DENGUE: A GLOBAL THREAT

Professor Usa Thisyakorn, M.D.
Chulalongkorn University
Bangkok, Thailand
Dengue Disease: Global Threat
30-fold increase in last decades

• Over 2.5 billion people now at risk
  • >40% of the world's population
• Dengue is the most common disease transmitted by a mosquito
• Now a major public health problem in many tropical and subtropical regions:
  • 100–200++ million infections / year
  • >100 tropical and subtropical countries
  • ~ 20,000 deaths annually
• Factors leading to increase include:
  1. Population growth and urbanization
  2. Inadequate water, sewer & waste management systems
  3. Rise in global commerce & tourism
  4. Global warming
  5. Changes in public health policy

Source: www.who.int/mediacentre/factsheets/fs117/en/
Undurraga PLoS Negl Trop Dis 2013
Gubler Expert Rev Vaccines 2011
Worldwide Threat of Dengue

Specific WHO Objective:
By 2020, reduce mortality and morbidity from dengue by at least 50% and 25% respectively
Dengue incidence is under-reported

• The case definition is not universally applied.

• There is limited access to dengue diagnostics.

• Misdiagnosis
  – Similarity to other febrile illnesses.

• Surveillance and reporting systems are not well established in many countries.

• There is a lack of knowledge about major regions theoretically at risk.

GLOBAL DISTRIBUTION & DENGUE BURDEN

The accurate estimation of dengue burden will help to guide improvements in disease control strategies and in their economic evaluation.

Nature 2013; 496: 504-7
Acknowledgements

The global distribution and burden of dengue


- The International Research Consortium on Dengue Risk Assessment, Management and Surveillance (IDAMS: [http://www.idams.eu]) is funded by the European Commission Seventh Framework Programme
- Green open-access with European PubMed Central ID: PMC3651993
GLOBAL DISTRIBUTION & DENGUE BURDEN

• An exhaustive assembly of known records of dengue occurrence worldwide
• Use an advance in disease modelling approaches to map the global distribution of dengue risk
• Pair the resulting risk map with detailed longitudinal information from dengue cohort studies and population surfaces to infer the public health burden of dengue

Nature 2013; 496: 504-7
From dengue risk to burden

- Pair probability of occurrence with cohort studies to infer inapparent (n=54) and apparent (n=39) incidence per pixel
- Then pair with population surfaces for 2010 to sum up global totals
- Consistent global estimates for BMGF, GAVI and surfaces for GBD2013
GLOBAL DISTRIBUTION & DENGUE BURDEN

Dengue infection is more than three times the dengue burden estimate of the World Health Organization

Nature 2013; 496: 504-7
GLOBAL SPREAD
OF
DENGUE VIRUS SEROTYPES

MAPPING THE 70 YEAR HISTORY
Figure 5. DENV Co-circulation. Cumulative number of DENV types reported by decade since 1943.
Global spread of dengue virus types: mapping the 70 year history

• Worldwide expansion of the types
• The expansion of disease hyperendemicity
• The establishment of an increasingly important infectious disease of global health significance

ECONOMIC & DISEASE BURDEN OF Dengue in SOUTHEAST ASIA

• Dengue poses a substantial economic and disease burden in SEA with a DALY burden per million inhabitants in the region

• The burden is higher than that of 17 other conditions, including Japanese encephalitis, upper respiratory infections, and hepatitis B

PLOS Neglected Tropical Diseases 2013; 7: e2055.
DENGUE

The most important arthropod-borne viral disease of humans
Is dengue eclipsing malaria as a global health threat?

