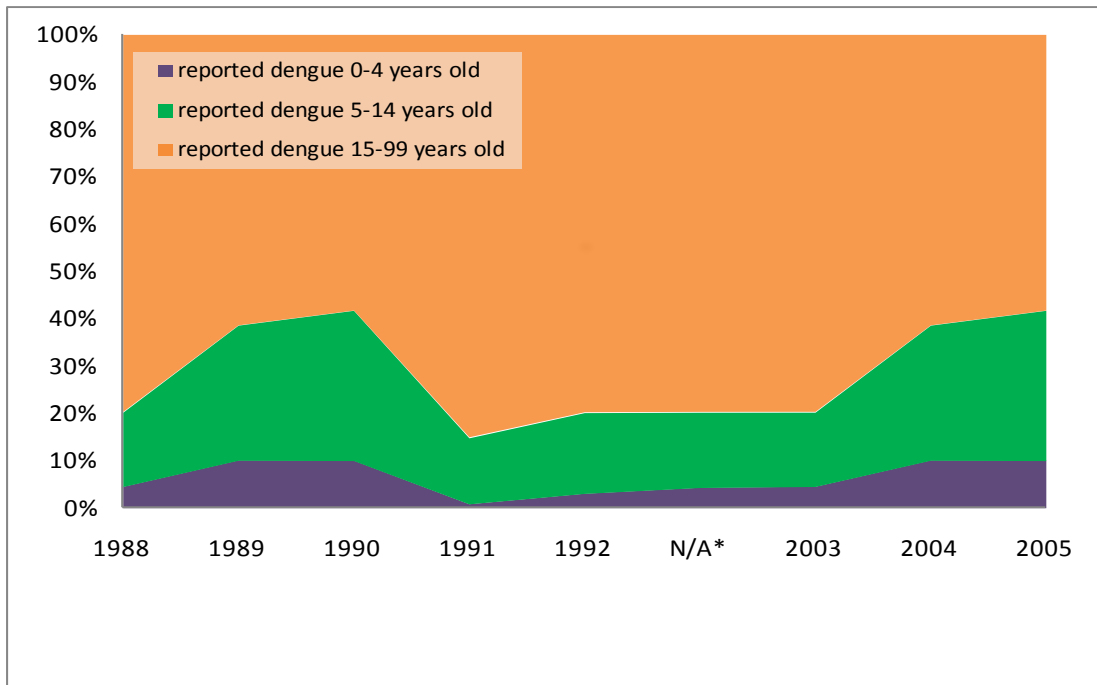
Between 2003 and 2005 there were 23,071 cases reported for persons over the age of 15 years, and 66% of reported cases in Malaysia are in adults, the economically active section of the population. It is interesting to note that this figure of 66% (from 2003-2005) is not too dissimilar to the proportion of dengue cases in adults estimated by Dr. Ho of 60% (an estimation made at the workshop in 2010), but that 17% of reported cases in 2009 were in children suggesting a decreasing number of cases in children in recent years. The data in Figure 3 (below) show a higher proportion of children in the latest year reported (2005). As Professor Lum has observed, the number and severity of cases in children is decreasing relative to those in adults, so that the change from 2005 to 2009 is reasonable.

Figure 2. Reported cases of dengue illness and estimated cases using EFs in Malaysia, 1988 – 2005



Sources: Ministry of Health Malaysia²²; WHO, Regional Office for the Western Pacific²³

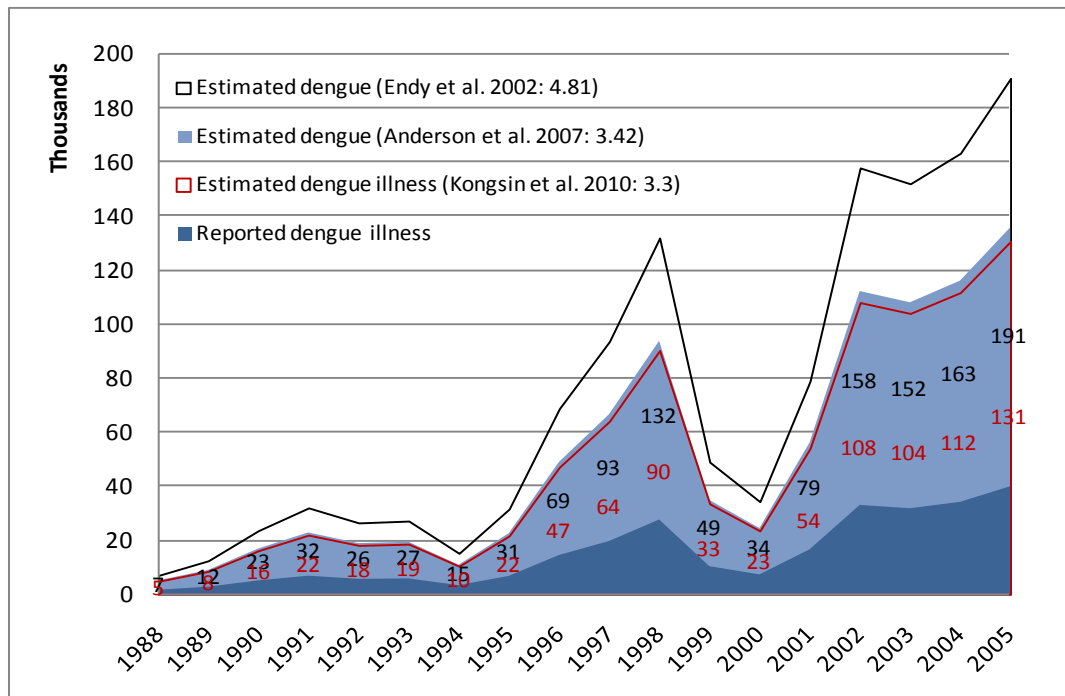
Figure 3. Age distribution of reported dengue illness cases by age group in Malaysia, 1988 – 2005.



Sources: Ministry of Health Malaysia²²; WHO, Regional Office for the Western Pacific²³; Poovaneswari, 1993¹⁹

Applying the EFs calculated in two other studies, 4.81 from Endy et al. (2002)⁴² and 3.3 from Kongsin et al. (2011)⁶, to the 30,846 reported dengue cases in Malaysia between 2001 and 2005 gives an upper estimate of the projected numbers of cases (using EFs derived by Endy et al.) of 148,368 a year (Figure 4). By way of comparison, the results of five studies in four South American countries (Brazil, Columbia, Nicaragua and Puerto Rico) are presented (Table 32-A) which had calculated EFs for dengue cases of between 1.4 and 9, with the exception of Nicaragua where EFs was estimated at 28, depending on the period of time under investigation. In this latter study all types of cases were included, not just hospitalized cases; the EF for ambulatory cases subject to routine passive surveillance, as in Malaysia, is likely to be much higher.

Figure 4. Reported and estimated cases of dengue illness in Malaysia using alternative EFs, 1988 – 2005.



Sources: Ministry of Health Malaysia²²; WHO, Regional Office for the Western Pacific²³

Is there a difference between the EFs applicable to children and adults?

Dr. Coudeville underlined the fact that the Thailand study³⁵ considered only dengue cases in children, and referred to the only documented comparison of dengue reporting in children versus adults that found under-reporting to be greater in adults than in children. This might suggest that this EF would be too low if applied to the Malaysian population as a whole. The breakdown of cases by age is important when considering, for example, the best age to vaccinate a population: under-reporting in children may lead to the conclusion that the best time to vaccinate is in adulthood, which would not be the case if a large number of infections occurred in children. However, Dr. Lum said that this comparison between children and adults would be affected by how groupings of cases by age was organized, and Dr. Ho said that whilst children generally recover quickly, there is more severe cases in adults and so the likelihood of an adult case being reported may be greater.

These considerations similarly apply to the level of hospitalization in children with dengue compared to that in adult cases. Dr. Ho believes that a greater proportion of adult cases are admitted to hospital: 10-20% of children with dengue, assessed in the public primary health care sector, are admitted, compared to 30-40% of adult cases. She estimated that of all hospitalized cases 20-30% of cases are in children and 70-80% are in adults, compared to suspected cases of which perhaps 40% are children under 15 years old and 60% are over 15. Given that a lower proportion of children than adults seem to be admitted to hospital, that the reported cases are primarily hospital-based, and that the rate

of under-reporting is much greater in ambulatory than hospitalized cases, there is likely to be a greater rate of under-reporting of cases in children than adults. In other words, you would tend to find more adult cases in the reported numbers than their share of actual cases. A larger EF would therefore need to be applied to the number of dengue cases in children than in adults in order to achieve a more realistic estimation of the actual number of cases.

This indeed seems to be the case. Using the WHO and Malaysian MoH definition of a child as being 14 years old and below, the 41,454 reported cases in the surveillance data from the Malaysian MoH can be classified into child cases and adult cases, based on the reported age of the patient. This gives a total of 7,062 cases of dengue in children reported in Malaysia in 2009, representing only 17% of the total number of reported cases. This is in the same magnitude as Dr. Ho's estimates of children making up 20-30% of hospitalized dengue cases, and if the estimate of 40% of suspected cases being in children is accurate, then it represents an under-reporting of over half the cases, or an EF from suspected to reported cases of at least 2 in children. As an additional observation, of the 93 deaths due to dengue reported in 2009, 14 (15%) were in children (under 15 years old).

Using the reported number of cases in children and adults and the estimation that 40% of actual cases are in children, it is possible to derive differential EFs for children and adults (Table 3), which if there is a large difference, should allow for a more accurate estimation of the real number of dengue cases in Malaysia. To calculate this, the number of adult cases is multiplied by an EF, adjusted for the relative proportion of adult to child cases, and then multiplied by the reported number of cases in children, to give an EF for children. Assuming an overall EF of 3 for adult cases, the EF would thus be 9.74 in children representing a much greater level of under-reporting in children than in adults. Multiplying the reported cases in children by this EF of 9.74 gives an estimate of 68,783 cases in under 15 year olds in Malaysia in 2009, combining with 103,176 cases in adults to give a total of 171,960 cases, 4 times greater than the reported number of cases.

Table 3. Deriving a differential EF for cases in children from available information, 2009

	REPORTED CASES IN 2009	EF	ADJUSTED DENGUE CASES	PROPORTION OF DENGUE CASES BY AGE GROUPS
Example 1				
Adult	34,392	1.1	37,831	60%
Children (derivation)	7,062	X	7,062X	40%
Children (result)	7,062	3.57	25,221	
Total (result)	41,454	1.52	63,052	100%
Example 2				
Adult	34,392	1	34,392	60%
Children (derivation)	7,062	X	7,062X	40%
Children (result)	7,062	3.25	22,928	
Total (result)	41,454	1.38	57,320	100%
Example 3				
Adult	34,392	3	103,176	60%
Children (derivation)	7,062	X	7,062X	40%
Children (result)	7,062	9.74	68,784	
Total (result)	41,454	4.15	171,960	100%

Notes:

i. Adjusted dengue case= reported numbers*EF

ii. The ratio of adult adjusted cases and children adjusted cases should equal the ratio of 60%/40%

iii. $x = \frac{\text{Adjusted adult cases} \cdot (\text{Proportion of cases in children} / \text{Proportion of cases in adults})}{\text{Reported children cases}}$

What is meant by a ‘hospital case’ in the reported dengue statistics?

A key problem in determining the number of hospitalized versus ambulatory cases is that cases are reported (and lab tests requested) as ‘hospital’ cases whether they are eventually admitted or whether they are tested/treated as outpatients. Although 97% of reported cases in 2009 were hospital-reported (Table 1), this does not necessarily indicate that 97% of cases were admitted to hospital. Participants examined the database, available from the Ministry of Health Malaysia, which lists all 41,454 cases reported in 2009, to see whether it was possible to determine whether a hospital reported case referred to an admitted or an ambulatory case which was seen as a hospital outpatient case. Considering the surveillance data giving records of all reported cases in 2009, It seems that the lack of an entry in the ‘date of admission’ field of a hospital-reported case indicated that it was an outpatient case – 138 cases have a dash in the ‘Ward’ column, and an additional 1,505 cases are left blank in this column, giving a total of 1,643. This figure is not too dissimilar to the reported figure of 1,394

ambulatory cases, seemingly accounting for to 3% of all data points, which would confirm that 97% of all reported cases were indeed hospitalized.

However, another way to determine from the data set which cases were ambulatory and which were hospitalized (distinct from those cases which were reported by hospitalized but not actually hospitalized) would be to quantify those cases where a ward was not listed, or where an outpatient unit or ward was listed in the 'Ward' column, assuming that this is an indication that they were not admitted and thus ambulatory. Filtering the cases to remove those whose 'Ward' column contained a blank, an entry such as 'N/A' or 'NIL', a dash, or a ward name which indicated it was an outpatient ward left 32,403 cases. If this classification were applied, the reported number of ambulatory cases in 2009 would represent 22% of all cases $((41,454-32,403)/41,454*100)$. However, this classification should be considered with caution. Of those cases which appeared to be outpatient cases many were reported as being positive for heametemesis, which is a symptom which is likely to trigger admission. However, of those cases which did not have a ward recorded but which were reported by a hospital, rather than by a clinic, most were not reported as being positive for the major symptoms, and so were very likely treated as outpatients. Hence there seems to be an imperfect correlation between the reporting (or not) of a ward in the database and the case being ambulatory, but the link seems to be stronger in hospital reported cases than in clinic reported cases, possibly highlighting a difference in the way cases are handled between the two. Note that there is not a clear correlation between those cases which were recorded without a date of admission and those for which no ward was listed.

When asked whether dengue leads to the majority of those affected being hospitalized; Dr. Ho estimated that about 70% of cases are ambulatory and 30% hospitalized, whereas Dr. Lum thought the ratio was more like 50:50. Taking the mid-point of these estimates would give a value of 60% of cases being ambulatory, which would make the EF of real cases compared to reported cases of 20 if the MoH reported proportion of ambulatory cases (3%) was considered, or of 2.72 if the proportion of reported cases was 22%.

How under-reporting impacts EFs

One possible source of evidence about the level of presumably underreporting of dengue in Malaysia comes from an examination of the data produced by the Foreign Worker Medical Examination Monitoring Agency (FOMEMA) system, a valuable suggestion from Dr. Hasan Abdul Rahman (Director for Disease Control) made during a planning meeting for this workshop. The FOMEMA system involves the routine testing of foreign workers in Malaysia for six reportable diseases on arrival and annually thereafter. Requests of laboratory tests for these diseases are entered into the system by the examining general practitioner (GP) physician and positive results automatically recorded. Although dengue is not included in the diseases which are tested for, the data from FOMEMA gives an idea of the reliability of the reporting process for reportable diseases, and the level of discrepancy between the automatically recorded positive tests and the number of cases which are independently reported by the examining GP. Comparing these two systems could act as a capture-recapture surveillance method, assessing the

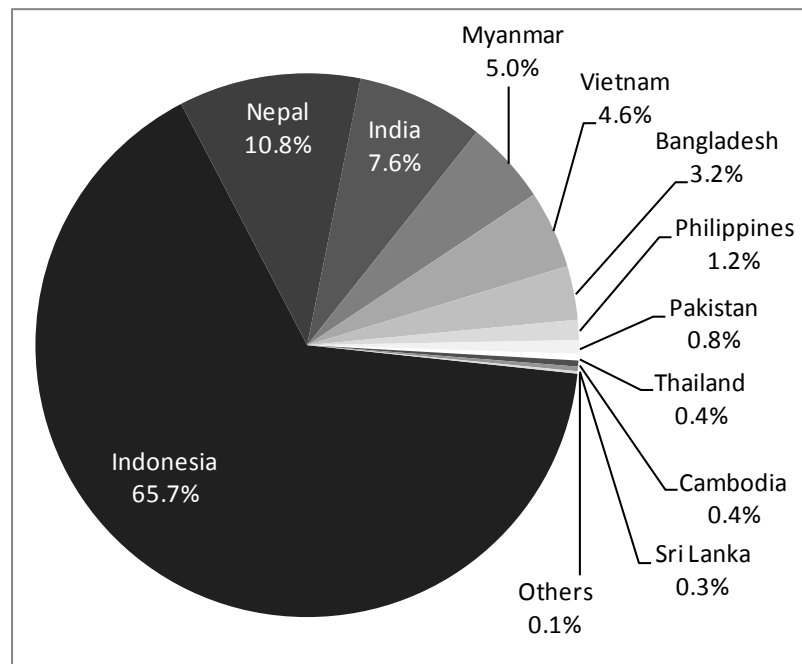
relative accuracy of two methods of reporting (in this case the electronic notification (ENOTIS) system and FOMEMA reporting procedures). This in turn could give a better idea of the true number of cases and the subsequent EF.

Foreign Worker Medical Examination Monitoring Agency (FOMEMA)

Background

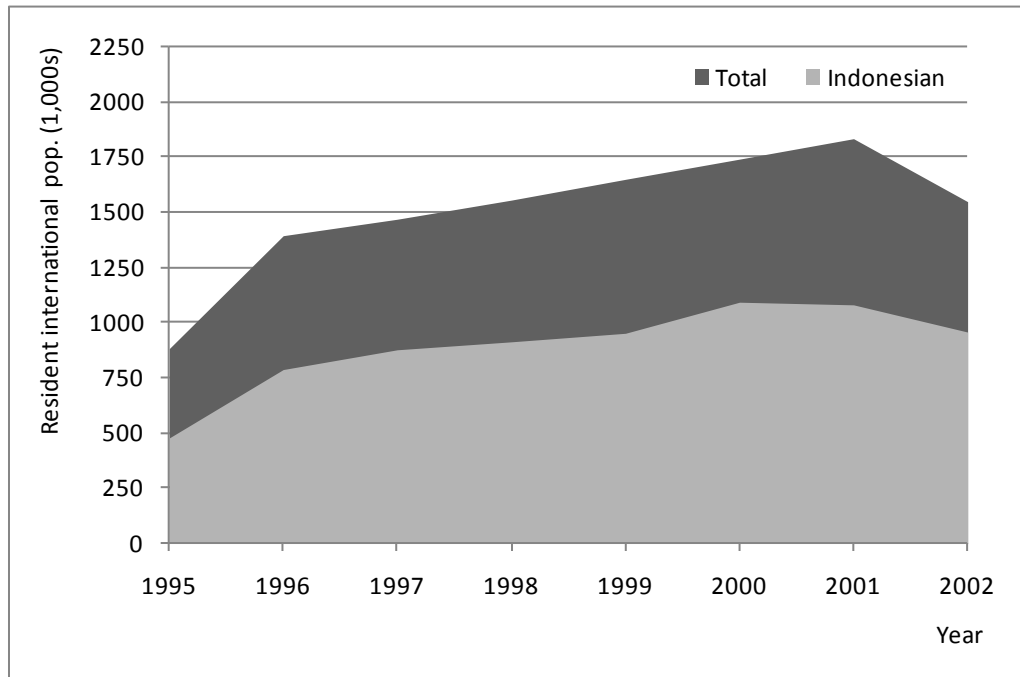
Malaysia has shown an outstanding economic development since its independence, with an average GDP growth rate of 6.5% between 1957 and 2005. Malaysia's economy is dynamic and diversified, largely based on manufacturing and services⁴³. As other middle-income countries in the region, Malaysia currently has significant amounts of emigration and immigration of workers⁴⁴, although the government estimates a net gain of one migrant worker every 5 minutes and 15 seconds⁴⁵. Foreign workers are an important part of the Malaysian economy, and are mostly employed in construction, agriculture, factories, and as domestic workers⁴⁶. The number of documented migrant workers in Malaysia was 1.7 millions in 2005 and 1.9 millions in 2009. According to government officials, numbers of undocumented workers are substantial, too, with an estimated ratio of documented/undocumented workers of 1/1^{47,48}. The biggest group of immigrant workers comes from Indonesia, followed by Nepal, India, Myanmar, Vietnam, and Bangladesh (Figure 5). Indonesians represented about 52% of the total of immigrant workers in 2009^{46,47}. Figure 6 shows the resident international population in Malaysia between 1995 and 2002.

