

The Pediatric Dengue Vaccine Initiative (PDVI)

Thailand, 2007



The Vaccine Enterprise-the disease

- Clinical data
- Surveillance data
- Laboratory data/diagnostics
- Input, analysis and reporting



The Vaccine Enterprise-the disease

- Clinicians/care givers
- Epidemiologists
- Statisticians
- Data monitors
- Outreach workers
- Health educators
- Health communicators
- Public health workers



The Vaccine Enterprise-the products

- Diagnostics
- Vaccines



Vaccine Enterprise-the products

- Scientists
- Product developers/distributors
- Regulators
- Policy makers
- Public health officials
- Communities/media
- Individuals

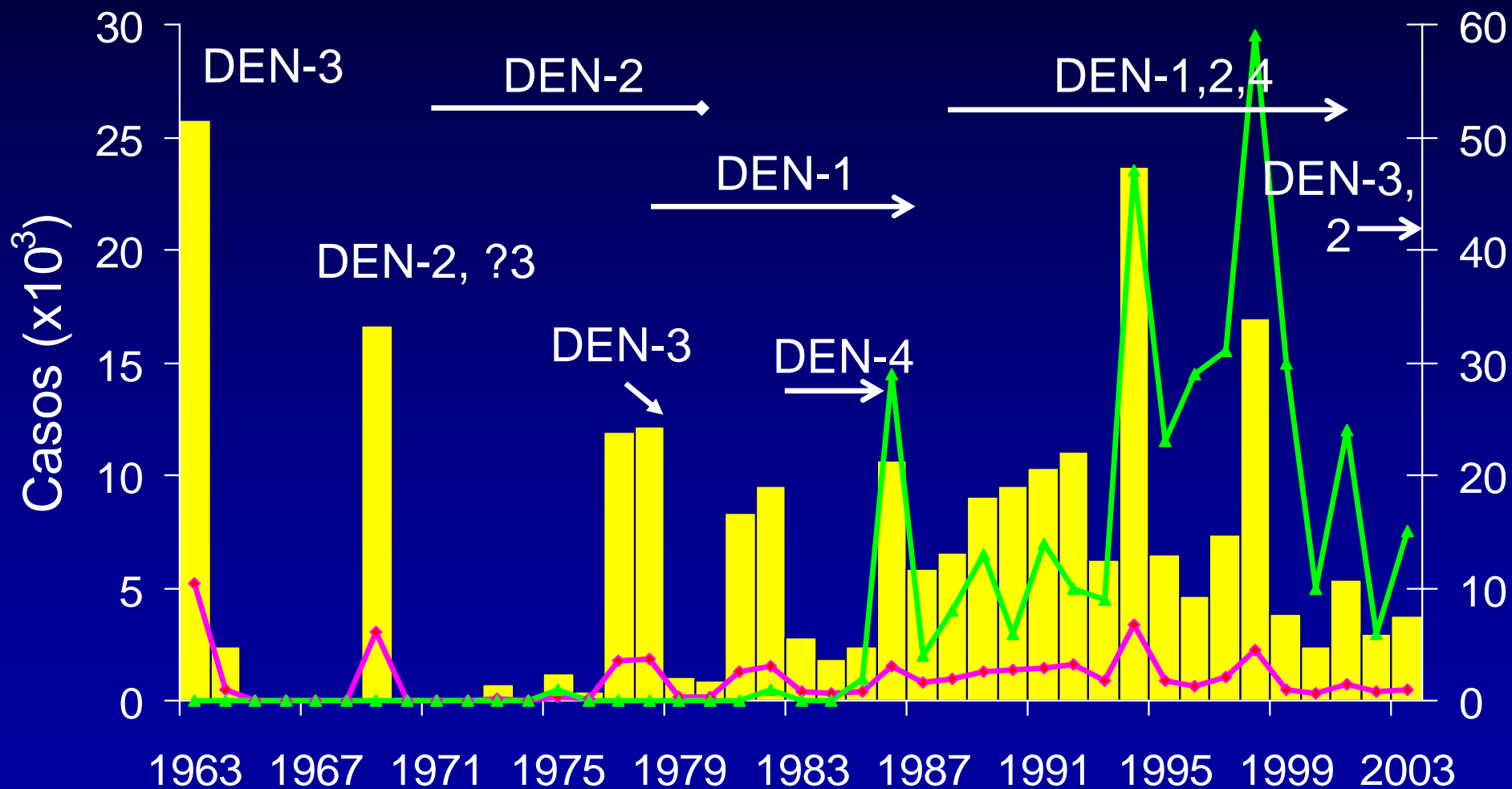


Dengue Burden

- **2.5- 3 billion people (40% of the world) at risk of infection**
- **An estimated 50 and 100 million cases of dengue fever occur annually**
- **250,000 and 500,000 people develop DHF and DSS each year**
- **20,000 deaths each year**