Professor Usa Thisyakorn, M.D.
Chulalongkorn University
Bangkok, Thailand
Dengue Transmission Cycle

1. Bites dengue infected person
2. Mosquito ingests blood with dengue virus. Takes 8-10 days for dengue virus to incubate.
3. Dengue infected mosquito bites another person
4. That person gets dengue 4-13 days later
Clinical Spectrum of DENV Infection

DHF/Severe Dengue

Hospitalized DF

Non-hospitalized DF

Inapparent DENV Infection

Host Response

Death of Organism

Classical and Severe Disease

Moderate Severity Mild Illness

Infection without Clinical Illness (Asymptomatic Infection)

Exposure without Infection

Iceberg Concept of Infection

Field’s Virology, 4th Ed. Chapter 9: Pathogenesis of Viral Infections, Kenneth L. Tyler and Neal Nathanson
Major pathophysiological changes in DHF

- Leakage of plasma
- Abnormal hemostasis
### 1997 WHO classification of dengue infection

<table>
<thead>
<tr>
<th>Severity</th>
<th>Platelet</th>
<th>Plasma leakage</th>
</tr>
</thead>
<tbody>
<tr>
<td>DF</td>
<td>variable</td>
<td>absent</td>
</tr>
<tr>
<td>DHF grade I</td>
<td>$&lt; 100,000$</td>
<td>present</td>
</tr>
<tr>
<td>grade II</td>
<td>$&lt; 100,000$</td>
<td>present</td>
</tr>
<tr>
<td>DHF grade III</td>
<td>$&lt; 100,000$</td>
<td>present</td>
</tr>
<tr>
<td>grade IV</td>
<td>$&lt; 100,000$</td>
<td>present</td>
</tr>
</tbody>
</table>
1997 WHO dengue classification

- Fever, headache, retro-orbital pain, myalgias, arthralgias +/- Haemorrhagic manifestations → Classic Dengue Fever
- Thrombocytopenia Haemoconcentration → Grade I DHF
- Spontaneous Bleeding → Grade II DHF
- Pulse Pressure 20 mmHg Hypotension, cold clammy skin, restlessness → Grade III DHF
- Profound shock Undetectable blood pressure & pulse → Grade IV DHF

DSS
The course of dengue illness

IgM = immunoglobulin M; IgG = immunoglobulin G. Temperature is given in degrees Celsius (°C).

Source: adapted from Yip, 1980 (2) by authors.
Major pathophysiologic changes in DHF

- Leakage of plasma
- Abnormal hemostasis
BLEEDING PRECAUTIONS
Mitrakul C, Thisyakorn U. Haemostatic studies in DHF

- Vasculopathy
- Coagulopathy
- Platelet abnormalities

HEMOSTATIC STUDIES IN DENGUE PATIENTS

- Laboratory evidences of DIC are demonstrated in all degrees of severity
- Only in severe dengue is profound DIC aggravated, leading to uncontrolled bleeding and death
- Plasma von Willebrand factor antigen is the best indicator of progression to severe dengue in a study to determine the extent of the activation of endothelial cells and the hemostatic system in correlation with severe dengue

Dengue infection during parturition complicated in severe hemorrhage and vertical transmission.
Reports of dengue patients with unusual manifestations

- 1976 Wuler, Indonesia
  Saguansermsri, Thailand
  Tin U, Burma
- 1978 Sumarmo, Indonesia
- 1981 Kho, Indonesia
- 1987 Nimmannitya & Thisyakorn, Thailand
- 1988 George, Malaysia
Thisyakorn U, Thisyakorn C. DHF: Unusual manifestations and problem in management

The unusual manifestations include encephalopathy, encephalitis and fulminant hepatitis

Neurological manifestations of dengue including alteration of consciousness, seizures, pyramidal tract signs, meningeal signs and headache. CSF showed lymphocytic pleocytosis in 1/5 while presence of IgM in few patients.

Solomon T, et al.  
Neurological manifestations of dengue infection  

In dengue endemic areas patients with encephalitis and encephalopathy should be investigated for this infection, whether or not they have other features of the disease.
Hepatic functions in dengue patients

Hepatocellular injury manifested by hepatomegaly, elevation of ALT and coagulopathy are common in DHF and even in DF, though hepatomegaly is absent.

Innis BL, et al. Acute liver failure is one important cause of fatal dengue infection.