Figure 5. Total immigrants in Malaysia in March 2006, by country of origin



Source: Nair 2006⁴⁹

Figure 6. Resident international population in Malaysia, 1995-2002



Source: ILO⁵⁰

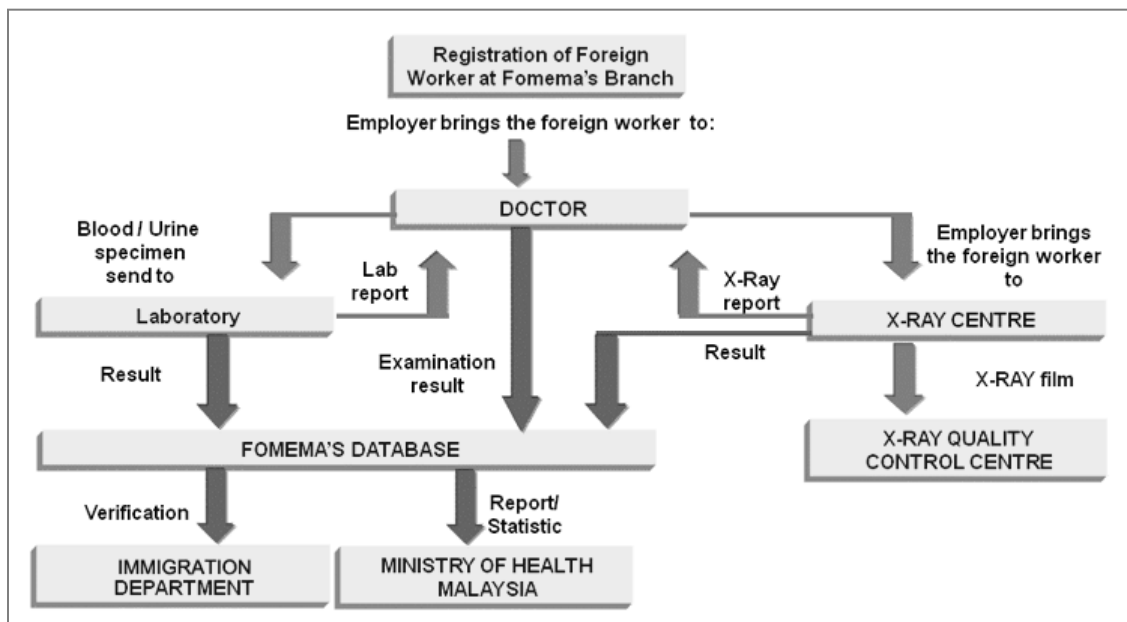
Workers migrating to Malaysia have to go through a medical examination in their country of origin. The Malaysian Ministry of Health appoints physicians in workers' home countries who reject any worker who is not deemed fit for employment in Malaysia. As of August 2005, mandatory pre-employment medical examination is also requested upon arrival in Malaysia, usually within the first month of the workers' stay^{46,48}. Medical baseline data for each worker are also created for future screening and supervision⁴⁸.

Medical screening of immigrant workers: FOMEMA

Even though all immigrant workers are required to be examined in their home countries before being employed in Malaysia, there is evidence that a proportion of them still have communicable diseases on their arrival to Malaysia⁴⁶. To reduce the number of immigrants who are unfit to work in Malaysia, the government requires a mandatory examination upon arrival. Pre-employment medical screening includes a series of mandatory laboratory examinations to test if the worker is free of an official list of communicable diseases, which include HIV, Hepatitis B, Malaria, Leprosy, VDRL/TPHA (syphilis), and Tuberculosis. FOMEMA operates as an independent agency, coordinating and managing the renewal of work permits for immigrant workers nationwide. The management and operation of the Malaysian national system of foreign workers medical screening was given in concession to Pantai FOMEMA and Systems Sdn Bhd in 1997⁵¹.

According to FOMEMA, some key features of the system include a centralized registration and payment, standardized examination as directed by the Ministry of Health, a centralized nationwide dataset on foreign workers' health status, independent and electronically submitted reports from physicians and laboratories, and an integrated system with Immigration Department Headquarters⁵¹. Overall, FOMEMA is a preventive health program which aims at avoiding the spread of communicable diseases, increasing average productivity by reducing absenteeism, and reducing the burden of illnesses in the health sector by avoiding the immigration of ill workers^{46,51}. Figure 7 shows the medical screening process of the FOMEMA system.

Figure 7. Medical Screening Process, FOMEMA System



Source: FOMEMA⁵¹

All the diseases that FOMEMA controls for are reportable diseases to the Malaysian Ministry of Health (MoH). ENOTIS is the MoH information system. Table 4 shows FOMEMA's panel doctor case register and notification data (2009) in ENOTIS, and Table 5 shows FOMEMA panel doctor notification data. It is interesting to note that the total cases of communicable diseases identified that are notified to the MoH are considerably less than the actual positive cases screened for all of these conditions. The underreporting found in these illnesses illustrates the necessity of using EFs when trying to estimate the true incidence of communicable diseases.

Dr. Shepard suggested that malaria might be the reported disease included in the FOMEMA system which most closely mirrors the case of dengue. Examining underreporting of Malaria to ENOTIS may shed a light on dengue illness too. Like dengue, malaria is a common arthropod-borne disease of humans in tropical areas. When symptomatic, malaria produces high fever and body pain which considerably reduces the patient's ability to work and reduces workers' productivity. In its acute phase,

malaria has active parasites and the person has to be ill when the medical screening is done. The estimated EF for Malaria is about 8, that is, for every reported case of Malaria, one would expect on average 8 unreported cases. This dataset includes a wide variety of Malaysian doctors in almost every state of Malaysia. Also, one would expect most of the immigrant workers to be located in urban areas, where dengue fever is most common. Malaria is the best case scenario in terms of expected reporting, and therefore one could expect the underreporting of dengue illness to be somewhat higher.

Dr. Coudeville pointed out that if malaria is assumed to be the most relevant disease to compare to the dengue situation, we would expect to see only around 10-12% of dengue cases being reported to the Ministry of Health Malaysia. If an EF were to be estimated from this example it would be as large as 52, representing substantial under-reporting of cases. However, Dr. Lum pointed out that the FOMEMA system only includes a skewed sample of the Malaysian population, and that more information is needed to assess the level of reporting overall. Dr. Singh expects the level of dengue reporting to be higher than this evidence would suggest, as dengue is covered in the press on a regular basis and awareness of the disease and its importance to the Malaysian population is high.

Table 4. FOMEMA panel doctor case register and notification data (2009) in ENOTIS by state

DOCTOR_STATES	DISEASES													
	HEPATITIS B		HIV		LEPROSY		MALARIA		SYPHILIS		TUBERCULOSIS		TOTAL	
	Reg.	Notif.	Reg.	Notif.	Reg.	Notif.	Reg.	Notif.	Reg.	Notif.	Reg.	Notif.	Register	Notification
JOHOR	1	1	0	0	0	0	0	0	0	0	0	0	1	1
KEDAH	0	0	0	0	0	0	0	0	0	0	0	0	0	0
KELANTAN	4	4	3	3	0	0	0	0	0	0	4*	3	11	10
KUALA LUMPUR	17*	15	0	0	0	0	0	0	4	4	98*	97	119	116
MELAKA	1	1	0	0	0	0	0	0	0	0	0	1	1	2
NEGERI SEMBILAN	0	0	0	0	0	0	4*	0	1	2	2	2	7	4
PAHANG	54	60	1*	0	0	0	3*	1	6	6	7*	6	71	73
PERAK	0	0	0	0	0	0	1	1	0	0	10*	0	11	1
PERLIS	1	1	0	0	0	0	0	0	0	0	0	1	1	2
PULAU PINANG	1	1	3	3	0	0	2	2	3*	2	11	11	20	19
SABAH (WP LABUAN)	3	3	1*	0	0	0	0	0	0	0	1*	0	5	3
SELANGOR	6	6	3*	1	1*	0	12*	5	0	1	38*	2	60	15
TERENGGANU	3	3	0	0	0	0	0	0	6	7	2	2	11	12
Grand Total	91	95	11	7	1	0	22	9	20	22	173	125	318	258

Notes:

DOCTOR_STATES = the location of examining doctor by States in Malaysia.

SABAH (WP LABUAN) = the data was from Wilayah Persekutuan Labuan. The state itself is under a different company.

ENOTIS = Ministry of Health (MoH) information system.

* This number cannot be precisely accurate because case register data must be same or less than notification data. This may caused by human or ENOTIS system error

Table 5. FOMEMA panel doctor notification data (2009) by state

Count of WORKER_CODE DOCTOR_STATES	DISEASES													
	HEPATITIS B		HIV		LEPROSY		MALARIA		SYPHILIS		TUBERCULOSIS		TOTAL	
	FOMEMA	ENOTIS	FOMEMA	ENOTIS	FOMEMA	ENOTIS	FOMEMA	ENOTIS	FOMEMA	ENOTIS	FOMEMA	ENOTIS	FOMEMA	ENOTIS
JOHOR	1,195	1	137	0		0	11	0	259	0	1,220	0	2,822	1
KEDAH	128	0	11	0	1	0	2	0	83	0	91	0	316	0
KELANTAN	100	4	8	3		0	10	0	29	0	51	3	198	10
KUALA LUMPUR	818	15	107	0		0	18	0	323	4	1,052	97	2,318	116
MELAKA	151	1	27	0		0	1	0	32	0	129	1	340	2
NEGERI SEMBILAN	260	0	23	0		0	3	0	77	2	193	2	556	4
PAHANG	471	60	29	0		0	3	1	87	6	218	6	808	73
PERAK	359	0	41	0		0	3	1	94	0	226	0	723	1
PERLIS	13	1		0		0		0	16	0	2	1	31	2
PULAU PINANG	219	1	37	3		0		2	105	2	368	11	729	19
SABAH (WP LABUAN)	36	3	4	0		0		0	18	0	4	0	62	3
SELANGOR	1,389	6	168	1	1	0	24	5	601	1	2,046	2	4,229	15
TERENGGANU	90	3	7	0		0	1	0	34	7	40	2	172	12
Grand Total	5,229	95	599	7	2	0	76	9	1,758	22	5,750	125	13,414	258
FOMEMA panel doctor notification rate (%)		1.8		1.2		0.0		11.8		1.3		2.2		1.9
EF		55		86		undefined		8		80		46		52

Notes:

ENOTIS = MoH INFORMATION SYSTEM

FOMEMA = Foreign Worker Medical Examination Monitoring Agency

SABAH (WP LABUAN) = the data was from Wilayah Persekutuan Labuan. The state itself is under different company.

There are 6 notifiable diseases under FOMEMA's Medical Examination of Foreign Workers: hepatitis B, HIV, leprosy, malaria, syphilis and tuberculosis.

Dengue illness in the private sector

Another way in which to reach an estimate of the number of dengue cases in Malaysia, which can be compared to the reported number of cases in an attempt to calculate relevant EFs, is to look at the number of laboratory tests for dengue requested from the private sector, specifically from Pantai Holdings, as reported to the workshop by Dr. Chiang.

Following Malaysia's economic growth and expansion in the last decades, Malaysian healthcare has also faced a considerable transformation, particularly in hospitals and specialized healthcare. Much of this transformation has been due to the increasing importance of the private health sector since the early 80s. For example, between 1980 and 2003 the number of hospital beds in the private sector increased by nine fold, going from 1,171 to 11,689 total hospital beds, and the share of hospital beds went from between 4 and 6 percent of total hospital beds to approximately 24 percent. There were only 10 private hospitals in 1980 and by 2003 there were already 209⁵². Table 6 shows a summary of hospital statistics from Malaysia.

Table 6. Malaysia hospital statistics, 2008-2009

Item	MoH general	Other gov't	All gov't gen.	Private	Total general	MoH special
Year 2008						
Hospitals	130	7	137	209	346	6
Beds	33,004	3,245	36,249	11,689	47,938	5,000
Admissions	2,062,925	126,677	2,189,602	754,378	2,943,980	9,708
Visits	15,273,036	1,544,581	16,817,617	2,464,756	19,282,373	153,830
<i>Percentages of total general</i>						
Hospitals	38%	2%	40%	60%	100%	2%
Beds	69%	7%	76%	24%	100%	10%
Admissions	70%	4%	74%	26%	100%	0%
Visits	79%	8%	87%	13%	100%	1%
Year 2009						
Hospitals	130	8	138	209	347	6
Beds	33,083	3,523	36,606	12,216	48,822	4,974
Admissions	2,130,784	128,726	2,259,510	828,399	3,087,909	9,122
Visits	17,295,971	1,900,047	19,196,018	2,861,443	22,057,461	161,955
<i>Percentages of total general</i>						
Hospitals	37%	2%	40%	60%	100%	2%
Beds	68%	7%	75%	25%	100%	10%
Admissions	69%	4%	73%	27%	100%	0%
Visits	78%	9%	87%	13%	100%	1%

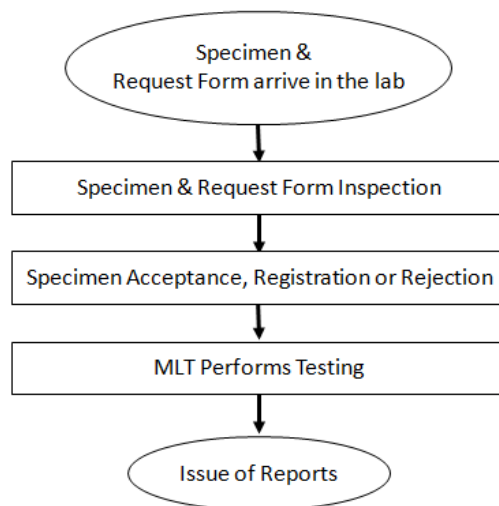
Source: Ministry of Health, Malaysia^{38,39}

One of the most important stakeholders in the private health sector in Malaysia is Pantai Holdings, which own seven important hospitals and hold the government contract for FOMEMA through Pantai Medivest. Pantai Holdings also hold two additional government concessions – a system of medical monitoring for the Ministry of Transport and privatized support hospital services⁵².

Laboratory testing as a mean to estimate the under reporting of dengue cases

Laboratories in Pantai hospitals implemented and analyzed approximately 20% of the total private sector tests of suspected dengue illness patients, according to information given by a provider of dengue test kits. Early detection of dengue fever is important for the treatment of the infected patients and also to plan an adequate public health response to the epidemic. Patients that are suspected of having dengue fever can get either serology (detection of antibodies) or, more recently, NS1 tests. NS1 tests enable earlier diagnoses than serological tests that produce antibodies only after 4 to 6 days^{53,54}. Recent studies suggest that NS1 tests have moderate sensitivity (approx. 60 percent) and high specificity (almost 100 percent) in the diagnosis of dengue^{54,55}. Figure 8 shows a workflow diagram of a laboratory for evaluating dengue specimens, and Table 7 shows a comparison between the total number of suspected dengue illness cases and the confirmed dengue illness cases (positive) between the two diagnosis tests by state. Table 7 suggests that there has been a decrease in the number of serology tests requested between 2009 and 2010 (approximately a 10 percent decline) and an increase in the number of dengue NS1 tests requested (approximately 40 percent rise). A total of 24,218 patients were screened for dengue illness in the private sector from January through November 2010, and about 20% of these showed positive results in the dengue tests.

Figure 8. Pantai Laboratory Workflow



Source: Dr. Chiang, Dengue Burden Study⁵⁶

Table 7. Total suspected dengue illness cases and diagnosis tests performed, by location of the laboratory

Location	Year	<u>SEROLOGY</u>			<u>NS1</u>			<u>ALL TESTS</u>		
		Number	Positive	%	Number	Positive	%	Number	Positive	%
Klang	2009	1,123	248	22%	581	160	28%	1,704	408	24%
	2010	916	192	21%	519	129	25%	1,435	321	22%
Ampang	2009	2,548	658	26%	205	85	41%	2,753	743	27%
	2010	2,377	555	23%	729	204	28%	3,106	759	24%
Melaka	2009	1,590	238	15%	498	94	19%	2,088	332	16%
	2010	2,408	521	22%	1,702	544	32%	4,110	1,065	26%
Penang	2009	3,474	373	11%				3,474	373	11%
	2010	2,131	408	19%	860		0%	2,991	408	14%
Bangsar	2009	2,908	553	19%	2,256	191	8%	5,164	744	14%
	2010	1,559	481	31%	2,671	49	2%	4,230	530	13%
Cheras	2009	1,778	1,021	57%	413	151	37%	2,191	1,172	53%
	2010	2,291	934	41%	389	164	42%	2,680	1,098	41%
Ipoh	2009	2,510	271	11%	998	76	8%	3,508	347	10%
	2010	2,422	255	11%	1,076	130	12%	3,498	385	11%
Batu Pahat	2009	1,447	318	22%	396	94	24%	1,843	412	22%
	2010	1,410	295	21%	758	132	17%	2,168	427	20%
Total	2009	17,378	3,680	21%	5,347	851	16%	22,725	4,531	20%
	2010	15,514	3,641	23%	8,704	1,352	16%	24,218	4,993	21%

Source: Sharon Chiang, Dengue Burden Study⁵⁶

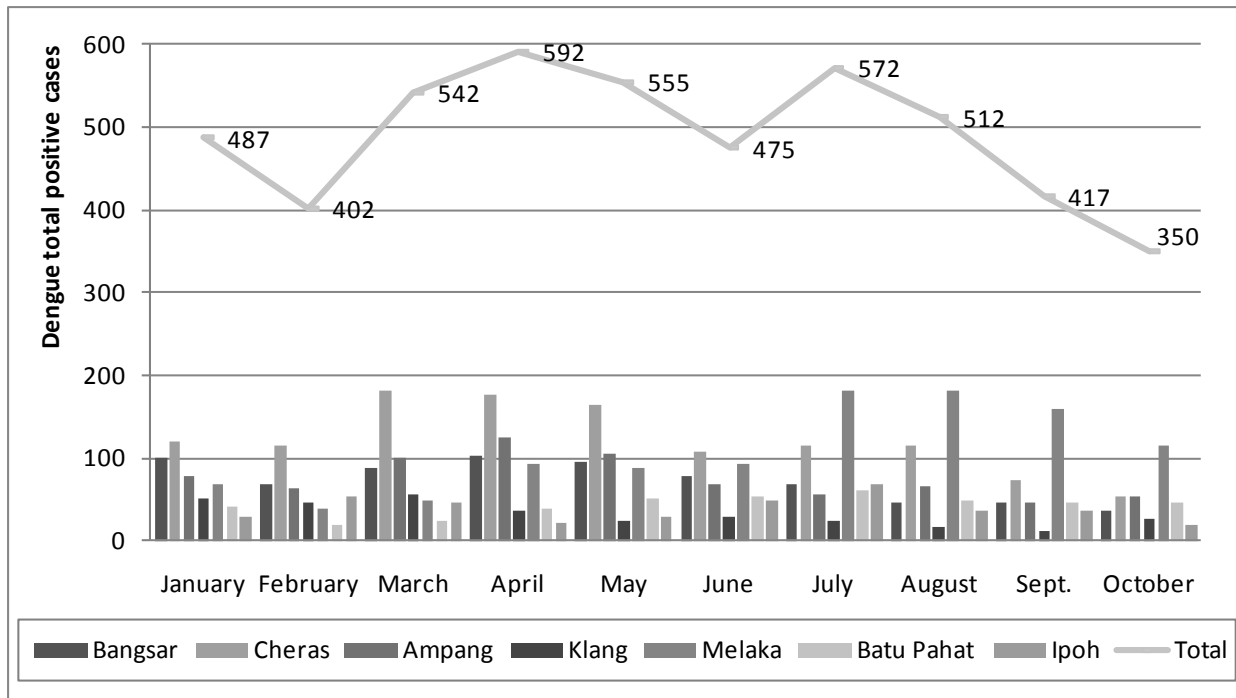
The number of requested and positive tests gives an estimate of the total number of suspected and confirmed dengue cases seen in the private sector, if they are multiplied by an EF of 5 to account for Pantai Holdings' 20% market share, of 121,090 and 24,965 cases, respectively (year 2010). Using the EF estimated from the FOMEMA data of 52 would give an actual number of cases of an enormous 1,298,180 cases.

When asked about the proportion of dengue cases requiring laboratory tests, the consensus among the participants was that in dengue reporting a routine surveillance approach is applied: there is no requirement on doctors to perform laboratory tests, though they may request a test in some cases to confirm a diagnosis. The tests are not always performed, due to cost, and public hospitals are more likely to request blood tests instead and report a case as 'probable dengue', rather than obtaining a laboratory confirmation.

Figure 9 shows the distribution of laboratory confirmed positive dengue illness cases by location in the year 2010. The distribution shows two peaks of dengue illness cases, in April and August. Dr. Lees noted that some patients may receive IgG testing when they are not in the acute stage, and the test may not be able to show dengue. An alternative analysis would exclude samples not taken at the ideal time. Figure 10 shows the comparison of the total cases of laboratory confirmed dengue illness in years 2009 and 2010 from

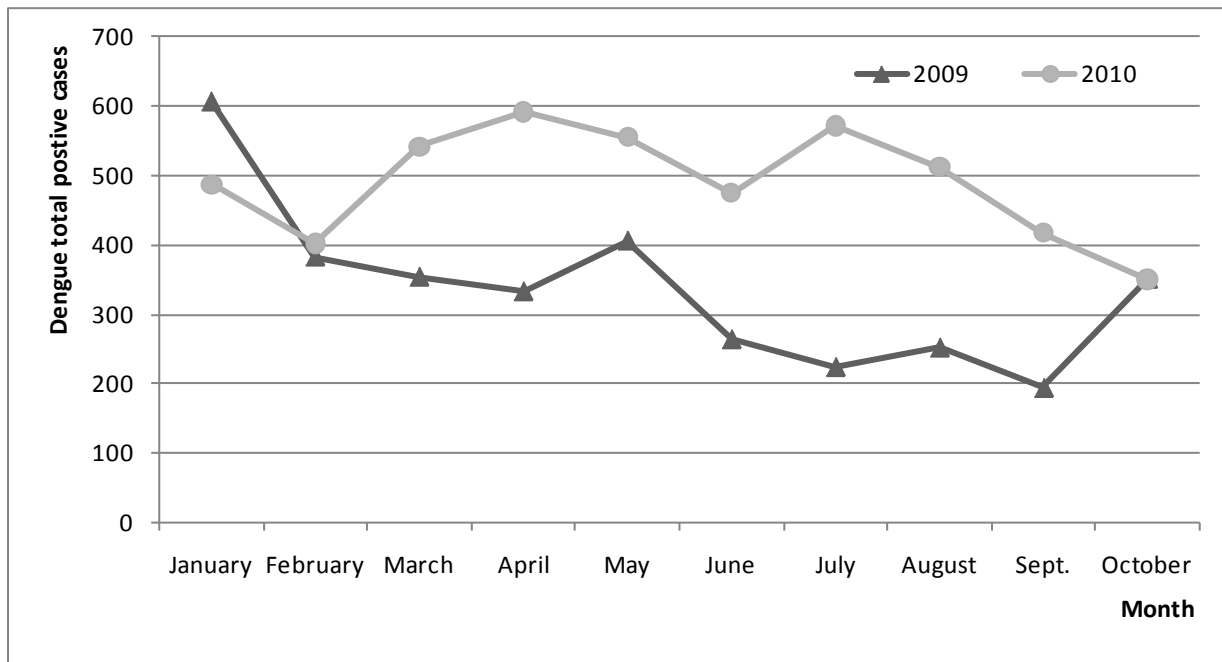
January to October. The curves show no clear pattern in the variation of total laboratory confirmed dengue illness cases between the two years.