Dengue en Puerto Rico, 1963-2003



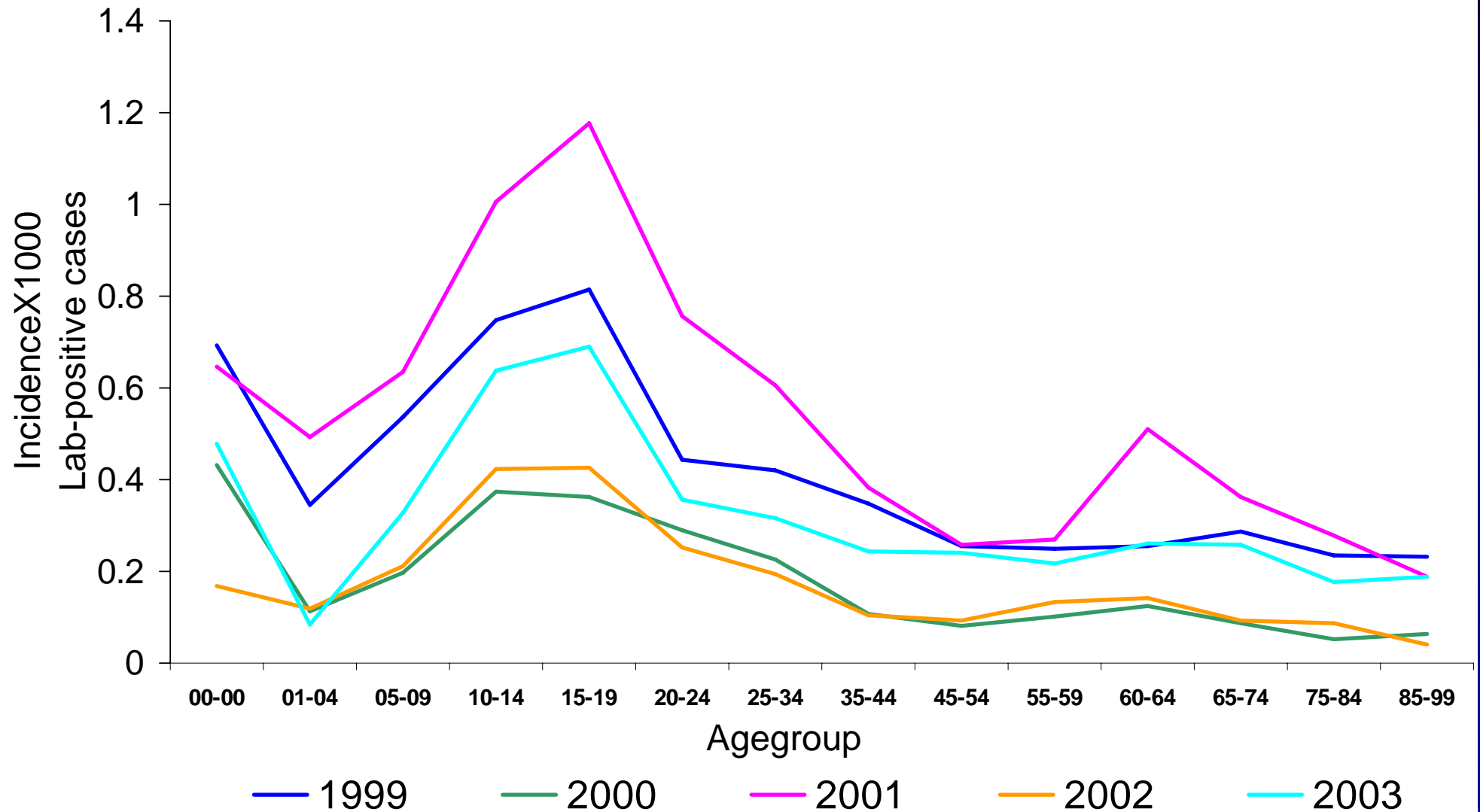
Casos

Tasa/1000

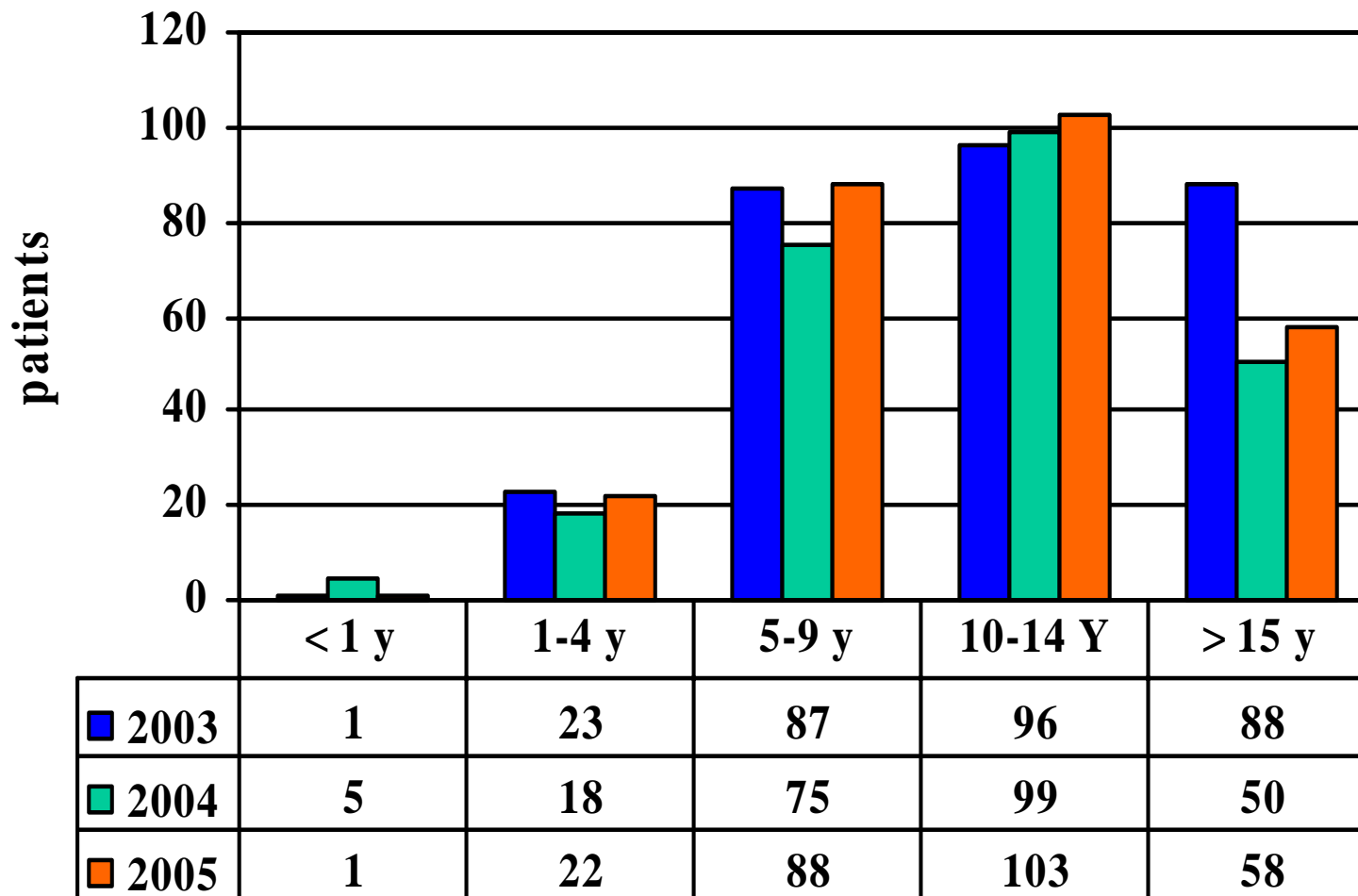
Casos DH positivos por lab



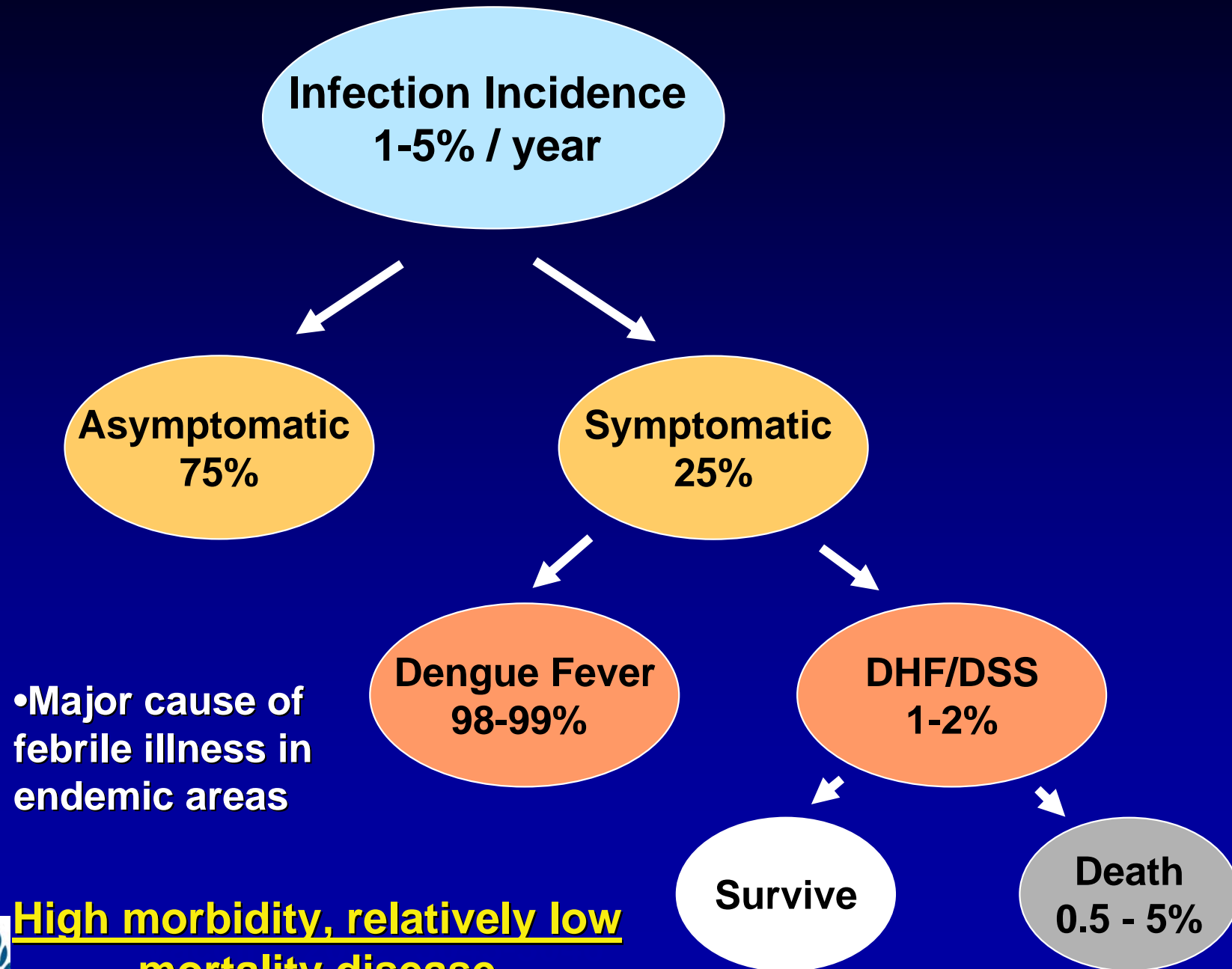
Age group-specific dengue incidence by year, Puerto Rico 1999-2003



Dengue cases by age, Ratchaburi Province, Thailand, 2003-2005



Dengue Virus Infection



High morbidity, relatively low mortality disease



Dengue Cost of Illness: Preliminary Data

- Costs were expressed in 2005 international dollars (I\$) to adjust for purchasing power parity
- Ambulatory patient
 - Mean total cost per case I\$514 (SD \$601)
 - Range: I\$158 (Guatemala) – I\$699 (Brazil)
- Hospitalized patients
 - Mean total cost per case I\$1491 (SD \$1052)
 - Range: I\$752 (Guatemala) – I\$2182 (Thailand)