Liver injury is either a direct effect of virus replication in the liver or a consequence of host responses to infection.
## Dengue: Unusual or Atypical Manifestations (1/2)

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurological</strong></td>
<td>Febrile seizures in young children. Encephalopathy.</td>
</tr>
<tr>
<td></td>
<td>Encephalitis/aseptic meningitis.</td>
</tr>
<tr>
<td></td>
<td>Intracranial haemorrhages/thrombosis.</td>
</tr>
<tr>
<td></td>
<td>Subdural effusions.</td>
</tr>
<tr>
<td></td>
<td>Mononeuropathies/polyneuropathies/Guillane-Barre Syndrome.</td>
</tr>
<tr>
<td></td>
<td>Transverse myelitis.</td>
</tr>
<tr>
<td>*<em>Gastrointestinal</em>/</td>
<td>Hepatitis/fulminant hepatic failure.</td>
</tr>
<tr>
<td><strong>Hepatic</strong></td>
<td>Acalculous cholecystitis.</td>
</tr>
<tr>
<td></td>
<td>Acute pancreatitis.</td>
</tr>
<tr>
<td></td>
<td>Hyperplasia of Peyer’s patches.</td>
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<tr>
<td></td>
<td>Acute parotitis.</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td>Acute renal failure.</td>
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<tr>
<td></td>
<td>Hemolytic uremic syndrome.</td>
</tr>
<tr>
<td><strong>Cardiac</strong></td>
<td>Conduction abnormalities.</td>
</tr>
<tr>
<td></td>
<td>Myocarditis.</td>
</tr>
<tr>
<td></td>
<td>Pericarditis.</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>Acute respiratory distress syndrome.</td>
</tr>
<tr>
<td></td>
<td>Pulmonary haemorrhage.</td>
</tr>
<tr>
<td>Organ system</td>
<td>Manifestation</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td>Myositis with raised creatine phosphokinase (CPK). Rhabdomyolysis.</td>
</tr>
<tr>
<td><strong>Lymphoreticular/Bone marrow</strong></td>
<td>Infection associated haemophagocytic syndrome (IAHS) or Haemophagocytic lymphohistiocytosis (HLH). Idiopathic thrombocytopenic purpura (ITP). Spontaneous splenic rupture. Lymph node infarction.</td>
</tr>
<tr>
<td><strong>Eye</strong></td>
<td>Macular haemorrhage. Impaired visual acuity. Optic neuritis.</td>
</tr>
</tbody>
</table>

2009 WHO Revised Dengue Classification

Dengue Case Classification by Severity
2009 WHO revised dengue classification

Dengue case classification by severity

Dengue ± warning signs

Severe dengue

1. Severe plasma leakage
2. Severe haemorrhage
3. Severe organ impairment

Criteria for dengue ± warning signs

Probable dengue
- Live in/travel to dengue endemic area
- Fever and 2 of the following criteria:
  - Nausea, vomiting
  - Rash
  - Aches and pains
  - Tourniquet test positive
  - Leucopenia
  - Any warning sign

Laboratory confirmed dengue
(Important when no sign of plasma leakage)

Warning signs:
- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy; restlessness
- Liver enlargement ≥2cm
- Laboratory: Increase in HCT concurrent with rapid decrease in platelet count

Criteria for severe dengue

1. Severe plasma leakage leading to:
   - Shock (DSS)
   - Fluid accumulation with respiratory distress

2. Severe bleeding
   - as evaluated by clinician

3. Severe organ involvement
   - Liver: AST or ALT ≥1000
   - CNS: Impaired consciousness
   - Heart and other organs

* Requiring strict observation and medical intervention
Co-infection in dengue patients

Co-infection can modify clinical presentations of dengue disease and result in missed or delayed diagnosis and treatment and possible misinterpretation as unusual manifestations.

Concurrent Infections

- Malaria + dengue
- Malaria + dengue + leptospirosis
- Malaria + dengue + leptospirosis + hepatitis E
- Dengue + Kawasaki syndrome
- Dengue + etc.
## Dengue & Kawasaki disease

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Kawasaki Disease</th>
<th>Dengue</th>
<th>Ref</th>
</tr>
</thead>
</table>
Clinical course

day 6

day 8
Clinical course

day 6

IVIG

ASA, echocardiogram
Thisyakorn U, Thisyakorn C. Diseases caused by arboviruses

Successful treatment of DHF depends on early recognition and careful monitoring of the development of shock.