Figure 9. Number of laboratory positive dengue illness cases (serology + NS1) by month, year 2010 (totals and breakdown by location)



Source: Sharon Chiang, Dengue Burden Study⁵⁶

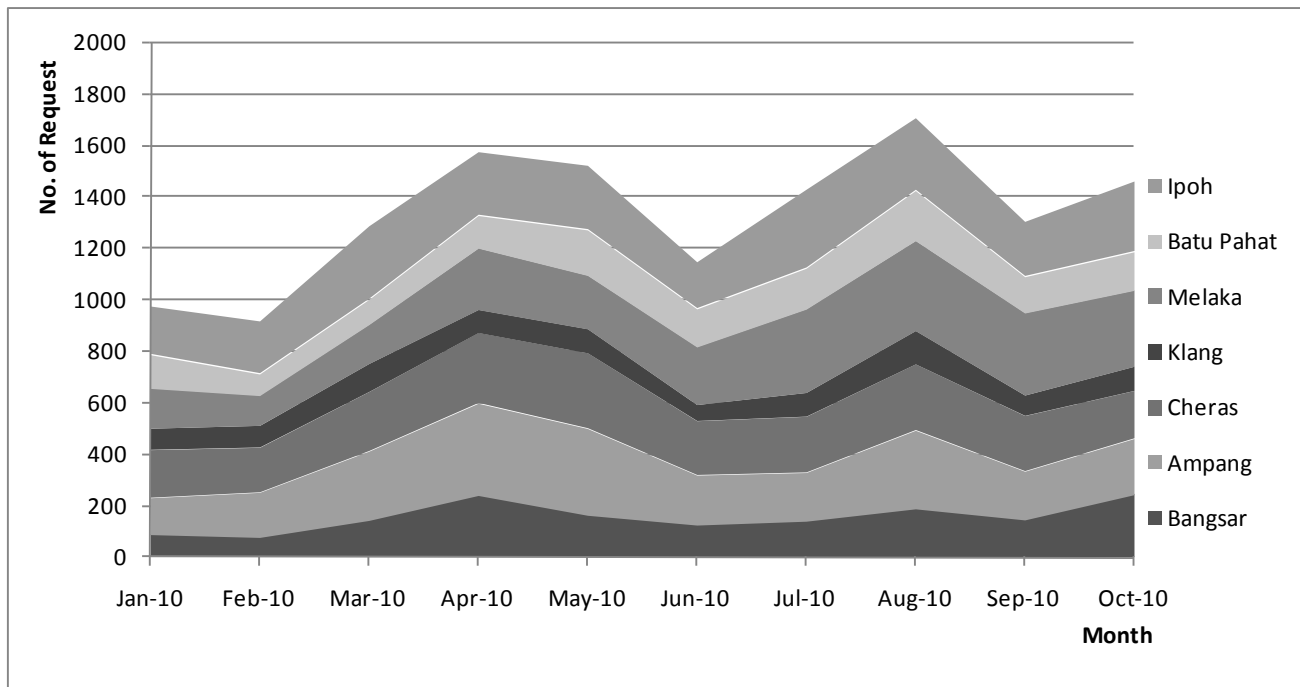
Figure 10. Distribution of positive dengue illness cases (serology + NS1), years 2009-2010



Source: Sharon Chiang, Dengue Burden Study⁵⁶

Figure 11 shows the monthly variation of the total number of dengue tests requested by location in Malaysia in 2010. There is a peak in the number of total tests requested in April and August 2010, which approximately coincides with the two peaks in the total laboratory-confirmed dengue illness cases shown in Figure 9. Also, facilities at the Klang Valley (Bangsar, Ampang, Cheras, and Klang) represent almost 50 percent of the total dengue tests requested in 2010.

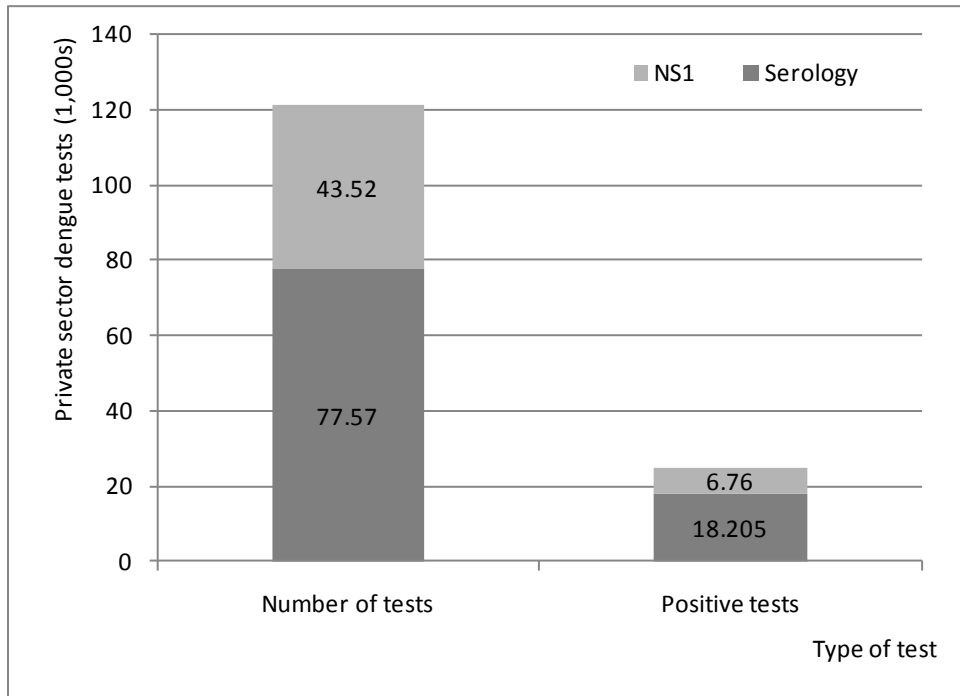
Figure 11. Total number of dengue tests requested by location, 2010



Source: Sharon Chiang, Dengue Burden Study

Figure 12 shows the projected total number of dengue tests requested during 2010. Note that the numbers presented are those estimated for Pantai’s laboratories multiplied by five, as Pantai represents approximately 20% of the total dengue illness tests requested by the private sector. The total number of true dengue illness cases is most probably somewhere between the total number of positive laboratory tests and the number of tests performed on patients who showed symptomatic dengue illness, since a negative test does not necessarily rule out dengue illness^{54,55}.

Figure 12. Projected total private sector dengue tests requests for year 2010



Source: Sharon Chiang, Dengue Burden Study

Differences between the public and private healthcare sectors

Using the proportion of cases of dengue seen in the private sector relative to the public sector, an estimate could be made from the Pantai Holdings data of the total number of suspected and actual dengue cases in the country. One source estimates that 54% of doctors in Malaysia work in the private sector, and that 20% of healthcare facilities in Malaysia are private⁵⁷. More specific data are provided by the Ministry of Health (Table 6). The majority of hospitals are private (60%), but only 24% of beds, 26% of admissions, and 13% of hospital visits are in the private sector. Comparable data from 2009 (828,399 private admissions and 2,861,443 private outpatient cases) suggests that utilization of, and spending on, private sector healthcare is growing faster than that in the public sector (corresponding figures in 2008 were 754,378 and 2,464,756). It was suggested that further information on dengue treatment in private hospitals might be available through Malaysia's health information system. It compiles numbers of hospitalizations by International Classification of Diseases (ICD) codes. As a condition of license renewal, private hospitals are required to report along with public hospitals. This source might be a further way to break cases down between children and adults. Dr Chong noted that data for an urban/rural breakdown would also be available.

From the Ministry of Health data (Table 6) we might expect 20% of dengue admissions to be in private hospitals, but Dr. Faudzi suggested that since dengue is over-represented in urban areas there may be more private admissions than the general data would suggest. The data in Table 8 could be used to correct for the over-representation of dengue cases in urban areas (note the similarity between the weighted average of 26% of hospital beds being private and the figure given in the 2008 Health Facts³⁸).

Another participant agreed that in general, dengue patients are more likely to seek private healthcare compared to type of healthcare sought for other diseases.

Table 8. Distribution of acute care hospital beds by sector, 2005

ITEM	URBAN	RURAL	TOTAL	URBAN	RURAL	WEIGHTED AVERAGE
	<u>% of beds</u>			<u>No. of beds</u>		
MoH	66%	34%	30,021	19,814	10,207	
Non-MoH	100%	0%	2,916	2,916	0	
All Public			32,937	22,730	10,027	
Private	90%	10%	10,794	9,715	1,079	
All Acute			43,731	32,444	11,287	
% of dengue cases						
Weight	80%	20%				
Private			25%	30%	10%	26%

Source: Source: Ministry of Health, Malaysia

Note:

Data exclude 4740 non-acute MoH beds

The consensus of the participants, implied throughout the workshop, seemed to be that in public hospitals the level of reporting of dengue cases is good. However, there is a general consensus that there are differences in how dengue cases are dealt with in Malaysia between the public and private sectors. For example, Dr. Zainuddin estimated that 45% of total healthcare expenditure in Malaysia was in the public sector, vs. 55% in the private sector, though in the specific case of dengue she guessed that hospitalized cases were more likely to be treated in the public sector compared to ambulatory cases.

When asked about the frequency of laboratory test in case of suspected dengue case, Dr. Chiang stated that it is common in the private sector for a GP to request a test, though she was less sure about the situation in the public sector. She did feel, however, that GPs and hospital doctors were more likely to request tests than were those seeing patients in clinics. It was felt by one participant that in the private sector it was more frequent to request a laboratory confirmation of dengue. Their experience was that in the public sector doctors were more likely to report cases to the Ministry of Health Malaysia based on clinical assessment (the MoH may subsequently decide that a report does not in fact represent an actual dengue case and remove it from the database), whereas in the private sector doctors were more likely to wait for a positive test result to report a case. Dr. Zainuddin noted that there were differences in patterns of treatment based on the age of the patient and regions of Malaysia.

Reaching a consensus on appropriate EFs

All participants were asked to fill in a survey giving their best estimates for the EFs which should be applied to the reported dengue case numbers in order to obtain an accurate estimate of the actual number of cases in Malaysia. Figures were requested for EFs for four groups of case: hospitalized and ambulatory cases in the public sector, and hospitalized and ambulatory cases in the private sector. They were asked to reach this estimate based on the information presented and discussed at the workshop, bearing in mind

which evidence, data, or specific values they felt were more reliable indicators. In addition to a best estimate, participants were asked if possible to provide a minimum and a maximum value which would seem reasonable for a given EF. From these values, mean and median value for the workshop participants' overall opinion on each EF could be calculated. Appendix F shows the values of these EFs, the projected number of cases in each of four categories, and a comparison between the total reported cases in 2009 and the projected cases using an adjusted EF.

In the weeks following the workshop, our initial analysis (Appendix F) showed, not surprisingly, some inconsistencies in the estimates. Considering all the information we gathered during those weeks, we asked participants' input to re-estimate the EFs for the different types of facilities and kind of treatment that the patients receive. This second round of the Delphi process of estimation of EFs allowed us to further refine our estimates of total dengue cases. Specifically, we asked participants to estimate underreporting for both public and private health sectors, and also the share of dengue cases that are ambulatory. Table 9 provides a summary of the workshop participants' new estimates.

Table 9. Participants' final estimates of EFs for hospitalized cases in the public and private sector and the total share of total dengue cases that are ambulatory

PARTICIPANT	EF FOR HOSPITALIZED CASES		% OF AMBULATORY DENGUE CASES
	Public	Private	
A	1.2	2.0	66%
B	1.3	2.8	50%
C	-	-	-
D	2.0	2.0	95%
E	-	-	-
F	1.2	1.4	60%
G	1.0	1.5	70%
H	-	-	-
I	-	-	-
J	1.1	1.3	60%
K	-	5.0	30%
L	1.5	2.0	60%
M	1.1	1.5	60%
N	-	5.0	30%
Median	1.20	2.00	60%
Mean	1.30	2.45	58%
Std. Dev.	0.32	1.41	19%
Minimum	1.0	1.3	30%
Maximum	2.0	5.0	95%

Notes:

* The blank lines mean that these respondents did not submit estimates of EFs.

Table 10 shows the mean estimates of expansion values calculated from the participants' best estimates. These EFs are used to calculate the projected number of cases in each of the four categories in

Table 11. At the bottom of Table 10, adjustment factors have been calculated that would make the distribution of dengue illness between hospitalized and ambulatory modalities consistent with the workshop estimates of 58% to ambulatory cases. Figure 13 shows the comparison between the total reported cases in 2009 and the total projected cases using an adjusted EF (58% share, following the results from the Delphi process). We are assuming that the proportion of public/private hospitalized cases is the same as the proportion of public/private ambulatory cases.

Table 10. Expansion factors for each of the four categories of dengue patients reported in Malaysia, 2009, calculated from the Delphi estimates made by workshop participants

Expansion Factors			
	Hospital cases	Ambulatory cases	Overall*
<i>Mean EF from latest Delphi process/q</i>			
Public	1.30	19.13 [‡]	2.01
Private	2.45	47.50 [‡]	3.29
Both*	1.65	23.79 [‡]	2.39
<i>Adjusted EFs (combining mean factors, using 58% share of ambulatory)</i>			
Public	1.30	43.08 [†]	2.97
Private	2.45	178.84 [†]	5.73
Both*	1.65	65.38 [†]	3.79

Notes:

*The "both" row and overall column are derived by comparing the projected and reported numbers from the table below.

[‡] EF for ambulatory cases correspond to first round of the Delphi process because the question was not repeated in the second round

[†] EF were estimated by comparing the projected and reported numbers from the table below, assuming that the total share of public/private ambulatory cases are the same as public/private hospitalized cases

Figure 13. Comparison between the total reported dengue cases in 2009 and the total projected cases using an adjusted EF (50% share of ambulatory cases)

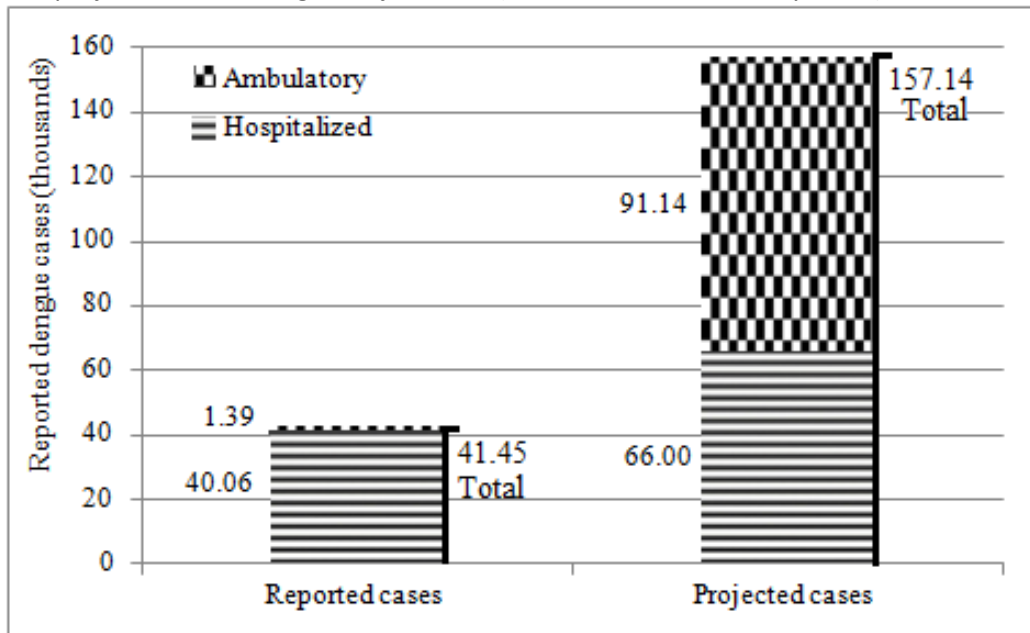


Table 11. Reported number of dengue cases in Malaysia, 2009, in each of four categories, and projected values calculated using the four estimated EFs

	HOSPITAL CASES	AMBULATORY CASES	TOTAL
<i>Reported Cases</i>			
Public	27,955	1,165	29,120
Private	12,105	229	12,334
Total	40,060	1,394	41,454
<i>Projected cases based on mean EFs only</i>			
Public	36,342	22,286	58,628
Private	29,657	10,878	40,535
Total	65,999	33,164	99,163
Row %	66.56%	33.44%	100.00%
<i>Approximate projected total cases considering 58% of total cases as ambulatory</i>			
Public	36,342	50,186	86,527*
Private	29,657	40,955	70,613*
Total	65,999	91,141	157,140
Row %	42.00%	58.00%	100.00%

Notes:

*The total cases of dengue (hospital + ambulatory cases) do not seem exact because of decimal points

During the workshop, Dr. Chong used the statistic that 40-50% of Malaysians are infected by dengue by the age of 50 (depending on whether they're living in an endemic area or not) to try and verify this total number of cases. As Malaysia has had all of the strains of dengue circulating, we assume that each infected

person has had 2 of the possible 4 types of infection. This statistic means that a Malaysian has a 1% chance of being infected with dengue each year. Multiplying this estimate by the population of Malaysia would give a total of 600,000 infections a yearⁱⁱ. Assuming that approximately 25% of infections are symptomatic⁵⁸, there should be an estimated total of approximately 150,000 dengue cases a year. This figure is remarkably close to the adjusted national number of 157,140 cases. Dr. Shepard added that there are four dengue serotypes, and presumably this initial statistic is assuming everyone is infected by at least one serotype of dengue by the age of 50. However, if everyone was infected by two serotypes then the number of cases a year would be doubled, and tripled if three infections was the average.

It is interesting to note that in the previous discussion on the proportion of dengue cases which were seen by a physician and then hospitalized, Dr. Ho estimated that 30% of cases assessed in the primary healthcare sector were admitted to hospital. However, the projected figures predict that 66% of all dengue cases are admitted (~66,000 hospitalized out of ~100,000 total cases, see Table 11). If in fact 30% of cases were hospitalized, and assuming that the hospitalized cases in the public sector are all reported (EF of 1), and that this is the same as 'hospital cases' in the reported cases, then the ~28,000 hospital cases would suggest a corresponding figure of ~65,000 ambulatory cases in the public sector (an EF of ~60).

In the case of the private sector, we can consider the adjusted number of tests for dengue performed in the private sector, corrected for the estimated 20% market share of Pantai Holding, of ~25,000 positive tests. The reported number of dengue cases in the private sector was ~12,000 (Table 11), half the figure which was projected from the data of Pantai Holdings. Even the value of ~25,000 may hide a level of under-representation; tests for serology may return a false negative at a rate of ~50% (according to previous MoH data). We expect that some cases are not tested, particularly those who are adults, so our estimates are consistent.

Correcting for this rate of false negatives would increase the projected number of dengue cases in the private sector to ~50,000 (~25,000 x 2). Assuming that reporting of hospitalized cases is accurate (EF of 1), then the remaining cases of dengue in the private sector, ~38,000 (~50,000 - ~12,000) cases should be ambulatory, giving a very high EF for hospitalized cases of ~166 (EF ambulatory private sector = 38,000/229 = 166). Interestingly this number is very close to our estimate of an expansion factor ~ 179 for ambulatory cases in the private sector we calculated using the best estimates from the second round of the Delphi process (Table 10, column 2, row 5).

There is yet another confounding factor in estimating the number of cases: in the private sector a number of laboratory-confirmed dengue patients are referred to the public sector following a positive result. This may lead to the above estimation of EF being inflated relative to the actual case; although such cases will be reported twice, this ~25,000 still may be an over-expansion. Appendix G contains a summary of the results of the workshop on reaching consensus on the proportion of dengue cases which are hospitalized and the proportion of cases treated in the private sector.

ⁱⁱ This number comes from the following estimation: 30 million people x 50% with one or more infections 2 infections per person infected = 30 million infections over 50 years, 30/50 million or 600,000 infections per year.

Overall cost of dengue in Malaysia

Estimation of public and private sector medical costs

Economic burden of dengue: Introduction

The framework for estimation of the economic burden of dengue infection in Malaysia requires, among others, information on the unit costs of providing inpatient and outpatient medical care both in public as well as private health care facilities. At this time, complete and reliable information on medical costs is not readily available and the purpose of this report is to document discussion and consensus reached at the workshop as to how available cost information could be used in this study. Subsequent to the workshop, further review on available cost information had been done. The results of this review and their proposed application in this dengue economic burden study (hereafter to be referred to as the 'Dengue Study' to avoid confusion) will also be included in this report. As the available information is mostly for public sector costs, this report is focused on costs of service provision in public healthcare facilities.