Some Background

- Formed in late 2001 at a meeting in Ho Chi Minh City, Vietnam
- 2001-2006 – Rockefeller Foundation funding (~\$1.7 million)
- July 2003 – 5-year grant from Bill and Melinda Gates Foundation for \$55 million
- A product development partnership (PDP)
- Program of International Vaccine Institute (IVI)



PDVI

Mission

To accelerate **evaluation** and **introduction** of dengue vaccine for use in developing countries

Measure of Success

Introduce dengue vaccine into national immunization program of at least one developing country in each dengue endemic region

Strategic Plan

Dengue Vaccines : The Role of the Pediatric Dengue Vaccine Initiative



www.pdvi.org



PDVI Program Directions

The Vaccine Pathway



Discovery

Evaluation
(Development)

Introduction
(Distribution)



PDVI Programs

Strategic Partnerships

Supportive R&D

Vaccine Evaluation

Vaccine Access



The Programs



Strategic Partnerships

- **Partnerships** with both public and private institutions
- **Portfolio** of vaccines



Public and Private Sector Partnerships

Private Sector

▪ Vaccine manufacturers

- Biologicals E
- Butantan
- GlaxoSmithKline
- Hawaii Biotech
- InViragen
- Panacea
- sanofi pasteur
- Shantha Biotechnics

▪ Diagnostics

- Standard Diagnostics, Korea
- Pentax, Japan
- Pan Bio, Australia



Public Sector

▪ World Health Organization

- Initiative for Vaccine Research (IVR)
- Special Programme in Tropical Disease Research (TDR)
- Developing Country Vaccine Regulators Network (DCVRN)

▪ US Department of Defense

▪ US Centers for Disease Control and Prevention

▪ Novartis Institute of Tropical Diseases



The PDVI Vaccine Portfolio

Developer	Commercial Partner	Approach
Live Attenuated		
WRAIR	GSK	Cell culture passage
Acambis	Sanofi Pasteur	17D Yellow fever – Dengue chimera
NIH / LID	Biological E Butantan Panacea	Dengue 4- dengue chimeras or attenuation by gene deletion
CDC	InViragen / Shantha	Dengue 2 - dengue chimeras and attenuated dengue 2
Subunit		
Hawaii Biotech	Hawaii Biotech	Envelope + NS1 recombinant proteins

Where are we Today with Dengue Vaccines ?