HEMODYNAMIC PROFILES OF PATIENTS WITH DHF DURING TOXIC STAGE: AN ECHOCARDIOGRAPHIC STUDY

- The mechanisms of decreased cardiac output during toxic stage of DHF is complex
- Decreased preload is accompanied by decreased left ventricular performance, and possibly a subnormal heart rate response in some patients

MYOCARDIAL DEPRESSION IN DHF: PREVALENCE AND CLINICAL DESCRIPTION

- Transient myocardial depression is not uncommon in patients with DSS.
- Cardiac dysfunction in children with DSS may contribute to the clinical severity and the degree of fluid overload in these patients.

Initial fluid resuscitation for children with DSS

There is no difference between crystalloids and colloids regarding initial fluid resuscitation in moderate DSS.

No significant evidence to support colloids as the fluid for initial resuscitation in serious DSS.

Any type of colloids is not significantly different from one another.

The decision in choosing appropriate type of fluid depends on the physician’s judgment.

CONTROVERSIES IN DENGUE PATHOGENESIS

• The 1997 WHO case definition is inadequate
• DHF is not significantly associated with second dengue infections
• DHF is caused by virulent viruses
• DHF results from an abnormal T cell response
• DHF results from dengue infection-induced autoimmunity
• DHF results from DENV-infected endothelial cells

DENGUE

Prevention and Control
Global strategy for dengue prevention & control, 2012-2020

GOAL:
TO REDUCE THE BURDEN OF DENGUE

OBJECTIVES:
- To reduce dengue mortality by at least 50% by 2020*
- To reduce dengue morbidity by at least 25% by 2020*
- To estimate the true burden of the disease by 2015

* The year 2010 is used as the baseline.

Technical element 1:
Diagnosis and case management

Technical element 2:
Integrated surveillance and outbreak preparedness

Technical element 3:
Sustainable vector control

Technical element 4:
Future vaccine implementation

Technical element 5:
Basic operational and implementation research

ENABLING FACTORS FOR EFFECTIVE IMPLEMENTATION OF THE GLOBAL STRATEGY:
- advocacy and resource mobilization
- partnership, coordination and collaboration
- communication to achieve behavioural outcomes
- capacity building
- monitoring and evaluation
Global Distribution of *Aedes aegypti* and *Aedes albopictus*

INTEGRATED VECTOR MANAGEMENT

- Advocacy, social mobilization and legislation
- Collaboration within the health sector and with other sectors
- Integrated approach to disease control
- Evidence-based decision-making
- Capacity-building

Dengue Vaccines:
Latest Developments and Future Directions

- Live attenuated virus
- Chimeric virus
- Inactivated virus
- Subunit
- DNA
- Vectored
- Recombinant E proteins
- VLP based
## Tetravalent Dengue Vaccines in Clinical Trial Pipeline

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi Pasteur</td>
<td>Chimeric, 17-D; DENV-1-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takeda/Inviragen LAV+Chimeric</td>
<td>DENV-2 PDK53; DENV-1/2, 3/2 &amp; 4/2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merck/NIH LAV+Chimeric</td>
<td>DENV-1 -3 and -4 Δ30/31; DENV-2/4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GSK Purified Inactivated</td>
<td>DENV-1-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NMRC; DNA</td>
<td>DENV-1-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merck/Hawaii Subunit</td>
<td>DENV-1-4</td>
<td>On hold</td>
<td></td>
</tr>
</tbody>
</table>
Yellow fever V 17D cDNA

Non-structural genes

Exchange with genes of wt dengue 1--4

Non-structural genes

4 chimeric cDNAs

Individually transcribed to RNA

Virus grown in Vero cells

Four individual chimeric Dengue viruses (CYD1-4)
Global strategy for dengue prevention & control, 2012-2020

GOAL:
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Technical element 1: Diagnosis and case management
Technical element 2: Integrated surveillance and outbreak preparedness
Technical element 3: Sustainable vector control
Technical element 4: Future vaccine implementation
Technical element 5: Basic operational and implementation research

ENABLING FACTORS FOR EFFECTIVE IMPLEMENTATION OF THE GLOBAL STRATEGY:
- advocacy and resource mobilization
- partnership, coordination and collaboration
- communication to achieve behavioural outcomes
- capacity-building
- monitoring and evaluation
1st ADVASC Meeting Report

The ASEAN Dengue Vaccination Advocacy Steering Committee (ADVASC) is a newly formed scientific forum dedicated to dengue vaccine advocacy. The committee consists of medical experts including virologists, paediatricians, physicians and experts in the fields of infectious disease, tropical medicine and immunisation. The first meeting of ADVASC was held on 16 December 2011 and served to define the objectives of ADVASC in relation to the introduction of a dengue vaccine in South-east Asia.