Costs of service provision in public hospitals

Currently available information on public hospital costs

There has been effort by diverse parties to produce estimates of unit costs for provision of medical care in the public hospitals in Malaysia. Of these, short descriptions and findings of three studies were presented at the workshop.

The Malaysia National Health Accounts (MNHA) unit, a Ministry of Health (MoH) entity, has been producing annual estimates of national health expenditures for the past few years. Thus far, national estimates are available for the years 1997 to 2008⁵⁹⁻⁶¹. In the process, the MNHA has carried out surveys of MoH hospitals to collect information on costs and workload. This information, combined with actual audited hospital expenditures, as provided by the Auditor-General of Malaysia, were used to estimate unit costs of inpatient, outpatient and daycare services in MoH hospitals. The initial survey was conducted in 2002. Subsequent to this, annual surveys were carried out from 2006 to 2008. However, to date the unit has yet to release their unit cost estimates but would make them available to the Dengue Study once they have been finalized. According to the study protocol, the MNHA should be able to provide unit costs for hospitals of differing complexities, from small district- to tertiary-level hospitals.

Dr. Shepard and his colleagues had made some estimates of the unit costs of inpatient and outpatient hospital services in the University of Malaya Medical Centre (UMMC) in 2005 (Table 12). These estimates were used in their eight-country comparative study of dengue costs in Asia and the Americas⁷. Using published information on the operating expenditures and workload of UMMC in 2005, the team estimated the cost per bed day to be RM 636 and the cost per outpatient visit to be RM 127.

These UMMC estimates had been derived using published 2005 hospital operating costs. For the Dengue Study, these estimates were updated using 2009 data (Table 12). The 2009 unit cost estimates also included salaries for academic clinicians not captured in the 2005 study. Academics were paid directly by the

university and information concerning their salaries was not kept by the hospital. Information on academic staffing and their salaries were obtained directly from the university. It was then assumed that 60% of the clinicians' time was spent on patient care in UMMC, the rest being for research and teaching duties. The portion of their salaries included in the 2009 estimate was derived appropriately from their total salaries. Table 12 shows the cost per bed day had increased from RM 636 in 2005 to RM 927 in 2009 and the cost per outpatient visit increased from RM 127 to RM 185.

Table 12. Method of estimation of unit costs at the University of Malaya Medical Centre, 2005 and 2009

ROW	ITEM	SOURCE	UMMC 2005	UMMC 2009
(1)	Admissions	Hosp. Report	41,000	46,977
(2)	Number of registered beds (official)	Hosp. Report	875	983
(3)	Occupancy rate	Hosp. Report	92%	69%
(4)	Occupied beds	(2) x (3)	805	681
(5)	Annual bed days	(4) x 365	293,825	248,645
(6)	Ambulatory clinic visits	Hosp. Report	491,000	776,420
(7)	Emergency visits	Hosp. Report	68,000	103,442
(8)	Total ambulatory visits	(6) + (7)	559,000	879,862
(9)	Rel. cost: visit/inpatient day	Shepard (2000)	0.20	0.20
(10)	Ambulatory bed-day equivalents	(8) x (9)	111,800	175,972
(11)	Total bed day equivalents	(5) + (10)	405,625	424,617
(12)	Operating expenditure, RM	Hosp. Report	258 mil.	393 mil.*
(13)	Cost per bed day equivalent, RM	(12) / (11)	636	927
(14)	Cost per ambulatory visit, RM	(13) x (9)	127	185

Source: Adapted from background tables for Suaya et al.⁷

Notes: * Includes salary of academic clinicians estimated to be RM 27 mil.

As part of the academic requirements towards a Master of Public Health (Health Services Management) degree in the University of Malaya, Sabrina examined the financial performance of six MoH district hospitals⁶². This study also provided estimates of the inpatient and outpatient unit costs for the year 2001. The estimates, inflated to 2009 values, are listed in Table 13. All the selected hospitals in this study were 93 bedded facilities with basic medical and surgical services provided by doctors without specialty qualifications, hospitals which were considered by the MoH as belonging to the category of "district hospitals without specialists."

Table 13. Estimates of unit costs for services in 11 district hospitals in Malaysia, 2009

DISTRICT HOSPITAL	COST PER BED DAY (2009 RM)	COST PER OUTPATIENT VISIT (2009 RM)
Kulai, Johore	459.34	89.39
Port Dickson, Negeri Sembilan	463.70	112.05
Sabak Bernam, Selangor	436.06	210.72
Sungai Siput, Perak	484.68	27.57
Sipitang, Sabah	685.36	115.68
Sik, Kedah	450.09	145.46
Average	496.54	116.81

Source: Sabrina, 2006⁶²

The WHO-CHOICE (World Health Organization – CHOosing Interventions which are Cost-Effective) project was initiated in 1998 to assist countries in making rational choices as to the use of limited health resources based on evidence generated by cost-effectiveness analyses⁶³. As part of the work, researchers collected a large database of unit hospital costs from 49 countries, both from the developed and developing world⁶⁴. Presumably because of the lack of suitable data, Malaysia had not been included in this list. Using econometric modeling, the project predicted the unit hospital costs for countries in which data were not available. The model predicted the cost per bed day using explanatory variables, GDP per capita of the country, hospital occupancy rate, drug and food costs, facility types, hospital ownership (public/private) and whether the hospital was located in the United States of America or not. The facility types, primary, secondary or tertiary-level hospitals, refer to the levels of technical sophistication of the hospitals (Table 14).

The workshop participants deliberated and agreed that the description of tertiary-level hospitals, as provided by WHO-CHOICE, could refer to the state-level, national referral centers or teaching hospitals in the public sector in Malaysia, including UMMC. The Malaysian district hospitals could be categorized as either primary-level or secondary-level hospitals depending on the services provided. In the case of smaller district hospitals without specialists or with few basic specialties, the participants agreed that they should be categorized as primary-level hospitals. These would include the district hospitals in Sabrina’s study⁶². The remaining district hospitals could be considered secondary-level hospitals.

Table 14. Definition of facility types as used in the WHO-CHOICE project

FACILITY TYPE	DESCRIPTION
Primary-level hospital	Has few specialties, mainly internal medicine, obstetrics-gynecology, pediatrics, and general surgery, or only general practice; limited laboratory services are available for general but not for specialized pathological analysis; bed capacity ranges from 30 to 200 beds; often referred to as a district hospital or first-level referral.
Secondary-level hospital	Highly differentiated by function with five to ten clinical specialties; bed capacity ranging from 200-800 beds; often referred to as provincial hospital.
Tertiary-level hospital	Highly specialized staff and technical equipment, e.g., cardiology, ICU and specialized imaging units; clinical services are highly differentiated by function; may have teaching activities; bed capacity ranges from 300 to 1,500 beds; often referred to as central, regional or tertiary-level hospital.

Source: WHO-CHOICE⁶³

The WHO-CHOICE project has made available on-line, predicted estimates for both costs per bed day as well as costs per outpatient visit in Malaysian public hospitals for the year 2005⁶³. These estimates are listed in Table 15. In considering the use of these country-level cost estimates, the workshop participants noted that these estimates included capital costs but excluded costs of provision of drugs, diagnostic tests, and procedures in the hospitals.

Table 15. Predicted estimates of unit costs of public hospitals services for Malaysia, 2005

FACILITY TYPE	COST PER BED DAY (2005 RM)	COST PER OUTPATIENT VISIT (2005 RM)
Primary-level hospital	115.21	40.33
Secondary-level hospital	150.31	57.21
Tertiary-level hospital	205.30	84.63

Source: WHO-CHOICE⁶³

Estimating public hospital costs for the Dengue Study

The 2009 UMMC cost estimates were combined with information from WHO-CHOICE to derive unit cost estimates for the Dengue Study. Table 16 illustrates the estimation process of the average unit cost per bed day. The workshop participants first agreed on the distribution of facility types by their total hospital beds in the country (column A). The number of tertiary-level beds made up 50% of all hospital beds in the country. The corresponding figures for secondary and primary level hospital beds were 30% and 20% respectively.

Using the WHO-CHOICE estimates (column B), the participants derived the ratio of WHO-CHOICE unit cost for secondary and primary-level hospitals to the tertiary-level hospital (column C). The unit cost per bed day in the primary-level hospital was found to be 56% of similar costs in the tertiary-level hospital. These cost-ratios were then applied to the 2009 UMMC unit cost estimates. Thus, the 2009 unit cost for

primary-level hospital amounted to RM 520.21 which was 56% of the UMMC estimates of RM 927.00 (Column D). These figures were then used in combination with the distribution of hospital beds by facility types (Column A) to provide a weighted average of the unit cost per bed-day in a public hospital in Malaysia. In this manner, the cost per bed day was estimated to be RM 771.15 in 2009.

Similar estimation methods were used to derive the average unit cost per outpatient visit in a public hospital as is shown in Table 17. The 2009 cost per public hospital outpatient visit was RM 147.65.

Table 16. Estimation of average unit costs per bed-day in a public hospital, 2009

	(A) Estimated % of total hospital beds	(B) Unit cost per bed- day (2005 RM) <u>WHO-CHOICE</u>	(C) Ratio cost of hospital type/tertiary hospital	(D) Unit cost per bed-day (2009 RM) <u>Shepard et al.</u>
Primary-level Hospital	20%	115.21	0.56	520.21
Secondary-level Hospital	30%	150.31	0.73	678.70
Tertiary-level Hospital	50%	205.30	1.00	927.00
Average cost				771.15

Source: Estimations using data from WHO-CHOICE⁶³ and Suaya et al.⁷

Table 17. Estimation of average unit costs per outpatient visit in a public hospital, 2009

	Estimated % of total hospital beds	Unit cost per outpatient visit (2005 RM) <u>WHO-CHOICE</u>	Ratio cost of hospital type/tertiary hospital	Unit cost per outpatient visit (2009 RM) <u>Shepard et al.</u>
Primary-level Hospital	20%	40.33	0.48	88.76
Secondary-level Hospital	30%	57.21	0.68	125.06
Tertiary-level Hospital	50%	84.63	1.00	185.00
Average cost				147.65

Source: Estimations using data from WHO-CHOICE⁶³ and Suaya et al.⁷

The district hospital costs obtained by Sabrina (2006)⁶² were used to check the accuracy of the public hospital cost estimates. Table 18 and Table 19 show the estimation process which is similar to that used in the workshop but combining WHO-CHOICE costs with district hospital costs as estimated by Sabrina. The new revised unit cost estimates for hospital services of RM 736.06 per bed day and RM 195.60 per outpatient visit. The main difference between this and the earlier estimate is in costs for outpatient visits where using Sabrina's data, the unit cost was about 32% higher than that obtained from UMMC's estimates. The difference between the costs estimates for inpatient services was only 5%.

In summary, it is proposed that the hospital costs derived from the 2009 UMMC estimates be used in this Dengue Study.

Table 18. Revised estimation of average unit costs per bed-day in a public hospital, 2009

	Estimated % of total hospital beds	Unit cost per bed-day (2005 RM)	Ratio cost of hospital type/primary hospital	Unit cost per bed-day (2009 RM)
Primary-level Hospital	20%	115.21	1.00	496.54
Secondary-level Hospital	30%	150.31	1.30	647.82
Tertiary-level Hospital	50%	205.30	1.78	882.82
Average cost				736.06

Source: Estimations using data from WHO-CHOICE⁶³ and Sabrina⁶²

Table 19. Revised estimation of average unit costs per outpatient visit in a public hospital, 2009

	Estimated % of total hospital beds	Unit cost per outpatient visit (2005 RM)	Ratio cost of hospital type/primary hospital	Unit cost per outpatient visit (2009 RM)
Primary-level Hospital	20%	40.33	1.00	116.81
Secondary-level Hospital	30%	57.21	1.42	165.70
Tertiary-level Hospital	50%	84.63	2.10	245.10
Average cost				195.60

Source: Estimations using data from WHO-CHOICE⁶³ and Sabrina⁶²

Costs of service provision in public clinics

Currently available information on public clinic costs

Short descriptions and findings of three studies on MoH clinic costs were presented during the workshop, a study from the Malaysian Ministry of Health, a project by WHO, and an unpublished study by Lim (1995)⁶⁵.

In 2008, a team of researchers from the MoH started a costing study of Putrajaya Clinic in preparation for a future case-mix based reimbursement system for public clinics. The Putrajaya Clinic is one of the few MoH clinics established along the lines of information-technology (IT) intensive 'paperless clinic' concept. Although the cost structure of this clinic may not be reflective of that of other 'typical' public clinics, cost estimates from this clinic may still be informative to the Dengue Study. The final outcome of the Putrajaya study has not been made available yet, but unofficially costs per visit ranging from RM 5 to RM 28 had been quoted.

The WHO-CHOICE project also provided estimates for unit cost for public clinic visits. Unlike hospital costs where available cost estimates were for hospitals of differing complexity, the cost estimates for clinics were provided for areas with differing population coverage and for different periods of clinic contact times. The population coverage here refers to percentage of population in a particular area living within 5 km from a clinic. Table 20 lists the Malaysian cost estimates made available online by the project⁶³. The Second National Health and Morbidity Survey (NHMS II), which was conducted by the MoH in 1996⁶⁶, revealed that

88.5% of the population in Malaysia lived within 5 km of a static health facility. As expected, the coverage was higher in urban compared to rural areas (96.3% vs. 76.9%)⁶⁷. The majority of the static health facilities were in the private sector and information on coverage by the public sector alone was not provided. The workshop participants noted that the estimates provided were for a 20 minute visit, which was rather longer than an average visit to a health clinic in the country.

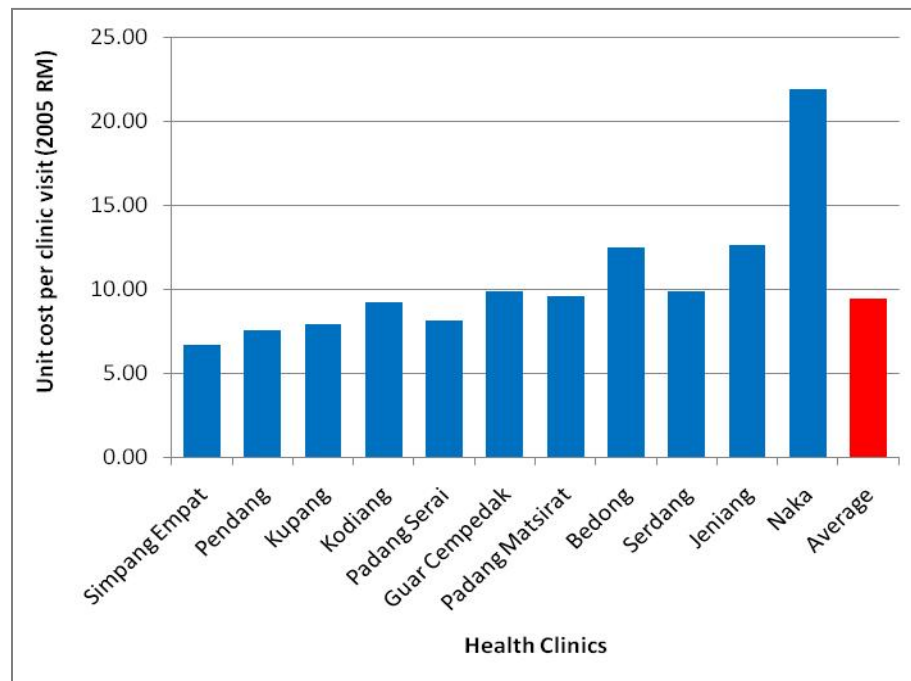
Table 20. Estimates of unit costs per health centre visit for Malaysia, 2005

POPULATION COVERAGE	COST FOR A 20 MINUTE VISIT (2005 RM)
50%	51.72
80%	51.72
90%	55.79

Source: WHO-CHOICE⁶³

The last study presented was an unpublished 1995 cost study on the provision of outpatient services in 11 MoH clinics in Kedah conducted by Lim (1995)⁶⁵. The unit costs were derived mainly from the operating budget of the clinics involved. Figure 14 suggests that on average the unit cost per visit, inflated to 2005 values, was RM 9.42.

Figure 14. Unit cost per clinic visit at 11 public health clinics in Kedah, 1995



Source: Lim (1995)⁶⁵

Estimating public clinic costs for the Dengue Study

The workshop participants discussed and came to the consensus that the average cost per clinic visit provided by Lim (1995) was more reflective of the actual costs of service provision in the MoH clinics.

Participants who had prior experience managing district health care recounted that rough estimates, derived from comparing clinic operating costs and workload, would give an approximate figure of RM 10 per visit.

Costs of service provision in private hospitals

Currently available information on private hospital costs

Estimating the unit costs for the provision of medical care in private hospitals is a significant challenge, given the scarce available data. Dr. Ng used data from the National Health and Morbidity Survey II (NHMS II) conducted by the Institute of Public Health, Ministry of Health Malaysia in 1996⁶⁶ to estimate private hospital costs. The NHMS II survey includes over 13,600 households and about 60,000 individuals. The survey has data on reported inpatient and outpatient out-of-pocket expenditures (OOP) for both public and private facilities. Dr. Ng examined a subset of individuals who reported OOP only for private care, with no recourse for reimbursement or payment from any third party payer (e.g. employer, health insurance, etc.). Assuming that the OOP payment approximates the costs (and profit) at these private hospitals, we can estimate the costs per bed -day in a private hospital in Malaysia, and the unit cost of an outpatient visit (facilities Table).

Table 21. Out of pocket expenditure (OOP) estimates for private health facilities

	N SAMPLE	MEAN	MIN	MAX	MEDIAN
	(2009 RM)				
<i>Hospitalized</i>					
OOP per hospital bed day	323	877	3	5,538	623
<i>Ambulatory</i>					
OOP per hospital outpatient visit	122	948	1	69,221	48
OOP per GP outpatient visit	2313	38	1	4,153	24

Source NHMS II 96⁶⁶

Note: The estimates are based on a subset of individuals who reported payment by OOP only (no third party payer involved e.g. insurer or employer)

Using the mean values to estimate the costs, the data suggests that the estimate of OOP per bed-day in a private hospital (RM 877) is approximately 14% higher than the weighted estimate we obtained for a bed-day in a public hospital (RM 771; Table 16); however it is in the range between bed-day costs for different public hospital types (RM 520 primary level hospital – RM 927 tertiary level hospital; Table 16). One possible interpretation of this difference in costs is that most of the capacity of private hospitals is in urban areas (90%, see Table 8) rather than in rural areas. Unfortunately we do not have detailed information about public hospitals to refine our estimates.

To obtain an estimate of the outpatient value, we took a weighted average between OOP per hospital outpatient visit and OOP per general practitioner (GP) outpatient visit. The values for OOP per outpatient hospital visit is RM 83.6 $((122*948+2,313*38)/(122+2,313))$, which is approximately 43% lower than our estimate for outpatient visits in a public hospital (RM 148; Table 17).

Summary: preliminary estimates of the cost of dengue

Indirect costs

The main source of indirect costs is work-time lost (i.e. productivity loss) due to illness. The indirect costs not only include the patient, but many times they include relatives' time spent in home nursing and also in trips to the hospital of both the patient and her or his relatives⁶⁸. Unfortunately, we do not have ready access to do further calculations, so we will rely on published data. For example, comparing the indirect cost and number of days affected in the Malaysia data in the eight-country study by Suaya et al.⁷, it appears that the average indirect cost per day was about 1.5 times the minimum wage (I\$17.46/I\$11.4; Table 22). Currently a minimum wage of RM700 per month is required only for private security guards⁶⁹. However, recent policy debates in Malaysia suggest that a National Wages Consultative Council may soon be set up to look at all sectors - and a benchmark of RM700 per month has also been mentioned⁷⁰. Assuming that this will happen, we can estimate the indirect costs of each day lost to dengue based on Suaya et al. by adjusting by the change in minimum wage.ⁱⁱⁱ

Table 22. Average indirect cost of dengue per day

	INDIRECT COST (I\$)	TOTAL DAYS AFFECTED*	INDIRECT COST PER DAY (I\$)
Ambulatory	219	11.2	19.55
Hospitalized	249	16.2	15.37
Average indirect cost (I\$)			17.46
Minimum daily wage (I\$)			11.40
Average indirect cost/minimum wage			1.5

Source: Suaya et al.⁷

Notes:

I\$ = international dollars.

* Total days affected include both the patient and the household impact (see Table 23 for details).

We also need to estimate how many work-days are lost to dengue. Analyzing patients from the University of Malaya Medical Center (UMMC), Suaya et al.⁷ estimated the total number of days lost to dengue fever in Malaysia (Table 23).

ⁱⁱⁱ To estimate the total indirect costs, we then do the following multiplication:

Indirect costs 2011 [RM] = Indirect costs in Suaya et al [I\$]*(Minimum daily wage 2011[RM]/minimum daily wage Suaya et al.[I\$])

Table 23. Impact per dengue cases in days lost (ambulatory and hospitalized)

	AMBULATORY CASES		HOSPITALIZED CASES	
	Mean	Stand. Dev.	Mean	Stand. Dev.
<i>Patient impact</i>				
If studying, days lost	3.2	2.3	4.1	2.1
If working, days lost	7.2	2.6	8.8	2.7
<i>Household impact</i>				
School days lost	1.0	2.0	2.2	2.6
Work days lost	6.0	4.2	6.7	5.1
<i>Total days affected</i>	<i>11.2</i>	<i>4.2</i>	<i>16.2</i>	<i>6.7</i>
Borne by patient (%)	78%		75%	

Source: Suaya et al.⁷

To include economic costs associated with deaths, we used the human capital approach based on productivity lost⁷¹, and estimated the years of premature life lost based on life expectancy using WHO life tables for Malaysia⁷². We used the age distribution of the 92 reported deaths related to dengue in the year 2009 (Ministry of Health, unpublished data, 2010). We assumed that the overall underreporting of dengue-related deaths is equal to the underreporting of hospitalized cases from the public and private sectors, and that the deaths in the public and private sectors are proportional to their shares of dengue cases. To be conservative, we assumed that all workers earn minimum wage and that students stay in school until they are 17 years old. We calculated the costs of school days lost using Suaya et al.'s estimates (2009 US\$5.05/day)⁷, and adjusted for time preferences using an annual discount rate of 3%.

To estimate the total costs per dengue case we have to make several assumptions. First, we need to assume that the duration of dengue cases from the UMMC data⁷ is on average representative of the national data (as regional breakdowns were not available, and dengue is primarily urban). The second assumption is that the impact on patients and households of dengue cases is the same as estimated from UMMC data. This assumption seems plausible, since in the proportion of dengue cases between adults and children were estimated at 2.3 in UMMC. Using the incidence of dengue fever and dengue hemorrhagic fever data between 2003 and 2005²², we estimated a proportion of 1.93 dengue cases between adults and children.^{iv} Third, we assume that all dengue cases affect productive individuals that are either working at a minimum wage if they are adults or attending school if they are children. Fourth, to update the indirect daily costs of dengue for both hospitalized and ambulatory cases from Suaya et al.'s study⁷, we are assuming that the proportion between the minimum wage and the indirect costs in both settings is on average constant. Fifth, we assume that our estimate cost for treatment at private facilities is accurate. We are assuming that

^{iv} To estimate the indirect costs associated to dengue, we multiply the total number of days lost to dengue by the indirect cost per day (separately for ambulatory and hospitalized patients). We are assuming that the total duration of dengue in Suaya et al. considers implicitly the proportion of adults and children (i.e. days lost to work and school, and the days of work loss when children get sick). We also assume that the average potential number of potential work days in a month remains unchanged from the analysis by Suaya et al, i.e. 21.67 days in a month (21.67=5*52/12).

the indirect daily costs of dengue cases are the same for the private and public sectors. This is a conservative assumption, since we would expect wealthier people to get treatment predominantly at private facilities, which would raise the average indirect costs of this setting. We do not have data to test this hypothesis and make a more accurate estimate. Using the total days affected from Table 23, we estimate the total costs per dengue case in Table 24. Finally, we are assuming that the impact of dengue illness on total days lost is due to the average duration of a dengue case. However, we are not including any costs associated with long-term consequences of dengue, possible chronic sequelae of dengue illness called post-infectious fatigue syndrome⁷³⁻⁷⁵.

Table 24. Summary of total costs per non-fatal dengue case [RM]

	AMBULATORY COSTS [RM]			HOSPITALIZED COSTS [RM]		
	INDIRECT	DIRECT	TOTAL AMB.	INDIRECT	DIRECT	TOTAL HOSP.
<i>Public Sector</i>	620.5	1,048.3	1,668.8	705.7	2,159.2	2,864.9
<i>Private Sector</i>	620.5	593.5	1,214.0	705.7	2,455.6	3,161.3

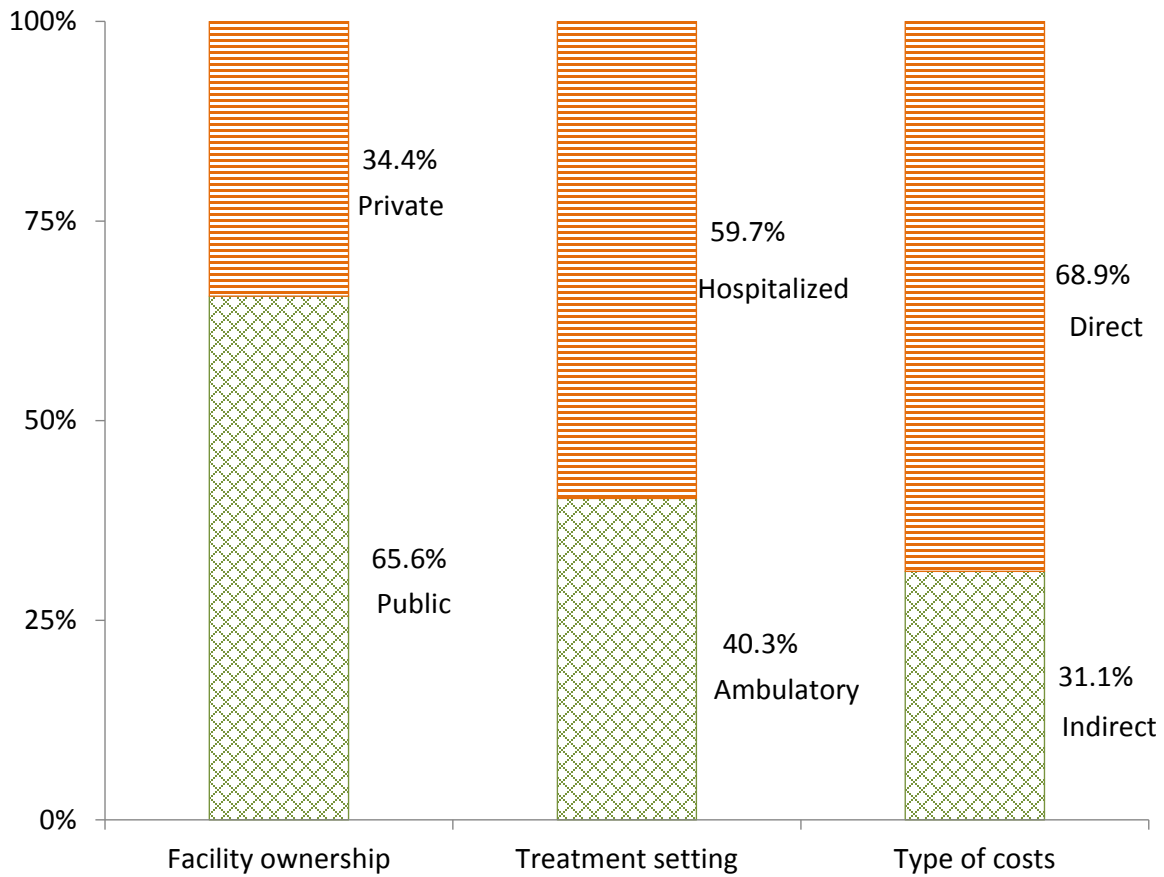
Total costs

Table 25 shows the summary of the estimated total costs of ambulatory and hospitalized dengue cases in the public and private sectors using the number of reported cases and the projected cases based on the adjusted factors (58% share; see Table 11). Figure 15 shows the proportions of dengue costs by type of facility, type of treatment, and type of cost.

Table 25. Summary of estimated total costs [RM 1000s]

	AMBULATORY			HOSPITALIZED			DEATHS	GRAND TOTAL
	INDIRECT	DIRECT	TOTAL AMB.	INDIRECT	DIRECT	TOTAL HOSP.	INDIRECT	
<i>Based on reported cases</i>								
Public	722.9	1,221.3	1,944.2	19,726.5	60,361.0	80,087.5	12,049	94,080
Private	142.1	135.9	278.0	8,541.9	29,725.0	38,266.9	5,217	43,762
Total	865.0	1,357.2	2,222.2	28,268.4	90,086.0	118,354.4	17,266	137,843
<i>Based on projected cases based on mean expansion factors (58% share of ambulatory cases)</i>								
Public	31,142.1	52,610.6	83,753	25,644.4	78,469.3	104,114	15,663	203,530
Private	25,414.1	24,307.5	49,722	20,927.7	72,826.3	93,754	12,782	156,258
Total	56,556.2	76,918.1	133,474.3	46,572.1	151,295.6	197,867.7	28,445	359,787

Figure 15. Proportions of dengue costs by facility, treatment setting, and type of cost based on adjusted factor (58% share of ambulatory cases)



Malaysia has a population of approximately 27.5 MM people, organized in 13 states and three federal territories. There is a considerable variation in size and population between these regions, ranging from the federal territory of Putrajaya with approximately 68,000 persons to the federal state of Selangor with almost 5.5 million.⁴⁵ The biggest urban area is the metropolitan area of Kuala Lumpur.

Table 26 shows demographic data by region and the reported dengue cases in 2009. Using this data, we can estimate a proportion of the total costs of dengue fever between Kuala Lumpur and the rest of the country, assuming that the costs are proportional to the number of dengue cases (Table 27).

Table 26. Dengue cases in 2009 by geographical region

REGION	AREA (Km ²)	POPULATION* (1,000)	POPULATION DENSITY (per km ²)	REPORTED DENGUE (2009)
Johor	19,210	3,459.4	180	2,528
Kedah	9,500	2,044.2	215	748
Kelantan	15,099	1,678.0	111	1,031
Melaka	1,664	786.2	472	769
Negeri Sembilan	6,686	1,033.0	155	1,056
Pahang	36,137	1,574.3	44	906
Perak	21,035	2,440.9	116	2,732
Perlis	821	245.6	299	191
Pulau Pinang	1,048	1,609.9	1,536	2,444
Sabah	73,631	3,271.9	44	1,170
Sarawak	124,450	2,557.1	21	4,490
Selangor**	8,108	5,287.9	652	18,650
Terengganu	13,035	1,148.5	88	968
Kuala Lumpur	243	1,681.6	6,920	3,746
Labuan	91	90.3	992	25
Putrajaya	46	-	-	0
TOTAL	330,804	28,908.8	87	41,454

Source: Department of Statistics, Malaysia⁴⁵; Costumed Dataset^v

Notes:

* Population projections 2010 by state

**Includes W.P. Putrajaya (population approx. 68.0; population density 1,478)

Table 27. Estimated costs of dengue by region (RM 1000)^{vi}

	AMBULATORY	HOSPITALIZED	DEATHS	GRAND TOTAL
<i>Estimated costs from reported cases</i>				
Kuala Lumpur	200.8	10,695.1	1,560.2	12,456.2
Malaysia	2,021.4	107,659.3	15,705.6	125,386.3
Total	2,222.2	118,354.4	17,265.9	137,842.5
<i>Estimated costs from projected cases based on mean expansion factors (58% share amb.)</i>				
Kuala Lumpur	12,061.4	17,880.4	2,570.5	32,512.3
Malaysia	121,412.9	179,987.4	25,875.0	327,275.2
Total	133,474.3	197,867.7	28,445.5	359,787.5

^v The dataset was given to Brandeis University by Sanofi-Pasteur as background for the workshop.

^{vi} The Ministry's dataset comes with data by region. If we included the whole metropolitan area of Kuala Lumpur, its proportion of costs would be much higher than what the table shows.

Sensitivity analysis of the cost estimates

We did a probabilistic analysis of the total costs of dengue illness in the sensitivity analysis, using RiskAMP, version 3.20⁷⁶. The probabilistic sensitivity analysis of total costs includes the simultaneous variation of five categories of parameters: (1) the expansion factors of hospitalized cases of dengue assuming a triangular distribution based on the results from the Delphi process (public sector EF, minimum: 1.0, likeliest:1.30; maximum:2.0; private sector EF, minimum: 1.3, likeliest:2.45, maximum:5.0); (2) the proportion of dengue cases treated that are ambulatory (versus hospitalized patients) assuming a triangular distribution based on the Delphi process with the minimum, likeliest, and maximum values set to the minimum, mean and maximum values from that process; (3) the cost of dengue in public hospitals using a combination of the estimates by the district hospitals study, UMMC 2009, and WHO-CHOICE, assuming a triangular distribution (hospitalized patients, minimum:736.07, likeliest:759.46, maximum:771.15; ambulatory patients, minimum:147.64, likeliest:163.62, maximum:195.60); (4) the total number of days lost due to dengue illness (indirect costs) per case assuming a normal distribution (ambulatory patients, mean:11.2, standard error:0.41; hospitalized patients, mean: 16.2, standard error:0.59);7 and (5) the total number of deaths due to dengue infection assuming a Poisson distribution (mean: 92 deaths). We computed 20,000 Monte Carlo simulations for each parameter. Iterations drew random values from the distribution of each input. We present results as 95% confidence intervals.

Because the estimates of direct costs derived from UMMC and the six district hospital study were similar, their contribution to the total variation of costs was only marginal. To illustrate, if we estimate public sector unit costs data from the six district hospitals instead of UMMC 2009 data, we find that the total annual economic burden of dengue illness in Malaysia is US\$106.09 million (m) (RM373.30), only a 3.8% increase from our original value. Varying all these parameters simultaneously, the estimated 95% certainty levels for the total economic burden of dengue were [RM 274.25m - RM 1,093.09m], for the total costs of hospitalized cases [RM 155.51.10m - RM 311.73m], for ambulatory cases of dengue [RM 60.35m - RM 822.09m], and finally, for the total long-term incremental costs of death [RM 22.69m - RM 34.32m]. The Monte Carlo simulations resulted in moderately wide certainty levels for the total cost estimates, due to the simultaneous variation of the parameters. While the mean values of costs we report here are based on our best informed assumptions and a variety of data sources, the size of the 95% certainty levels illustrate the uncertainty of estimates of economic burden when using incomplete data. The inter-quartile range for the total costs of dengue is [RM 363.18m; RM 546.63m].

Limitations of the cost estimates

Our estimates of the economic burden of dengue infection in Malaysia have been carefully calculated; however, they have several limitations and we have made a number of assumptions. In an ideal world, to estimate the real costs of dengue we would need information on the unit costs of inpatient and outpatient medical care in both private and public facilities, and in rural and urban areas. The Malaysia National Health Accounts (MNHA) unit has not yet provided unit cost estimates on the costs of health care, but we have reached some consensus on how to use the available information.

Dr. Shepard and several colleagues estimated the unit costs of inpatient and outpatient services at UMMC in 2005⁷. Even though UMMC costs are not necessarily representative of all health care facilities in Malaysia, we combined those estimates with information from WHO-CHOice to derive unit cost estimates based on the facility type. Even if there was agreement among the workshop participants, we believe this estimates could be further refined by distinguishing not only by facility type (based on the number of beds), but also by region, GDP, population, number of specialist physicians, healthcare coverage, etc. The costs for public clinics were estimated from the Putrajaya study, which is probably not very representative of the quality of health care provided elsewhere. Estimates in the study are based on 20 minute-visits, which is probably somehow above average for the country.

Estimating unit costs for the private sector proved to be challenging as well. Dr. Ng suggested that we use the data collected from the National Health and Morbidity Survey II (NHMS II) conducted by the Institute of Public Health, Ministry of Health Malaysia, in 1996⁶⁶. Using a selected sample to estimate out-of-pocket expenditures we derived an estimation of private care costs for those who did not receive any reimbursement of payment from third parties.

To estimate the indirect costs of dengue (mainly associated with work time lost), we rely on previous work done by Dr. Shepard and colleagues⁷. In estimating indirect costs, we make several assumptions (already discussed in the previous section). The most relevant are the assumptions that (i) UMMC data is representative of national health care; (ii) that all individuals affected by dengue are either working or attending school; (iii) that the proportion between minimum wage and health care costs is constant on average; and finally (iv) we assume that the indirect costs associated to dengue are the same between people who get treatment in either private or public facilities.

Finally, the total number of dengue cases remains an area of uncertainty. The section on EFs earlier in this report discussed these factors, but they remain a topic of uncertainty.

Estimating the costs of dengue vector control activities: study design^{vii}

Objectives of a study of vector control

Dr Raviwharmman designed a study to evaluate dengue vector control activities in Peninsular and Eastern Malaysia. Through this study, the author hopes to generate data for better policy development and improved operational management of dengue vector control activities in Malaysia. The project aims to

^{vii} Presented by Dr P. Raviwharmman, University of Malaya

determine the burden of vector control on the country, and not any measure of spending per case, and so per activity costs will be divided by the regional or national population to give a per capita spending. Dr Raviwharmman aims to submit results for publication, and as a thesis, by June 2012 (Figure 16).

Figure 16. Gantt chart plotting the projected progress of the study

	Project proposal	Submission	Approval	Data collection	Data analysis	Prep journal paper	Follow-up research	Write / edit thesis	Feedback / review	Submission
Jul-10	█									
Aug-10	█									
Sep-10	█									
Oct-10	█									
Nov-10		█								
Dec-10			█							
Jan-11				█						
Jun-11				█	█					
Jul-11				█	█					
Oct-11				█	█					
Nov-11				█	█	█	█			
Dec-11				█	█	█	█			
Jan-12								█		
Feb-12								█	█	
Mar-12								█	█	
Apr-12									█	
May-12									█	
Jun-12										█

Methodology

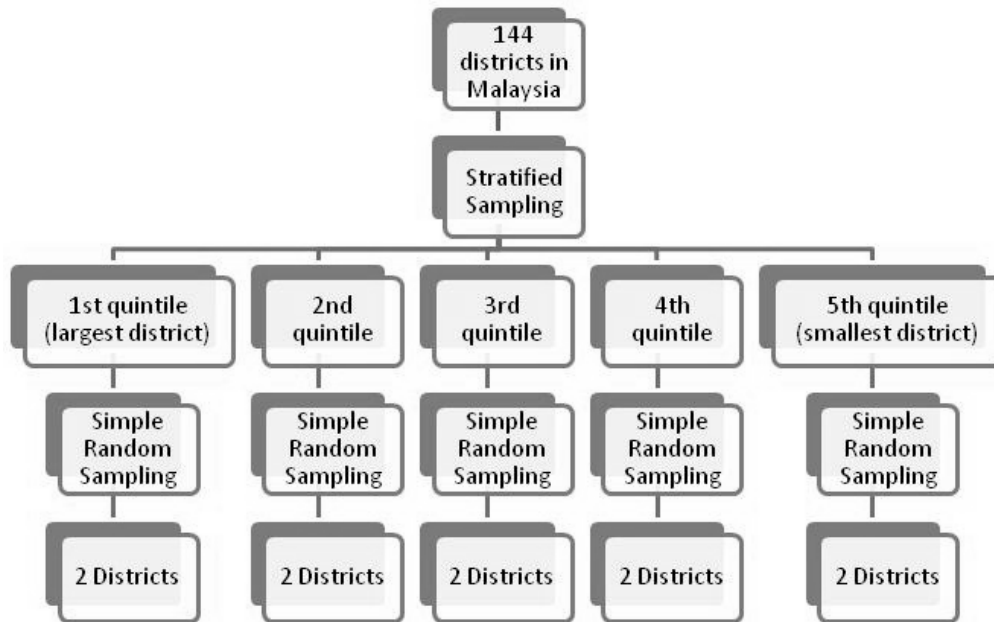
Sampling

The Malaysian Ministry of Health (MoH) and local councils both have vector control units, and so both must be sampled to ensure a clear and complete picture of vector control in Malaysia is obtained. There are vector control activities conducted by the MoH at the National level, at the State level, of which five out of 13 states will be included as a sample, and at the District level. There are 144 districts in Peninsular and Eastern Malaysia, which will be divided into five equal groups according to population size (quintiles); two districts will be randomly selected out of each quintile for inclusion in the study (Figure 17).

Through this multi-stage sampling procedure the study is designed to be comprehensive and inclusive, giving a fair representation of MoH vector control units from a range of districts. When considering how to sample Local Councils it is not so clearly organized. Currently there are a total of 151

local authorities in Malaysia: One City Hall - City Hall of Kuala Lumpur; 11 City Councils; 36 Municipal Councils; 96 District Councils; and seven modified local authorities. Usually it is only the larger Local Councils which perform vector control activities (city hall, city councils, municipal councils), but it should be possible to find out which ones involve in dengue vector control activities through a telephone survey. It is estimated that ten Local Councils will be sampled, based on a stratified sampling method.