The mosquito-borne dengue virus is a potential threat to almost half of the world’s population, with an estimated 60 million people infected annually. Around 500,000 of these infected each year develop dengue haemorrhagic fever (DHF), a severe form of the disease that can lead to dengue shock syndrome and death. DHF is a leading cause of hospitalisation and places a large economic burden on affected countries. South-east Asia and the Western Pacific carry the majority of the global burden, with over 76% of the population at risk of dengue infection living in those regions. The incidence of dengue fever has been rising dramatically, facilitated by increased urbanisation and travel.

Current efforts to halt the spread of dengue focus on mosquito control and reducing virus transmission; however, such efforts alone are not sufficiently effective. A vaccine that protects against the virus would translate into tremendous benefit in the fight against dengue. Vaccines against dengue are in development, with the lead candidate currently undergoing Phase III clinical trials. Estimates suggest that the vaccine will be available for the global market by 2016. Early preparation for vaccine introduction is essential to maximise the benefits of the vaccine.

ADVASC aims to assist the introduction of the dengue vaccine in South-east Asia. This initial meeting provided an opportunity to develop and clarify the group’s identity, objectives and activities. In the first session of the meeting, nine presentations were given by the attendees to provide country-specific background information on the current dengue situation across South-east Asia, as detailed in the following table.

<table>
<thead>
<tr>
<th>Table 1: ADVASC Meeting Presentations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Professor Usa Thayller</strong></td>
</tr>
<tr>
<td>Dengue in the Asia-Pacific region</td>
</tr>
<tr>
<td>75% of global burden is in Asia-Pacific region. Need preparation in advance of vaccine release to ensure rapid introduction.</td>
</tr>
<tr>
<td><strong>Professor Usa Thayller</strong></td>
</tr>
<tr>
<td>Dengue surveillance in Thailand</td>
</tr>
<tr>
<td>Dengue surveillance system in place since 1995, reporting mandatory, usually within 24 hours. Reports are public.</td>
</tr>
<tr>
<td><strong>Dr Mario Raquejo</strong></td>
</tr>
<tr>
<td>The Global Dengue d2V Initiative</td>
</tr>
<tr>
<td>d2V aims to establish and document burden of dengue, raise awareness of vaccination benefits, provide guidance in relation to introduction and advocate for funding.</td>
</tr>
<tr>
<td><strong>Dr Mario Raquejo</strong></td>
</tr>
<tr>
<td>Dengue and vaccination programmes in the Philippines</td>
</tr>
<tr>
<td><strong>Dr Daniel Goh</strong></td>
</tr>
<tr>
<td>Dengue in Singapore</td>
</tr>
<tr>
<td>High attack rate for inhabitants for child healthdiseases. Good vaccine acceptance and coverage. Infrastructure for implementation already, but some concerns over new vaccine. National Environment Agency (NEA) currently undergoing mosquito control.</td>
</tr>
</tbody>
</table>
OBJECTIVES

• Identifying & making practical recommendations on:
  - Improved surveillance and case diagnostics
  - Select initial groups for vaccination
  - Address program feasibility
  - Prepare and implement risk management plan
• Communicating recommendations to all stakeholders
• Collaborating with other relevant dengue initiatives

Thisyakorn U. Vaccine 2012; 30: 5587-8
Letter to the Editor

ADVASC—New regional initiative supporting transition from dengue vaccine to vaccination in Southeast Asia

Keywords:
Advocacy
ASEAN
Dengue
Vaccination

Dear Editor,

I am pleased to announce the formation of a new scientific forum dedicated to dengue vaccine advocacy in Southeast Asia. The ASEAN Member States Dengue Vaccination Advocacy Steering Committee (ADVASC) aims to disseminate information and make recommendations on dengue vaccine introduction strategies in Southeast Asia.

ADVASC members (Table 1) include virologists, paediatricians, physicians and experts across the fields of infectious disease, tropical medicine and immunisation. Countries represented include Indonesia, the Philippines, Malaysia, Singapore and Thailand. ADVASC recognises the value of partnerships with other groups working on dengue and vaccine introduction in the region, and intends to work wherever possible with the World Health Organization (WHO), the Dengue Vaccine Initiative (DVI) and the Dengue Vaccine to Vaccination Initiative (dengue v2V) [1].

The objectives of ADVASC were agreed at the inaugural Steering Committee meeting held in Bangkok on 16 December 2011 (Box 1). Presentations at the meeting addressed topics of dengue epidemiology—documenting the increasing prevalence of the disease across the ASEAN region and at the individual country level—and dengue infection in adults, which is often misdiagnosed due to the perception of dengue as a paediatric disease.

Dengue is a mosquito-borne viral disease found throughout equatorial regions and is a potential threat to almost half of the world’s population [2]. Many factors have contributed to a recent dramatic rise in dengue fever cases, including increased urbanisation and travel [3]. Recent studies estimate that 50–100 million people are infected per year, of whom about 500,000 develop dengue haemorrhagic fever (DHF) – a severe form of the disease and 22,000 die [4].

More than 70% of the population at risk for dengue worldwide (around 1.8 billion people) live in the regions of Southeast Asia and the Western Pacific that bear nearly 75% of the current global dengue burden [5].

There is currently no specific antiviral treatment for dengue and preventing the disease through vector control methods alone is problematic. Vaccines for dengue are in development, with the lead candidate currently in Phase III clinical trials and estimated to be available by 2015 [6].

Box 1: Objectives of ADVASC

1. Identifying opportunities and making practical recommendations about how to:
   a. Improve surveillance and laboratory capacity for dengue disease confirmation, including:
      i. Documenting and standardising existing systems and coverage
      ii. Standardising case confirmation and diagnostics
   b. Select initial target groups for vaccination
   c. Address programme feasibility by improving existing infrastructure (cold chain, pharmacovigilance, vaccination compliance monitoring, and vaccine supply and distribution logistics)
   d. Prepare and implement a risk management plan
2. Communicating recommendations to:
   a. National and local government bodies
   b. International, regional, and local medical and academic societies
   c. Other stakeholders including WHO (Southeast Asia and Western Pacific Regional Offices)
   d. The public/media
3. Collaborating with other relevant dengue initiatives including v2V and DVI

Table 1

<table>
<thead>
<tr>
<th>ADVASC members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor Uta Thongsuk (Chair)</td>
</tr>
<tr>
<td>Dr Maria Rosalina Clavellino</td>
</tr>
<tr>
<td>Dr Daniel Coh</td>
</tr>
<tr>
<td>Dr Zaifuddin Hamid</td>
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<tr>
<td>Professor Taepong Tanawirun</td>
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<tr>
<td>Dr Satire Yehas</td>
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<tr>
<td>Professor Sri Rezeki Hadiningro</td>
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</tbody>
</table>

Early preparation for vaccine introduction will ensure that the vaccine can reach those who need it as early as possible. In 2012, ADVASC intends to focus on understanding dengue surveillance systems in Southeast Asia, making recommendations on regional standardisation and identifying gaps in diagnostic capabilities and case classification. Robust surveillance of dengue will allow valid assessment of vaccine impact and aid control of the disease.

Financial disclosure

ADVASC is supported by an unrestricted educational grant from Sanofi Pasteur.
Recommendations from ADVA

Standardizing the monitoring & reporting of dengue in the ASEAN region
CONCLUSION

• The human and economic cost of dengue are significant and likely to be even higher than estimated

• Disease prevention is a key to public health
ACPID 2016
Bangkok, Thailand
8th Asian Congress of Pediatric Infectious Diseases
15-18 November, 2016

Join Us in Bangkok!

We look forward to welcoming you to the spectacular city of Bangkok in November 2016!

www.pidst.or.th
THANK YOU