Figure 17. Sampling Strategy for Malaysian Ministry of Health Districts



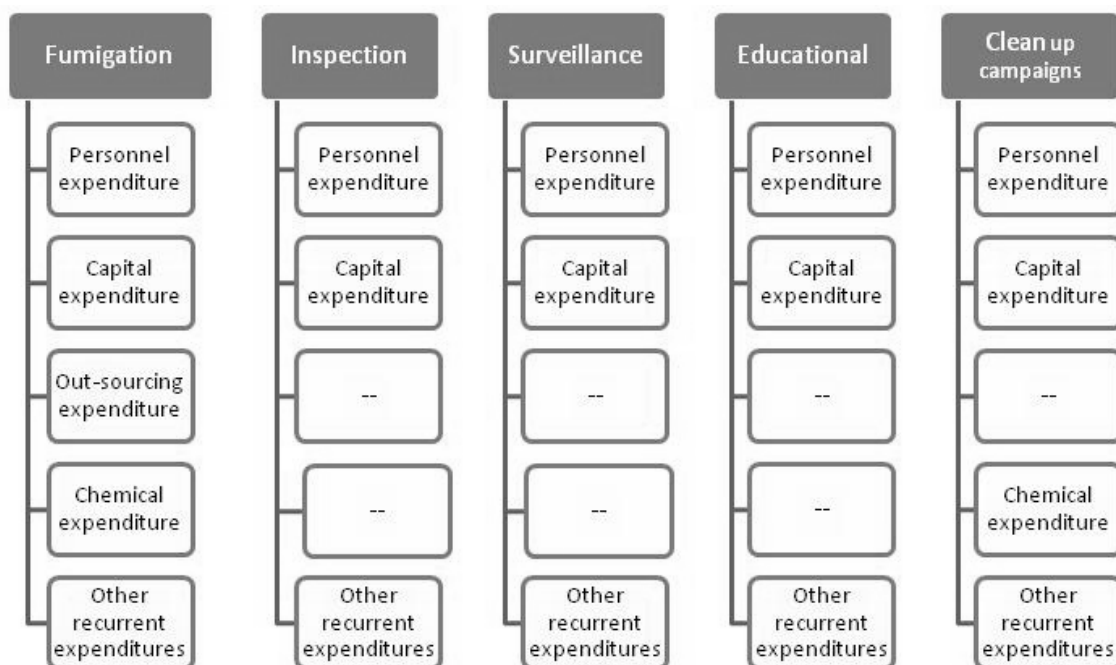
Study design

Dr Raviwharman’s study will employ a mixed-model approach consisting of three phases: Quantitative analysis, Economic analysis, and Qualitative analysis. The Quantitative analysis will consist of secondary data analysis: Descriptive data of dengue vector control activities for 2009, structured questionnaires, on-site interviews and telephone follow-ups. Descriptive analysis of data will be conducted using SPSS software. The Qualitative section of the study will consist of face to face interviews with Key Informants, and with senior vector control officers (with at least 5 years of experience). The interviewees will be chosen equally from Local Authority (municipal council) and MoH Vector Control Unit (federal, state, district). The analysis of this data will rely on subjective judgment based on non-quantifiable information, such as management expertise, strength of research and development and labor relations, and will employ nVIVO software.

The most complex and probably time-consuming section of the study will be the Economic analysis, which will consist of micro-costing of dengue vector control activities in Local Councils and Ministry of Health units, using costing data for 2009. A comparison can be made between municipal council expenditures and MoH expenditures. Line item analysis will be conducted; costs, or input indicators, to be considered include personnel, capital expenditure, consumables (chemicals) and the costs of outsourcing,

along with other recurrent expenditure. Analysis of these costs will be based on the vector control functions achieved, i.e. the costs involved with fumigation, inspection, surveillance, education of the public and clean up campaigns (Figure 18). Output and outcome indicators will be chosen which should be attributable to the activities of which the costs are being measured. Examples of output indicators might include the number of households or area sprayed number of premises inspected, number of premises fined or amount of fines (RM). Outcome indicators will include measures of mosquito population (the house index, container index, pupal index or and Breteau index) and the incidence of dengue cases. In order to collect data for the Economic analysis, structured questionnaires and on-site interviews will be conducted, as well as telephone follow-up where required.

Figure 18. Vector control functions and associated costs to be considered for the Economic analysis



Burden of dengue in DALYs ^{viii}

Introduction to DALY calculations

A DALY, or Disability-adjusted Life Year, is a unit used to describe the impact of a disease or injury not just in terms of a shortened lifespan (life lost) but also considering the impact on health, quantifying the resulting time spent with a reduced level of health. According to the WHO methodology used to calculate the 'Global Burden of Disease'⁷⁷, one DALY represents one year lost of healthy life, and is calculated from the years of life lost (YLL) and years of life lived with disability (YLD). In turn, YLL is calculated by multiplying mean life expectancy, and number of deaths caused, both of which are age- and sex-specific. YLD is

^{viii} Presented by Dr. Faudzi Yusoff Isa, Unit of Epidemiology & Biostatistics, Medical Research Resource Centre, Institute for Medical Research

calculated by multiplying the number of cases, incidence, by average duration of disability (in years) and a 'disability weight', which measures the loss of healthy life using an average health state weight.

Major causes of mortality and morbidity in Malaysia

In 2005 the life expectancy in Malaysia was 71 years for men and 74 years for women, and the top three causes of death for males were ischaemic heart disease, road traffic injuries and stroke, and in women the top three killers were ischaemic heart disease, stroke and septicaemia, in order (Data not shown)⁷⁸. Dengue did not appear in the list of top ten causes of death for either sex, and the only infectious diseases to appear on the list were respiratory infections. Considering the burden of infectious disease, the 2008 data from the notifiable disease database listing the top ten causes of YLL places dengue as the seventh biggest cause of reduced survival (Table 28). As discussed earlier in this report, the notifiable disease database is based on reported cases, whereas the actual number is higher—perhaps several fold higher. This adjustment has not yet been factored into this analysis. As a result, these disease burden estimates to date probably underestimate the true burden of dengue.

When causes of YLL are further categorized by sex, dengue is seen to be the seventh biggest cause of lost life years in males, causing 1.7% of all YLL lost to men, but in women dengue is more significant, ranking fifth and causing 2.2% of all YLLs. If instead of considering years lost (YLL) we look at years lived with disability (YLD) caused by disease in Malaysia, the 2008 data (Table 29) shows chronic infections, unsurprisingly, to be the major causes of disability, and dengue is not among the top ten.

Table 28. Top ten communicable diseases causing YLL Burdens, Malaysian Population, 2008 (total, and subdivided by sex).

RANK	MALE			FEMALE			TOTAL		
	DISEASE CATEGORIES	YLL	%	DISEASE CATEGORIES	YLL	%	DISEASE CATEGORIES	YLL	%
1	Septicaemia	108,488	45.1	Septicaemia	92,809	54.5	Septicaemia	201,298	49.0
2	Lower respiratory infections	71,217	29.6	Lower respiratory infections	53,822	31.6	Lower respiratory infections	125,039	30.4
3	Tuberculosis	25,956	10.8	Tuberculosis	7,973	4.7	Tuberculosis	33,929	8.3
4	HIV/AIDS	10,933	4.5	Meningitis	5,241	3.1	Meningitis	12,742	3.1
5	Meningitis	7,501	3.1	Dengue	3,829	2.2	HIV/AIDS	11,987	2.9
6	Hepatitis B	4,800	2	Other Diarrhoeal diseases	3,668	2.2	Other Diarrhoeal diseases	8,293	2.0
7	Other Diarrhoeal diseases	4,625	1.9	Hepatitis B	1,118	0.7	Dengue	7,974	1.9
8	Dengue	4,145	1.7	HIV/AIDS	1,054	0.6	Hepatitis B	5,917	1.4
9	Malaria	965	0.4	Varicella (chickenpox)	248	0.1	Malaria	1,199	0.3
10	Varicella (chickenpox)	733	0.3	Malaria	234	0.1	Varicella (chickenpox)	980	0.2
	Total (23 diseases)	240,443	100	Total (23 diseases)	170,280	100	Total (23 diseases)	410,723	100

Source: Ministry of Health Malaysia⁷⁸

Table 29. Top ten communicable diseases causing YLD Burdens, Malaysia, 2008 (total, and subdivided by sex).

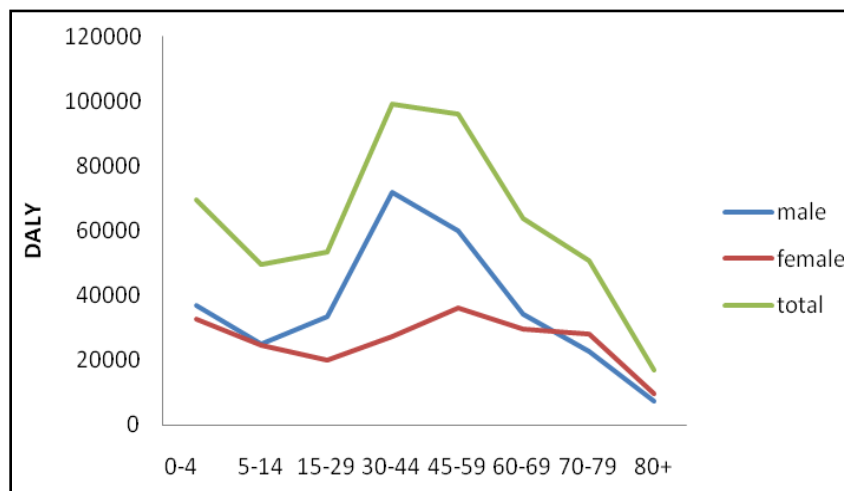
RANK	MALE			FEMALE			TOTAL		
	DISEASE CATEGORIES	YLD	%	DISEASE CATEGORIES	YLD	%	DISEASE CATEGORIES	YLD	%
1	Otitis media	20,885	40	Otitis media	19,822	52	Otitis media	40,707	45
2	HIV/AIDS	9,277	18	Lower respiratory infections	5,220	14	Tuberculosis	12,829	14
3	Tuberculosis	8,601	17	Tuberculosis	4,228	11	HIV/AIDS	11,255	12
4	Lower respiratory infections	5,846	11	Hepatitis B	2,624	7	Lower respiratory infections	11,066	12
5	Hepatitis B	2,759	5	HIV/AIDS	1,978	5	Hepatitis B	5,383	6
6	Meningitis	1,722	3	Upper respiratory infections	1,377	4	Meningitis	3,040	3
7	Upper respiratory infections	1,355	3	Meningitis	1,318	3	Upper respiratory infections	2,732	3
8	Syphilis	406	1	Chlamydia	399	1	Syphilis	765	1
9	Septicaemia	298	1	Food Poisoning	394	1	Food Poisoning	692	1
10	Food Poisoning	297	1	Syphilis	359	1	Chlamydia	688	1
	Total (23 diseases)	51,977	100	Total (23 diseases)	38,108	100	Total (23 diseases)	90,085	100

Source: Ministry of Health Malaysia⁷⁸

DALY calculations for Malaysia

Using the above YLL and YLD data and the WHO equation ($DALY = YLL + YLD$) it is possible to calculate the top causes of DALY burden on Malaysia, and in this case dengue is ranked ninth (Table 30), causing a similar level of burden as diarrheal diseases and only marginally less of a burden than Hepatitis B. When these figures are broken down by sex and age (Figure 19) it is clear that overall the DALY burden is greatest on males, and on adults aged 30-60 years, although dengue affects females more than males (Table 30), and is known to be a more significant disease in the lowest age groups. Already included in the data from the notifiable disease database (Table 28 and Table 29) is some correction for under-reporting of disease. But if the DALY calculations were adjusted for under-reporting on a scale predicted by this report, then it seems likely that dengue would be promoted into the top three causes of DALY burden in Malaysia.

Figure 19. DALY by sex and age group, Malaysia, 2008



Source: Estimated by Dr. Faudzi Yusoff from MoH Malaysia database⁷⁸

Table 30. Top twelve communicable diseases causing a DALY Burden, Malaysia, 2008 (total, and subdivided by sex).

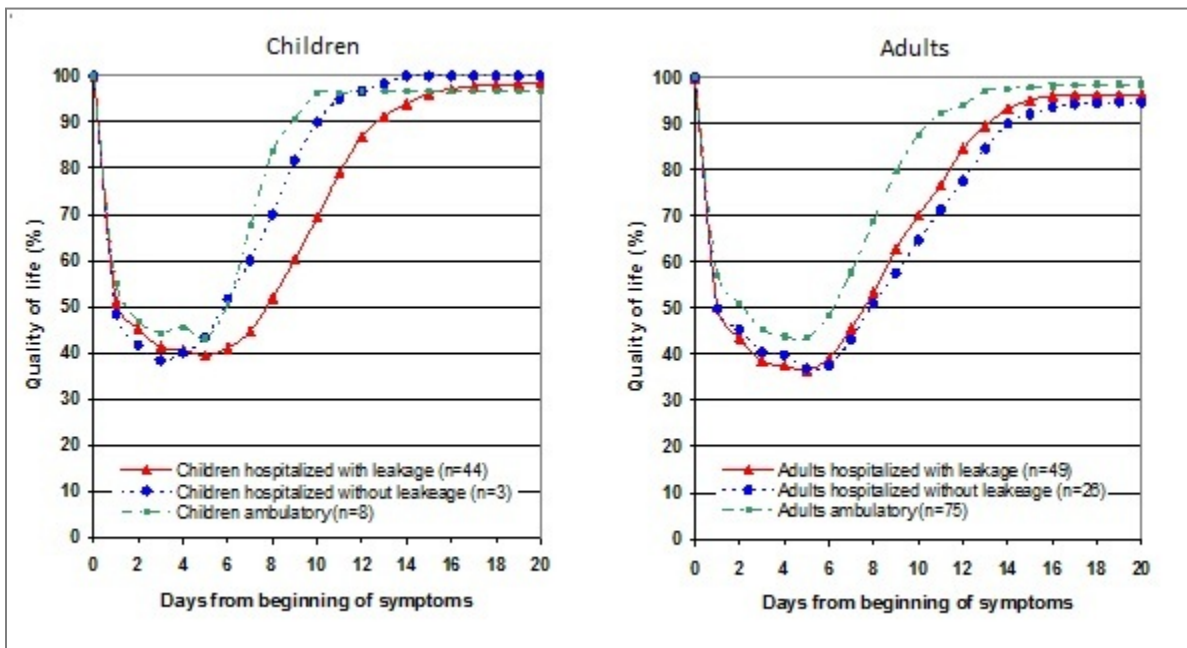
RANK	MALE			FEMALE			TOTAL		
	DISEASE CATEGORIES	DALY	%	DISEASE CATEGORIES	DALY	%	DISEASE CATEGORY	DALY	%
1	Septicaemia	108,787	37.2	Septicaemia	93,062	45	Septicaemia	201,849	40.3
2	Lower respiratory infections	77,064	26.35	Lower respiratory infections	59,041	28	Lower respiratory infections	136,105	27.2
3	Tuberculosis	34,557	11.82	Otitis media	19,822	10	Tuberculosis	46,758	9.3
4	Otitis media	21,042	7.2	Tuberculosis	12,201	6	Otitis media	40,864	8.2
5	HIV/AIDS	20,209	6.91	Meningitis	6,559	3	HIV/AIDS	23,242	4.6
6	Meningitis	9,223	3.15	Dengue	3,892	2	Meningitis	15,783	3.2
7	Hepatitis B	7,558	2.58	Hepatitis B	3,742	2	Hepatitis B	11,300	2.3
8	Other Diarrhoeal diseases	4,635	1.58	Other Diarrhoeal diseases	3,676	2	Other Diarrhoeal diseases	8,310	1.7
9	Dengue	4,251	1.45	HIV/AIDS	3,032	1	Dengue	8,144	1.6
10	Upper respiratory infections	1,746	0.6	Upper respiratory infections	1,377	1	Upper respiratory infections	3,123	0.6
11	Malaria	974	0.33	Chlamydia	399	0	Malaria	1,213	0.2
12	Varicella (chickenpox)	756	0.26	Food Poisoning	394	0	Varicella (chickenpox)	1,022	0.2
Total (23 diseases)		292,420	100	Total (23 diseases)	208,389	100	Total (23 diseases)	500,809	100

Source: Ministry of Health Malaysia⁷⁸

Dengue infection and Quality of Life

Dengue appeared in the top ten YLL causing diseases in Malaysia (Table 28), and in the top twelve DALY causing diseases in Malaysia (Table 30) in 2008, and yet it was not listed among the top ten YLD causing diseases (Table 29). This suggests that although dengue is a substantial cause of reduced life expectancy in Malaysia, it is not a serious disease in terms of the disability caused in those who are infected. There is, however, evidence that dengue does cause a significant reduction in quality of life in patients during the course of their infection²¹. The data on quality of life by day (Figure 20) gives quantitative evidence of the reduction in quality of life, which is comparable to disability caused as considered in Table 29, albeit on a personal and not population scale and over a short time frame. By calculating the area above the graph as a proportion of the total graph area it is possible to quantify the average quality of life lost to a dengue patient. For example, a 30% reduction in quality of life, which seems to be the burden on a child suffering with plasma leakage, over 20 days of acute disease equates to the equivalent of 6 days of healthy life lost. This can be scaled up to consider the cost to the Malaysian population as a whole: multiplying 6 days by the reported number of dengue cases in Malaysia in a year (for example 41,454 cases in 2009) gives a total of 248,724 days, or 681 years, of healthy life lost, which would make it comparable to the diseases listed in the top ten causes of YLD causing diseases in Dr. Faudzi's study (Table 30). Indeed, it is surprising that dengue does not appear on this list, when food poisoning and URTIs, also acute diseases, do. This is likely due to an under-reporting of the quality of life cost of dengue infections, which is probably the case, given the under-reporting of dengue cases at all, especially ambulatory cases.

Figure 20. Quality of life measured daily in children (1a) and adults (1b) suffering from dengue



Source: Lum et al. 2008²¹

Discussion

Our findings suggest that there is substantial underreporting of symptomatic dengue fever in Malaysia, and that the economic burden of dengue fever in Malaysia is considerable. Combining multiple sources of data is critical in order to achieve reliable estimates of the total cases and economic burden of dengue fever. The EFs we used to adjust for underreporting were estimated based on several data sources including existing literature, expert knowledge, and laboratory evidence. The Delphi process led to an overall EF of 3.79, adjusted using the mean value of 58% share of ambulatory cases. This EF is well in the range of previously published studies from Southeast Asia (EF: 3.1 to 9.1), and lower than the average from these studies (7.8 times as many cases of dengue as those officially reported)⁷⁹. On balance, however, our estimates are probably conservative, understating the overall burden of dengue in Malaysia, for several reasons.

First, a thorough study of EFs in Thailand and Cambodia with EFs of 8.7 and 9.1, respectively⁸⁰, was not available at the time of the workshop. If that study been available, the EF estimates from the Delphi process might have been somewhat higher.

Second, our estimates include only the acute phase of dengue illness. Recent evidence indicates that dengue causes a substantial reduction in quality of life (QoL) in patients during the course of their infection. A previous study in Malaysia found that the reduction in QoL for dengue patients lasted longer than the duration of the fever²¹. For some patients, symptoms are more persistent but we do not know for how long these symptoms may last, and how they affect a patients' QoL. Dengue Chronic Fatigue (DCF) refers to the long-term consequences of dengue fever⁷⁴, but only a few published studies have examined this phenomenon. A study of adults in Cuba suggests that 57% of the symptomatic dengue patients reported having persistent symptoms for 2 years following their infection⁸¹. Other studies suggest that 25% of discharged patients had symptoms after two months (Singapore)⁷⁴, 47% of patients had symptoms after 6 months (Cuba)⁸², and finally, 8.5% of patients reported having difficulty in their daily activities after 2 months and 5.1% after 6 months (Brazil)⁷⁵. If DCF is as common as these studies suggest, then our calculations of the total economic burden of dengue in Malaysia would be considerably underestimated.

Finally, our cost estimates do not include the costs of prevention, surveillance, and dengue vector control activities. These activities significantly increase the total economic burden of dengue, as suggested by studies elsewhere. For example they add 39% to the estimated economic burden of dengue in Thailand⁶, 43% in Panama⁸³, and 29% in Puerto Rico⁸⁴. There are vector control units administered both by the Malaysian MoH and also by local councils (city hall, city councils, and municipal councils). There are yet other costs not considered, such as the impact of dengue illness on tourism or the effects of the seasonal clustering of dengue on health systems⁸⁵.

More generally, limited data required to extrapolate EFs and costs across calendar years, age groups, locations, and countries, creating substantial uncertainty in our estimates. This variation is reflected in our wide sensitivity analysis. Several limitations and areas of uncertainty deserve special acknowledgment.

First, underreporting of cases in children is probably more extreme than in adults for several reasons. A lower proportion of children than adults is hospitalized, and since the reported cases are primarily hospital-based, and the rate of underreporting is much greater in ambulatory than hospitalized cases, there is likely to be a greater rate of underreporting of cases in children than adults. In other words, the share of adults among reported cases is probably greater than their share in actual cases. A larger EF would therefore need to be applied to the number of dengue cases in children than in adults in order to achieve a more realistic estimation of the actual number of cases.

Second, our estimates of unit costs of inpatient and outpatient could be further refined by distinguishing not only by facility type (based on the number of beds), but also by region, GDP, population, number of specialist physicians, healthcare coverage, etc. Unfortunately this data is not readily available.

In conclusion, information about economic burden is needed for setting health policy priorities and deciding about the implementation of existing and new technologies, but accurate estimation is difficult due to incomplete data. We overcame this limitation by drawing on multiple data sources. While hospital-based reporting appeared relatively complete, the data indicate that in the ambulatory and private sectors there is considerable underreporting of dengue cases. After adjusting for underreporting we found that dengue imposes a considerable economic burden in Malaysia. Our results and previous studies suggest that health policies aimed at controlling dengue efficiently would most likely be economically valuable.

References

- 1 Shepard, D. S., Undurraga, E. A. & Halasa, Y. A. Economic and Disease Burden of Dengue in Southeast Asia. *Plos Neglect. Trop. Dis.* **in press** (2013).
- 2 Shepard, D. S. *et al.* Use of Multiple Data Sources to Estimate the Economic Cost of Dengue Illness in Malaysia. *Am. J. Trop. Med. Hyg.* **87**, 796-805 (2012).
- 3 x-rates. *Currency calculator*, <<http://www.x-rates.com/>> (2011).
- 4 Gubler, D. J. & Meltzer, M. in *Advances in Virus Research, Vol 53* Vol. 53 *Advances in Virus Research* 35-70 (Academic Press Inc, 1999).
- 5 Shepard, D. S. & Suaya, J. A. in *Handbook of Disease Burdens and Quality of Life Measures* (eds V.R. Preedy & R.R. Watson) Ch. 73, 1281-1296 (Springer, 2009).
- 6 Kongsin, S. *et al.* Cost of Dengue in Thailand. *Dengue Bulletin* **34**, 77-88 (2010).
- 7 Suaya, J. A. *et al.* Cost of Dengue Cases in Eight Countries in the Americas and Asia: A Prospective Study. *Am. J. Trop. Med. Hyg.* **80**, 846-855 (2009).
- 8 Guzman, A. & Isturiz, R. E. Update on the global spread of dengue. *Int. J. Antimicrob. Agents* **36**, S40-S42, doi:10.1016/j.ijantimicag.2010.06.018 (2010).
- 9 Barclay, E. Is climate change affecting dengue in the Americas? *Lancet* **371**, 973-974 (2008).
- 10 Rigau-Perez, J. G. & Gubler, D. J. Is there an inapparent dengue explosion? Reply. *Lancet* **353**, 1101-1101 (1999).
- 11 Ooi, E. E., Goh, K. T. & Gubler, D. J. Dengue prevention and 35 years of vector control in Singapore. *Emerg. Infect. Dis* **12**, 887-893 (2006).
- 12 Tapia-Conyer, R., Mendez-Galvan, J. F. & Gallardo-Rincon, H. The growing burden of dengue in Latin America. *J. Clin. Virol.* **46**, S3-S6 (2009).
- 13 Ooi, E. E. & Gubler, D. J. Dengue in Southeast Asia: epidemiological characteristics and strategic challenges in disease prevention. *Cad. Saude Publica* **25**, S115-S124 (2008).
- 14 Gubler, D. J. Dengue and dengue hemorrhagic fever. *Clin. Microbiol. Rev.* **11**, 480-496 (1998).
- 15 Gubler, D. J. The changing epidemiology of yellow fever and dengue, 1900 to 2003: full circle? *Comp. Immunol. Microbiol. Infect. Dis.* **27**, 319-330, doi:10.1016/j.cimid.2004.03.013 (2004).
- 16 Torres, J. R. & Castro, J. The health and economic impact of dengue in Latin America. *Cad. Saude Publica* **23**, S23-S31 (2007).

- 17 Jacobs, M. Dengue: emergence as a global public health problem and prospects for control. *Trans. Roy. Soc. Trop. Med. Hyg.* **94**, 7-8 (2000).
- 18 Halstead, S. B. Dengue in the Americas and Southeast Asia: Do they differ? *Rev. Panam. Salud Publica* **20**, 407-415 (2006).
- 19 Poovaneswari, S. Dengue Situation in Malaysia. *Malays. J. Pathol.* **15**, 3-7 (1993).
- 20 Holmes, E. C., Tio, P. H., Perera, D., Muhi, J. & Cardoso, J. Importation and co-circulation of multiple serotypes of dengue virus in Sarawak, Malaysia. *Virus Res.* **143**, 1-5, doi:10.1016/j.virusres.2009.02.020 (2009).
- 21 Lum, L. C. S., Suaya, J. A., Tan, L. H., Sah, B. K. & Shepard, D. S. Quality of life of dengue patients. *Am. J. Trop. Med. Hyg.* **78**, 862-867 (2008).
- 22 Ministry of Health Malaysia *Vector Borne Disease Control Section*, <http://www.dph.gov.my/vektor/eng/kes_dd_tahunan.htm> (2010).
- 23 World health Organization. *Data Query by Country - Global Health Atlas*, <<http://apps.who.int/globalatlas/dataQuery/default.asp>> (2010).
- 24 Meltzer, M. I., Rigau-Perez, J. G., Clark, G. G., Reiter, P. & Gubler, D. J. Using disability-adjusted life years to assess the economic impact of dengue in Puerto Rico: 1984-1994. *Am. J. Trop. Med. Hyg.* **59**, 265-271 (1998).
- 25 Shepard, D., Coudeville, L., Halasa, Y. A., Zambrano, B. & Dayan, G. H. Economic Impact of Dengue in the Americas. *Am. J. Trop. Med. Hyg.* **84**, 200-207 (2011).
- 26 Vong, S. *et al.* Estimating the incidence of dengue fever in Cambodia: Results of a capture recapture analysis. *Am. J. Trop. Med. Hyg.* **77**, 26 (2007).
- 27 Chairulfatah, A., Setiabudi, D., Agoes, R., van Sprundel, M. & Colebunders, R. Hospital based clinical surveillance for dengue haemorrhagic fever in Bandung, Indonesia 1994-1995. *Acta Trop.* **80**, 111-115 (2001).
- 28 Duarte, H. H. P. & Franca, E. B. Data quality of dengue epidemiological surveillance in Belo Horizonte, Southeastern Brazil. *Rev. Saude Publica* **40**, 134-142 (2006).
- 29 Camacho, T. *et al.* Incomplete surveillance of a dengue-2 epidemic in Ibague, Colombia, 1995-1997. *Biomedica* **24**, 174-182 (2004).
- 30 Gubler, D. J. How Effectively is Epidemiological Surveillance Used for Dengue Programme Planning and Epidemic Response? *Dengue Bulletin* **26**, 96-106 (2002).
- 31 Ooi, E. E., Gubler, D. J. & Nam, V. S. Dengue research needs related to surveillance and emergency response. *Report of the Scientific Working Group Meeting on Dengue, Geneva, 1-5 October 2006*, 124-133 (2007).

- 32 Deen, J. L. *et al.* The WHO dengue classification and case definitions: time for a reassessment. *Lancet* **368**, 170-173 (2006).
- 33 Clark, D. V., Mammen, M. P., Nisalak, A., Puthimethee, V. & Endy, T. P. Economic impact of dengue fever/dengue hemorrhagic fever in Thailand at the family and population levels. *Am. J. Trop. Med. Hyg.* **72**, 786-791 (2005).
- 34 Garg, P., Nagpal, J., Khairnar, P. & Seneviratne, S. L. Economic burden of dengue infections in India. *Trans. Roy. Soc. Trop. Med. Hyg.* **102**, 570-577, doi:10.1016/j.trstmh.2008.02.015 (2008).
- 35 Anderson, K. B. *et al.* Burden of symptomatic dengue infection in children at primary school in Thailand: a prospective study. *Lancet* **369**, 1452-1459 (2007).
- 36 World Health Organization (WHO). *Country health information. National health accounts*, <<http://www.who.int/nha/country/en/>> (2010).
- 37 United Nations Development Program (UNDP). *International Human Development Indicators*, <<http://hdr.undp.org/en/data/profiles/>> (2010).
- 38 Ministry of Health Malaysia. Health Facts 2008. 12 (Health Informatics Center, Planning and Development Division, 2009).
- 39 Ministry of Health Malaysia. Health Facts 2009. 14 (Health Informatics Center, Planning and Development Division, 2010).
- 40 Ministry of Public Health Thailand. Report 2005-2007. (Ministry of Public Health, 2007).
- 41 Phupoksakul, N. Thailand: Clinical Laboratory Testing Devices and Equipment. (US Commercial Service. Department of Commerce, United States of America, 2008).
- 42 Endy, T. P. *et al.* Epidemiology of inapparent and symptomatic acute dengue virus infection: A prospective study of primary school children in Kamphaeng Phet, Thailand. *Am. J. Epidemiol.* **156**, 40-51 (2002).
- 43 United States Department of State. *Background Note: Malaysia*, <<http://www.state.gov/r/pa/ei/bgn/2777.htm>> (2010).
- 44 Hugo, G. Migration in the Asia-Pacific region. (National Centre for Social Applications of GIS, University of Adelaide, 2005).
- 45 Department of Statistics Malaysia. *Official Website. The Source of Malaysia's Official Statistics*, <<http://www.statistics.gov.my/portal/>> (
- 46 Leong, C. C. Pre-Employment Medical Examination of Indonesian Domestic Helpers in a Private Clinic in Johor Bahru. An Eight Year Review. *Med. J. Malaysia* **5**, 592-598 (2006).
- 47 Asian Migration News. *Malaysia: 1.9M foreigners in the country in 2009*, <<http://www.smc.org.ph/amnews/amn1005/amn1005.htm#MALAYSIA>> (May 2010).

- 48 Jayakumar, G. Pre-Employment Medical Examination of Migrant Workers. The Ethical and Legal Issues. *Med. J. Malaysia* **61**, 516-518 (2006).
- 49 Nair, P. L. & Jantan, N. in *Expert Group Meeting on ESCAP Regional Census Programme* (Department of Statistics, Malaysia, Bangkok, 2006).
- 50 International Labour Organization ILO. *International Labour Migration Statistics Malaysia*, <<http://laborsta.ilo.org>> (
- 51 FOMEMA. *FOMEMA: Caring for Malaysia*, <<http://www.fomema.com.my/html/>> (2010).
- 52 Leng, C. H. *The Emergence of a Transnational Healthcare Service Industry in Malaysia* (Catalogue No. 76, Asia Research Institute, National University of Singapore, 2006).
- 53 Selectscience. *Bio-Rad Launches Test for Early Diagnosis of Dengue Virus*, <<http://www.selectscience.net/product-news/bio-rad-laboratories-informatics-division/bio-rad-launches-test-for-early-diagnosis-of-the-dengue-virus/?artID=9997>> (2010).
- 54 Guzman, M. G. *et al.* Multi-Country Evaluation of the Sensitivity and Specificity of Two Commercially-Available NS1 ELISA Assays for Dengue Diagnosis. *Plos Neglect. Trop. Dis.* **4**, e811 (2010).
- 55 Dussart, P. *et al.* Evaluation of Two New Commercial Tests for the Diagnosis of Acute Dengue Virus Infection Using NS1 Antigen Detection in Human Serum. *Plos Neglect. Trop. Dis.* **2**, doi:e280 10.1371/journal.pntd.0000280 (2008).
- 56 Chiang, S. in *Dengue Burden in Malaysia Workshop* (Shangri-La Hotel, Putrajaya, Malaysia, December 6, 2010).
- 57 Health Tourism in Asia. *Hospitals in Malaysia*, <<http://www.healthtourisminasia.com/malaysia.htm>> (2010).
- 58 Shepard, D. S. *et al.* Cost-effectiveness of a pediatric dengue vaccine. *Vaccine* **22**, 1275-1280, doi:10.1016/j.vaccine.2003.09.019 (2004).
- 59 Ministry of Health Malaysia. Health Expenditures Report 1997 - 2002. (Ministry of Health, Putrajaya, Malaysia, 2006).
- 60 Ministry of Health Malaysia. Health Expenditures Report 1997-2006. (Ministry of Health, Putrajaya, Malaysia, 2008).
- 61 Ministry of Health Malaysia. Health Expenditures Report (2007-2008). (Malaysia National Health Accounts Unit, Planning and Development Division, Ministry of Health Malaysia, Putrajaya, Malaysia, 2009).
- 62 Sabrina, A. R. *Unit cost of patient care in district hospitals in the Ministry of Health, Malaysia* (Department of Social and Preventive Medicine, Faculty of Medicine. University of Malaya., Kuala Lumpur, Malaysia, 2006).

- 63 World Health Organization. *CHOosing Interventions that are Cost Effective (WHO - CHOICE)*, <<http://www.who.int/choice/en/>> (2011).
- 64 Adam, T., Evans, D. B. & Murray, C. J. Econometric estimation of country-specific hospital costs. *Cost Effectiveness and Resource Allocation* **1** (2003).
- 65 Lim, K. J. *Costing of OPD services at main health clinics Kedah Darul Aman* (Ministry of Health, Malaysia, 1995).
- 66 Institute of Public Health. (Ministry of Health Malaysia (MoH), Kuala Lumpur, Malaysia, 1996).
- 67 Institute for Public Health. *Recent Illness/Injury, Health Seeking Behaviour and Out-of-Pocket Health Expenditure* (Ministry of Health, Kuala Lumpur, Malaysia, 1997).
- 68 Drummond, M. F., Sculpher, M. J., Torrance, G., W., O'Brien, B. J. & Stoddart, G. L. *Methods for the Economic Evaluation of Health Care Programmes*. Third edn, (Oxford University Press, 2005).
- 69 Berita Nasional Malaysia (Bernama). in *The Star Online* (Kuala Lumpur, Malaysia, 2011).
- 70 Anis, M. N. in *The Star Online* (Kuala Lumpur, Malaysia, 2011).
- 71 Bahl, R. *et al.* Costs of illness due to typhoid fever in an Indian urban slum community: Implications for vaccination policy. *J. Health Popul. Nutr.* **22**, 304-310 (2004).
- 72 World Health Organization. *Life Tables for WHO Member States for Year 2009*, <http://www.who.int/healthinfo/statistics/mortality_life_tables/en/> (2009).
- 73 Seet, R. C. S. *et al.* Oxidative damage in dengue fever. *Free Radic. Biol. Med.* **47**, 375-380, doi:10.1016/j.freeradbiomed.2009.04.035 (2009).
- 74 Seet, R. C. S., Quek, A. M. L. & Lim, E. C. H. Post-infectious fatigue syndrome in dengue infection. *J. Clin. Virol.* **38**, 1-6, doi:10.1016/j.jcv.2006.10.001 (2007).
- 75 Teixeira, L. D. S. *et al.* Persistence of dengue symptoms in patients in Uberaba, Minas Gerais State, Brazil. *Cad. Saude Publica* **26**, 625-630 (2010).
- 76 Structured Data LLC. *RiskAMP User Guide. User Guide for the RiskAMP Monte Carlo Add-in*, <www.riskamp.com> (2007).
- 77 World Health Organization (WHO). *Global Burden of Disease*, <http://www.who.int/topics/global_burden_of_disease/en/> (2011).
- 78 Ministry of Health Malaysia. in *Notifiable Disease Database* (Institute for Medical Research, Epidemiology and Biostatistics Unit, Kuala Lumpur, Malaysia, 2010).
- 79 Undurraga, E. A., Halasa, Y. A. & Shepard, D. S. Expansion Factors: A Key Step in Estimating Dengue Burden and Costs in Southeast Asia. *Am. J. Trop. Med. Hyg.* **85**, 318 (2011).

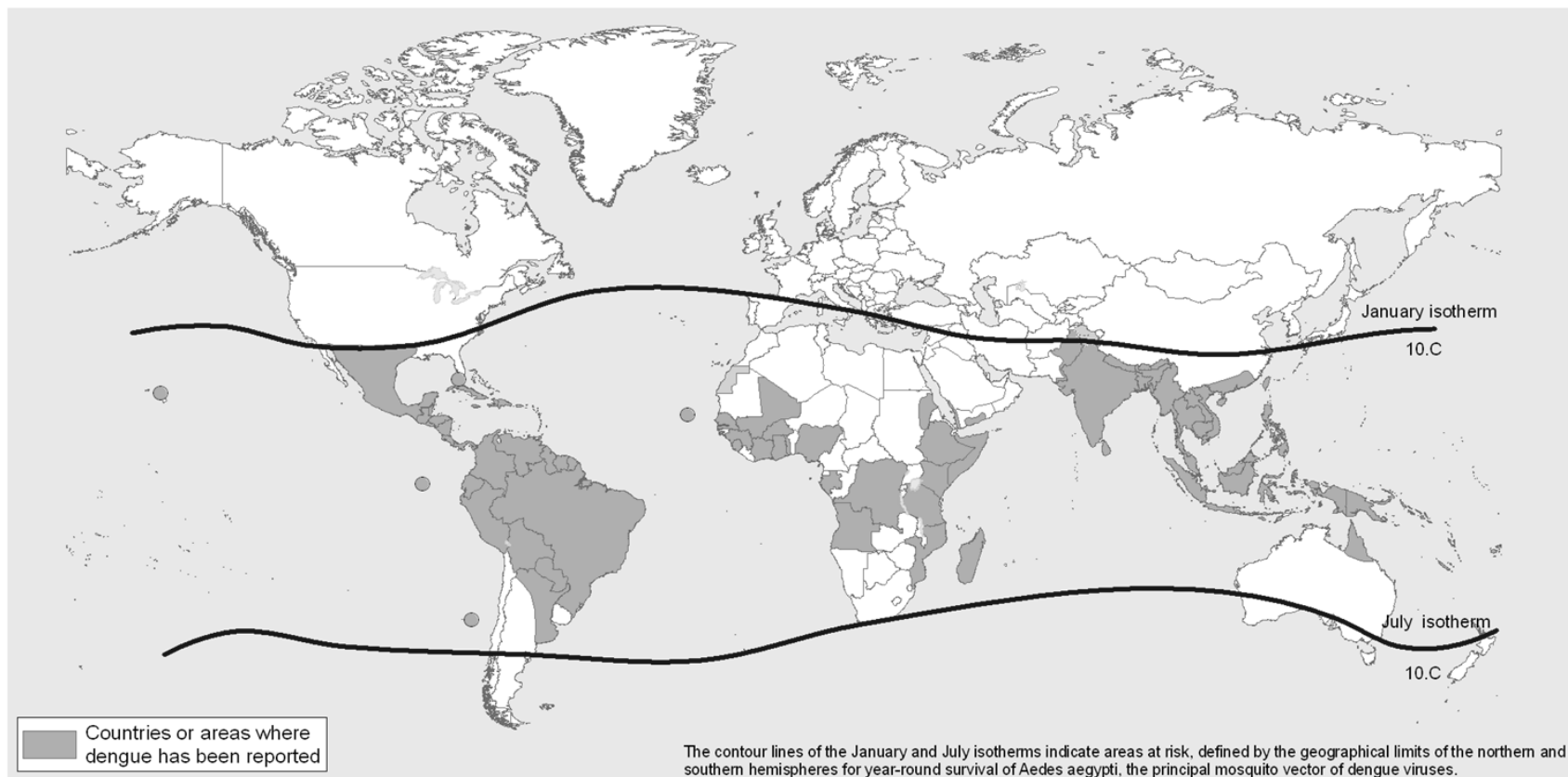
- 80 Wichmann, O. *et al.* Dengue in Thailand and Cambodia: An Assessment of the Degree of Underrecognized Disease Burden Based on Reported Cases. *Plos Neglect. Trop. Dis.* **5**, e996, doi:e99610.1371/journal.pntd.0000996 (2011).
- 81 Garcia, G. *et al.* Long-term persistence of clinical symptoms in dengue-infected persons and its association with immunological disorders. *Int. J. Infect. Dis.* **15**, E38-E43, doi:10.1016/j.ijid.2010.09.008 (2011).
- 82 Gonzalez, D. *et al.* Evaluation of Some Clinical, Humoral, and Immunological Parameters in Patients of Dengue Haemorrhagic Fever Six Months After Acute Illness. *Dengue Bulletin* **29**, 79-84 (2005).
- 83 Armien, B. *et al.* Clinical characteristics and national economic cost of the 2005 dengue epidemic in Panama. *Am. J. Trop. Med. Hyg.* **79**, 364-371 (2008).
- 84 Shepard, D. S., Halasa, Y. A., Dieppa, M. & Perez-Guerra, C. L. Aggregate Economic Cost of Dengue in Puerto Rico. *Am. J. Trop. Med. Hyg.* **81**, 224-225 (2009).
- 85 Kuo, H. I., Chang, C. L., Huang, B. W., Chen, C. C. & McAleer, M. Estimating the impact of avian flu on international tourism demand using panel data. *Tour. Econ.* **15**, 501-511 (2009).
- 86 World Health Organization (WHO). *International Travel and Health. 2011 Edition - Dengue*, <<http://www.who.int/ith/en/>> (2011).
- 87 Standish, K., Kuan, G., Aviles, W., Balmaseda, A. & Harris, E. High Dengue Case Capture Rate in Four Years of a Cohort Study in Nicaragua Compared to National Surveillance Data. *Plos Neglect. Trop. Dis.* **4**, e633, doi:e63310.1371/journal.pntd.0000633 (2010).
- 88 Dechant EJ & Rigau-Pérez JG. Hospitalizations for suspected dengue in Puerto Rico, 1991-1995: estimation by capture-recapture methods. The Puerto Rico Association of Epidemiologists. *Am J Trop Med Hyg* **61**, 574-578 (1999).
- 89 Rigau-Perez, J. G. Surveillance for an emerging disease: dengue hemorrhagic fever in Puerto Rico, 1988-1997. Puerto Rico Association of Epidemiologists. *P. R. Health Sci. J.* **18**, 337-345 (1999).
- 90 Shepard, D. S., Coudeville, L., Halasa, Y. A., Zambrano, B. & Dayan, G. H. Economic Impact of Dengue Illness in the Americas. *Am. J. Trop. Med. Hyg.* **84**, 200-207, doi:10.4269/ajtmh.2011.10-0503 (2011).
- 91 Vong, S. *et al.* Dengue Incidence in Urban and Rural Cambodia: Results from Population-Based Active Fever Surveillance, 2006-2008. *Plos Neglect. Trop. Dis.* **4**, e903, doi:e90310.1371/journal.pntd.0000903 (2010).
- 92 Porter, K. R. *et al.* Epidemiology of dengue and dengue hemorrhagic fever in a cohort of adults living in Bandung, west Java, Indonesia. *Am. J. Trop. Med. Hyg.* **72**, 60-66 (2005).
- 93 Yew, Y. W. *et al.* Seroepidemiology of Dengue Virus Infection Among Adults in Singapore. *Ann. Acad. Med. Singap.* **38**, 667-675 (2009).

- 94 Shepard, D. *et al.* Burden of Dengue in Malaysia: Report from Ministry of Health Workshop of December 6 2010, Putrajaya, Malaysia. (Schneider Institutes for Health Policy, Brandeis University, & University of Malaya, 2013).
- 95 Shepard, D. S. *et al.* Economic Cost of Dengue in Malaysia: Merging Multiple Data Sources. *Am. J. Trop. Med. Hyg.* **85**, 156 (2011).
- 96 Phuong, H. L. *et al.* Dengue as a cause of acute undifferentiated fever in Vietnam. *BMC Infect. Dis.* **6**, doi:12310.1186/1471-2334-6-123 (2006).
- 97 Tien, N. T. K. *et al.* A prospective cohort study of dengue infection in schoolchildren in Long Xuyen, Viet Nam. *Trans. Roy. Soc. Trop. Med. Hyg.* **104**, 592-600, doi:10.1016/j.trstmh.2010.06.003 (2010).

Appendices

Appendix A: Countries or areas at risk of dengue fever in the world, 2010

Figure 21-A. Countries or areas at risk of dengue fever in the world, 2010



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization



© WHO 2010. All rights reserved.

SOURCE: WHO⁸⁶

Appendix B: Workshop participants

Table 31-B. List of workshop participants

NAME	ORGANIZATION	EMAIL	TELEPHONE
Dr Chee Kheong Chong	Ministry of Health	drchongck@moh.gov.my	+603 88834275
Dr Jeremy Brett	Sanofi Pasteur	jeremy.brett@sanofipasteur.com	+6564312512
Ms. Sharon Chiang	Pantai Premier Pathology Sdn Bhd	chiang@premierpathology.com.my	+603 4297 9911
Dr Laurent Coudeville	Sanofi Pasteur	laurent.coudeville@sanofipasteur.com	+33 (689) 32.10.21
Dr Ahmad Faudzi bin Yusoff	Institute for Medical Research	faudzi@imr.gov.my	+60122018414
Dr. BK Ho	Ministry of Health	hobk@hotmail.com	
Dr Shree Jacob	Sanofi Pasteur	jeyashree.jacob@sanofipasteur.com	+60-12 280 3051
Dr Ahamad Jusoh	Ministry of Health	dr_ahamad@sel.moh.gov.my	
Dr Rosemary Lees	University of Malaya	rosemarylees@um.edu.my	+60102631480
Prof Lucy Lum	University of Malaya	Lumcs@ummc.edu.my	+60 (13) 390 7898
Dr. Chiu Wan Ng	University of Malaya	chiuwan.ng@ummc.edu.my	+60-16 394 1135
Dr P Ravi Raviwharmman	University of Malaya	raviwharmman_p@yahoo.com	+60 12 261 7486
Dr Puan Shanaliza Sulaiman	Pantai Premier Pathology Sdn Bhd	shanaliza@premierpathology.com.my	+603 4297 9911
Prof Donald Shepard	Brandeis University	shepard@brandeis.edu	+1 781 736 3975
Dr Satwant Singh	Ministry of Health	satwant70@hotmail.com	+60 (12) 353-4744
Dr Jameela Zainuddin	Ministry of Health	jzmohealth@yahoo.com	+603 8883-2095

Appendix C: Workshop photographs

Figure 22-C. Left to right: Ahmed Faudzi; Laurent Coudeville; Shree Jacob; Jeremy Brett; Shanaliza Sulaiman; Sharon Chiang; Rosemary Lees



Figure 23-C. Left to right: Ahamad Jusoh; Satwant Singh; Chiu Wan Ng; Jameela Zainudeen; BK Ho; Lucy Lum; CK Chong; A Faudzi; Jeremy Brett; Shanaliza Sulaiman; Rosemary Lees



Figure 24-C. Left to right: Shree Jacob, Jeremy Brett, Laurent Coudeville, Donald Shepard



Appendix D: Use of EFs to estimate the incidence of dengue illness in Malaysia

Table 32-D. Sensitivity of dengue surveillance systems in American countries and corresponding EFs

Study	Country	Period	Type of dengue	Method used	EFs
Duarte et al. ²⁸	Brazil	1996-2002	Hospitalized dengue case	Sensitivity of the surveillance system using hospital records as the reference	Overall : 1.6 [1.4-1.8] DHF : 1.4 [1.3-1.5] DF : 2.1 [1.6-3]
Camacho et al. ²⁹	Colombia	1995-1997	All types of Dengue cases	Sensitivity of the surveillance system using emergency room medical records as the reference	Overall : 9
Standish et al. ⁸⁷	Nicaragua	2004-2008	All types of Dengue cases	Comparison of incidence obtained through active surveillance with reported incidence in the same area	Clinically diagnosed : 20.4 (2004-2008), 16 (2007-2008) 28 (2005-2006) Lab-confirmed : 23.1 (2004-2008), 14 (2006-2007), 28 (2005-2006)
Dechant et al. ⁸⁸	Puerto Rico	1991-1995	Hospitalized dengue case	Capture-recapture method	1991-1995 : 2.4 1991 : 2.3 1993 : 3.4
Rigau-perez ⁸⁹	Puerto Rico	1988-1997	Hospitalized dengue case	Sensitivity and specificity of the surveillance system when compared to hospital records	Overall : 3

Source: Shepard et al, 2011⁹⁰

Table 33-D Other studies of EFs in South East Asia.

Study	Country	Period	Type of Dengue	Method	EFs
Vong et al. 2007 ²⁶	Cambodia	Not available	Confirmed dengue cases	Capture-recapture, active surveillance for febrile illness and DF. Assessment of National Dengue Surveillance System (NDSS) in children <16 yrs	E.F.: 3.1 [Total confirmed dengue cases in children <16 yrs/ reported dengue cases in children <16 yrs] E.F.: 2.1 [Total confirmed hospitalized dengue children <16 yrs/ reported cases of hospitalized dengue <16 yrs]
Vong et al. 2010 ⁹¹	Kampong Cham, Cambodia	2006-2008	Laboratory confirmed dengue cases	Population-based active fever surveillance of children aged 0 to 19 yrs. Convenience sample of rural villages (20) and urban areas (5)	E.F.: 16.9 [Total laboratory confirmed dengue cases/ total patients hospitalized for dengue]
Chairulfatah et al. 2001 ²⁷	Bandung, Indonesia	1994-1995	Clinically diagnosed DHF/DSS patients and laboratory confirmed DHF	Active surveillance in 4 major hospitals. Comparison of total DHF cases in hospitals & cases reported to Municipality Health Office	E.F. DHF & DSS: 4.3 [Total diagnosed DHF & DSS hospitalized patients/ diagnosed DHF & DSS hospitalized patients reported to Municipal Health Office]
Porter et al. 2005 ⁹²	Bandung, Indonesia	2000-2002	Clinically diagnosed and laboratory confirmed dengue	Active surveillance and periodic blood exam of a cohort of 2,536 adult volunteers (>18 yrs) from two textile factories	E.F.: 2.3 [Total laboratory confirmed dengue cases / total laboratory confirmed dengue hospitalized cases]
Yew et al. 2009 ⁹³	Singapore	2004	Laboratory confirmed cases	18-74 yrs. Representative sample adults, part of National Health Survey (n=4,152).	E.F.: 8.5 [†] [Total dengue cases / laboratory confirmed dengue cases reported]
Shepard et al. 2011 ^{94,95}	Malaysia	2009	All types of dengue fever	Delphi process based on multiple data sources	E.F.: 3.8 [Total estimate of dengue cases/ reported cases of dengue] E.F.: 1.7 [Total estimate of hospitalized dengue cases/ reported hospitalized dengue cases] E.F.: 65.4 [Total estimate of ambulatory dengue cases/ reported]
Wichmann et al. 2011 ⁸⁰	Kampong Cham (KC)	KC: 2006-2007	Laboratory confirmed dengue	Cambodia: cohort study of children aged 0 to 19 yrs	<i>Cambodia</i> E.F.: 9.1 [Total laboratory-confirmed dengue cases < 15 yrs]

	Cambodia & Kamphaeng Phet (KP), Ratchaburi (R) Thailand	KP: 2004-2007; R: 2006-2007	cases (e.g. RT-PCR)	Thailand: Cohort studies of children aged 0 to 14 yrs	/reported dengue cases < 15 yrs] EF: 1.4 [Total laboratory-confirmed hospitalized dengue cases <15 yrs /reported hospitalized dengue cases <15 yrs] <i>Thailand</i> E.F.: 8.7 [Total laboratory-confirmed dengue cases <15 yrs / reported dengue cases < 15 yrs old] EF: 2.6 [Total laboratory-confirmed hospitalized dengue cases <15 yrs/ reported hospitalized dengue cases <15 yrs]
Endy et al. 2002 ⁴²	Kamphaeng Phet Thailand	1998-2000	All types of dengue (laboratory confirmed)	Cohort of 2,119 children aged 5 to 15 at 12 local primary schools (2 nd -6 th grade).	E.F.: 4.8 [Total laboratory confirmed dengue cases 5-15 yrs/ laboratory confirmed hospitalized dengue cases 5-15 yrs]
Anderson et al. 2007 ³⁵	Kamphaeng Phet Thailand	1998-2002	All types of dengue (laboratory confirmed)	Cohort of 2,214 children aged 5 to 15 at 12 local primary schools.	E.F.: 3.4 [Total laboratory-confirmed dengue cases 5-15 yrs/ laboratory confirmed hospitalized dengue cases 5-15 yrs]
Phuong et al 2006 ⁹⁶	Binh Thuan, Viet Nam	2001-2002	Laboratory confirmed dengue	Evaluation of all patients with febrile illness in 12 community health posts and one clinic at the provincial malaria station (n=2,096).	E.F.: 5.2 [Total laboratory-confirmed dengue cases/ total patients diagnosed with dengue]
Tien et al. 2010 ⁹⁷	Long Xuyen, Viet Nam	2004-2007	Laboratory confirmed dengue	Active surveillance children aged 2 to 15 yrs	E.F.: 5.8 [Laboratory confirmed dengue cases/ reported dengue cases]

Appendix E: Literature review procedure

We conducted a systematic literature review of articles published between 1995 and 2011 to identify the most appropriate EFs for total, hospitalized, and ambulatory cases for countries in Southeast Asia where empirical studies have taken place. We performed a literature search in the Web of Science and MEDLINE databases using the keywords “dengue” and “surveillance”; “dengue” and “capture recapture”; or “dengue” and “sensitivity”. In the original search, we only included articles that were published between 1995 and 2011 in English, Spanish, or Portuguese. We obtained a total of 1,371 articles. We then reviewed the titles and abstracts of these articles and selected 39 that contained information relevant to the study of expansion factors for dengue in Asia. We collected these 39 studies in full text, and added 14 related articles that we had collected from previous literature reviews. We examined the 53 articles and checked the cited references, looking for additional articles that we could have missed in our search (including any year). Eight new articles resulted from reviewing the references. We looked for studies that explicitly reported data on expansion factors or included the necessary data to estimate them. In some cases we combined existing studies to calculate better estimates. The selection criteria to identify the most reliable studies were based on the (1) use of original, empirical data; (2) implementation of a scientifically valid approach; and (3) the external validity of the data gathered (plausible patterns among age groups, geographic regions, years, and study sites).

Appendix F: First round of Delphi estimates of EFs

Participants in the workshop were asked to provide their best estimates of EFs for dengue cases using the evidence on dengue cases available at that moment. In addition to a best estimate, participants were asked if possible to provide a minimum and a maximum value which would seem reasonable for a given EF. From these values, mean and median value for the workshop participants' overall opinion on each EF could be calculated. Table 34-D shows the values of these EFs. The best estimate expansion values from the workshop as calculated using the estimates and minimum/maximum values of the participants are given in Table 35-D and are used to calculate the projected number of cases in each of the four categories in Table 36-D.

At the bottom of Table 35-D, adjustment factors have been calculated that would make the distribution of dengue illness between hospitalized and ambulatory modalities consistent with the workshop estimates of 50% to 60% ambulatory. Figure 25-D shows the comparison between the total reported cases in 2009 and the total projected cases using an adjusted EF (50% share) estimated in the workshop.

Table 34-F. Participants' estimates of EFs suitable to apply to four subdivisions of dengue cases reported in Malaysia based on evidence discussed during the workshop

Participant*	EF PUBLIC						EF PRIVATE					
	Hospitalized			Ambulatory			Hospitalized			Ambulatory		
	Best	Min	Max	Best	Min	Max	Best	Min	Max	Best	Min	Max
A	1.5	1.1	2	5	1	10	1.5	1	2	15	10	50
B	1.1			10			1.2			100		
C	1.1	1	1.2	2	1.5	3	1.5	1.2	2	3	2	5
D	1.2	1	1.4	10	8	12	1.5	1.3	1.7	30	28	32
E	1.3	1.2	1.4	10	10	15	2	1.5	2.2	30	25	35
F												
G	1			56			1			52		
H	1	0.8	1.2	50	10	80	1	1	1	100	80	100
I	1			10			1			50		
Mean	1.15	1.02	1.44	19.13	6.10	24.00	1.34	1.20	1.78	47.50	29.00	44.40
Median	1.1	1	1.4	10	8	12	1.35	1.2	2	40	25	35
Minimum	1	0.8	1.2	2	1	3	1	1	1	3	2	5
Maximum	1.5	1.2	2	56	10	80	2	1.5	2.2	100	80	100

Notes:

* The blank lines mean that these respondents did not submit estimates of EFs.

Table 35-F. EFs for each of the four categories of dengue patient reported in Malaysia, 2009, calculated from the estimates made by workshop participants

	EF		
	<u>Hospital cases</u>	<u>Ambulatory cases</u>	<u>Overall*</u>
<i>Mean of workshop participants within the range of estimates made by participants</i>			
Public	1.15	19.13	1.87
Private	1.34	47.50	2.20
Both*	1.21	23.79	1.97
<i>Supplemental multiplicative factor required for ambulatory cases (to be multiplied times existing EFs) needed to bring the ambulatory share to the alternative specified shares of total cases)</i>			
50%	1.00	1.46	1.19
60%	1.00	2.19	1.48
<i>Adjusted EFs (combining mean and supplemental factors, using 50% share)</i>			
Public	1.15	27.96	2.22
Private	1.34	69.43	2.60
Both*	1.21	34.77	2.34

Figure 25-F. Comparison between the total reported dengue cases in 2009 and the total projected cases using an adjusted EF (50% share of ambulatory cases) based on estimates during the workshop

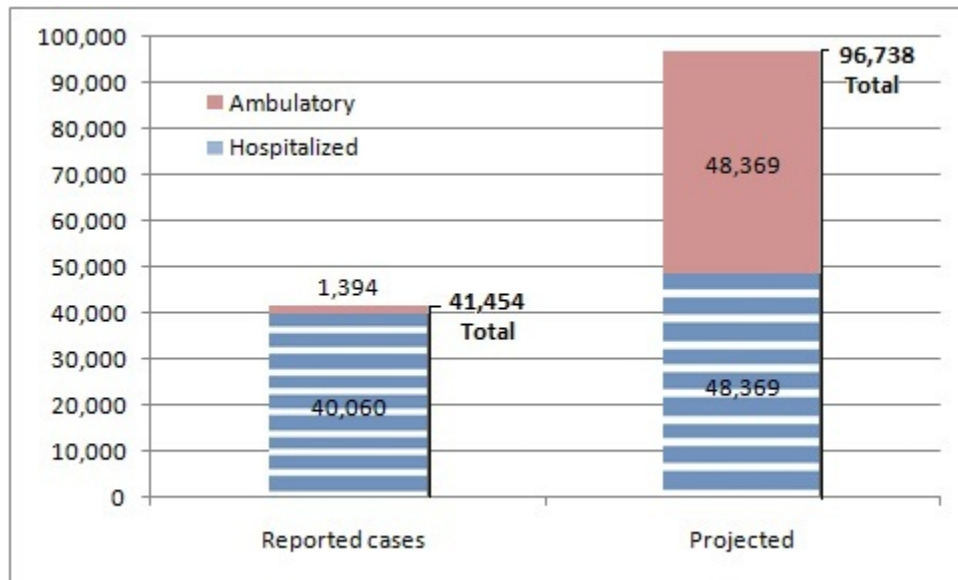


Table 36-F. Reported number of dengue cases in Malaysia, 2009, in each of four categories, and projected values calculated using the four estimated EFs

	HOSPITAL CASES	AMBULATORY CASES	TOTAL
<i>Reported Cases</i>			
Public	27,955	1,165	29,120
Private	12,105	229	12,334
Total	40,060	1,394	41,454
<i>Projected cases based on mean EFs only</i>			
Public	32,148	22,286	54,434
Private	16,221	10,878	27,099
Total	48,369	33,164	81,533
Row %	59.3%	40.7%	100.0%
<i>Approximate projected total cases with supplemental multiplicative factors incorporated</i>			
50% target*	48,369	48,369	96,738
Row %	50.0%	50.0%	100.0%
60% target	48,369	72,554	120,923
Row %	40.0%	60.0%	100.0%
<i>Projected total cases with adjusted factor (50% share)*</i>			
Public	32,148	32,504	64,652
Private	16,221	15,865	32,086
Total	48,369	48,369	96,738
Row %	50.0%	50.0%	100.0%

Note:

* 50% share considered base estimate

Appendix G: Reaching a consensus on proportion of dengue cases which are hospitalized and the proportion of cases treated in the private sector

Table 37-G. Reaching a consensus on proportion of dengue cases which are hospitalized

PARTICIPANT (NO)	% HOSPITALIZED PUBLIC			% HOSPITALIZED PRIVATE		
	Best	Min	Max	Best	Min	Max
1	33%			33%		
2	30%			20%		
3	40%	20%	50%	10%	5%	20%
3	60%	58%	62%	40%	38%	42%
5	70%	65%	75%	30%	25%	35%
6	70%			30%		
7						
8	70%	70%	80%	30%	10%	30%
9						
Median	60%	62%	69%	30%	18%	33%
Minimum	30%	20%	50%	10%	5%	20%
Maximum	70%	70%	80%	40%	38%	42%

Table 38 G. Reaching a consensus on proportion of dengue cases which are treated in the private sector

	% PRIVATE HOSPITALIZED			% PRIVATE AMBULATORY		
	Best	Min	Max	Best	Min	Max
A	30%	20%	40%	54%	50%	60%
B	20%			50%		
C	20%	10%	30%	50%	30%	70%
D	30%	28%	32%	30%	28%	30%
E	30%	30%	35%	70%	60%	75%
F	85%			15%		
G						
H	30%	20%	30%	70%	50%	70%
I						
Median	30%	20%	32%	50%	50%	70%
Minimum	20%	10%	30%	15%	28%	30%
Maximum	85%	30%	40%	70%	60%	75%

Appendix H: Correction of labeling error

In the course of related research,¹ we uncovered a labeling error in our recent article on dengue costs in Malaysia.² In columns 3 and 6 of Table 5, p.801 of that article, we endeavored to report direct costs per ambulatory and hospitalized dengue case. The numbers presented actually corresponded to the costs per outpatient visit and per bed-day, respectively. Due to that error, our subsequent calculations were also incorrect. Applying the methods in our article with the appropriate data, the corrected version of Table 5 is:

Table 5 (corrected). Cost of dengue illness by sector, setting, and component, Malaysia

Sector	Ambulatory			Hospitalized			Indirect deaths	Total
	Indirect	Direct	Total	Indirect	Direct	Total		
<i>Estimated costs per case (2009 US\$)</i>								
Public	176.36	297.93	474.29	200.55	613.65	814.20	53,336.50	668.49
Private	176.36	168.68	345.03	200.55	697.88	898.43	53,336.50	628.90
Total	176.36	239.85	416.21	200.55	651.50	852.05	53,336.50	650.70
<i>Estimated aggregate costs from EF-adjusted dengue cases (58% ambulatory; 2009 US\$1,000s)</i>								
Public	8,851	14,952	23,803	7,288	22,301	29,589	4,451	57,843
Private	7,223	6,908	14,131	5,948	20,697	26,645	3,633	44,409
Total	16,073	21,860	37,933	13,236	42,998	56,234	8,084	102,252
Range			(17,150-233,637)			(44,197-88,593)		(77,942-310,657)

*EF = expansion factor. The unit cost of death reported is the average cost; the actual values were estimated on the basis of the age distribution of reported deaths caused by dengue in 2009 (Ministry of Health Malaysia, unpublished data)

†The range corresponds to the 95% certainty levels (centered on the median) in our projections, and is given by the simultaneous variation of parameters as indicated in Table 3²

In the published article, we mistakenly reported an economic burden of dengue illness of US\$56 million or approximately US\$2.03 per capita. Our corrected estimate of the economic burden of dengue illness in Malaysia is US\$102 (95%CI: 78– 311) million per year (MYR 359.79 million), approximately US\$3.72 (MYR 13.08) per capita. This update was published in the Errata of the *American Journal of Tropical Medicine and Hygiene*, vol. 88, number 3, page 606, March 2013.