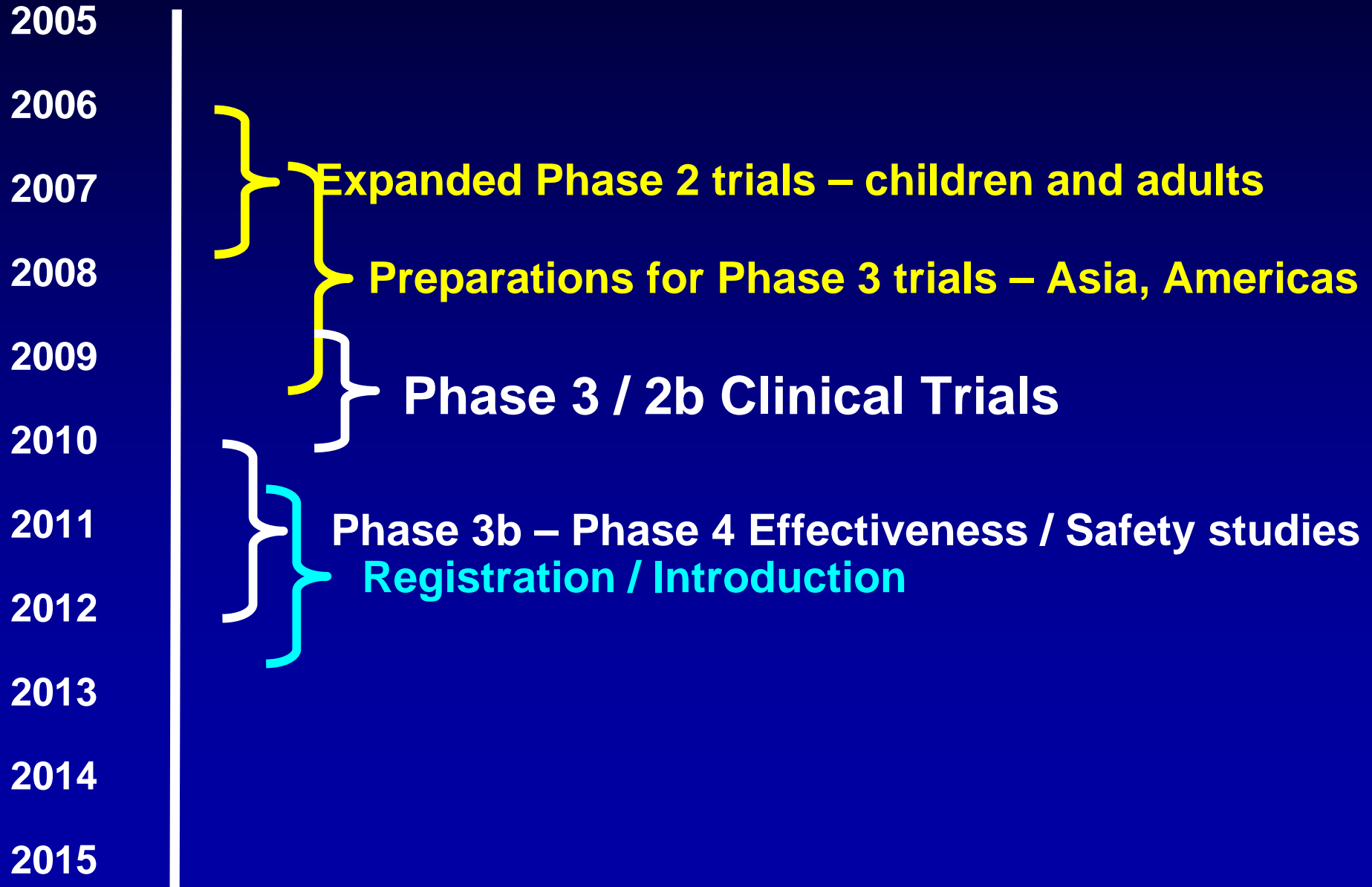


Status of Dengue Vaccines- 2007

- 5 candidates – different vaccine types
- Phase 2 trials – 2 vaccines
 - GlaxoSmithKline
 - sanofi pasteur
- Phase 1 trials
 - NIH vaccine
- Pre-clinical – 2 vaccines
 - Hawaii Biotech
 - InViragen / Shantha

No large-scale proof of concept trials

Estimated Dengue Vaccine Timeline



Why PDVI is Working with a Portfolio of Dengue Vaccines

- No assurance that any one vaccine will be successful in a Phase 3 trial – getting multiple types of vaccines into clinical trials
- Availability of multiple vaccines is more likely to ensure:
 - An affordable vaccine
 - Sustained and sufficient availability of product



What are we Doing - 2007

- **'Big' Companies**

- Collaboration / participation in PDVI program activities
 - Supportive R&D, Vaccine Evaluation, Vaccine Access

- **'Small' Companies**

- Direct funding:
 - Process development – cGMP vaccine to enter Phase 1-2 trials



Supportive Research and Development



Supportive Research and Development

The Gaps - 2003

- No high throughput assays to measure virus-type specific protective antibody to dengue virus infection (correlate of protection)
- No assays to measure antibodies associated with antibody enhanced disease (AED)
- No tools to validate existing dengue diagnostics or plaque reduction neutralization assay



Filling the Gaps

- **Network of research laboratories** (virology, structural biology, cell biology, immunology, assay development) **has developed a portfolio of specialized assays to measure:**
 - **protective antibody to dengue virus infection**
 - **immune enhancing antibody**
- **Tools to evaluate diagnostic tests and specialized assays**
 - **Dengue Diagnostics Laboratory Network**
 - **Evaluation Panel for IgM anti-dengue tests**
 - **Commercially available IgM anti-dengue tests evaluated**



Guidance document for performance of PRNT



Vaccine Evaluation



Vaccine Evaluation

The gaps - 2003

- Multiple vaccines under development with no plan forward to evaluation
- Limited sites in dengue endemic countries with adequate data on disease (dengue fever) incidence and capacity to conduct clinical trials
- No agreement on key elements for clinical trials of dengue vaccines (e.g., primary endpoint)



PDVI Vaccine Evaluation Program

- Facilitate evaluation of vaccines, primarily in large-scale clinical trials
- Develop guidelines for large-scale clinical trials of dengue vaccines
- Develop provisional guidelines for dengue immunization strategies

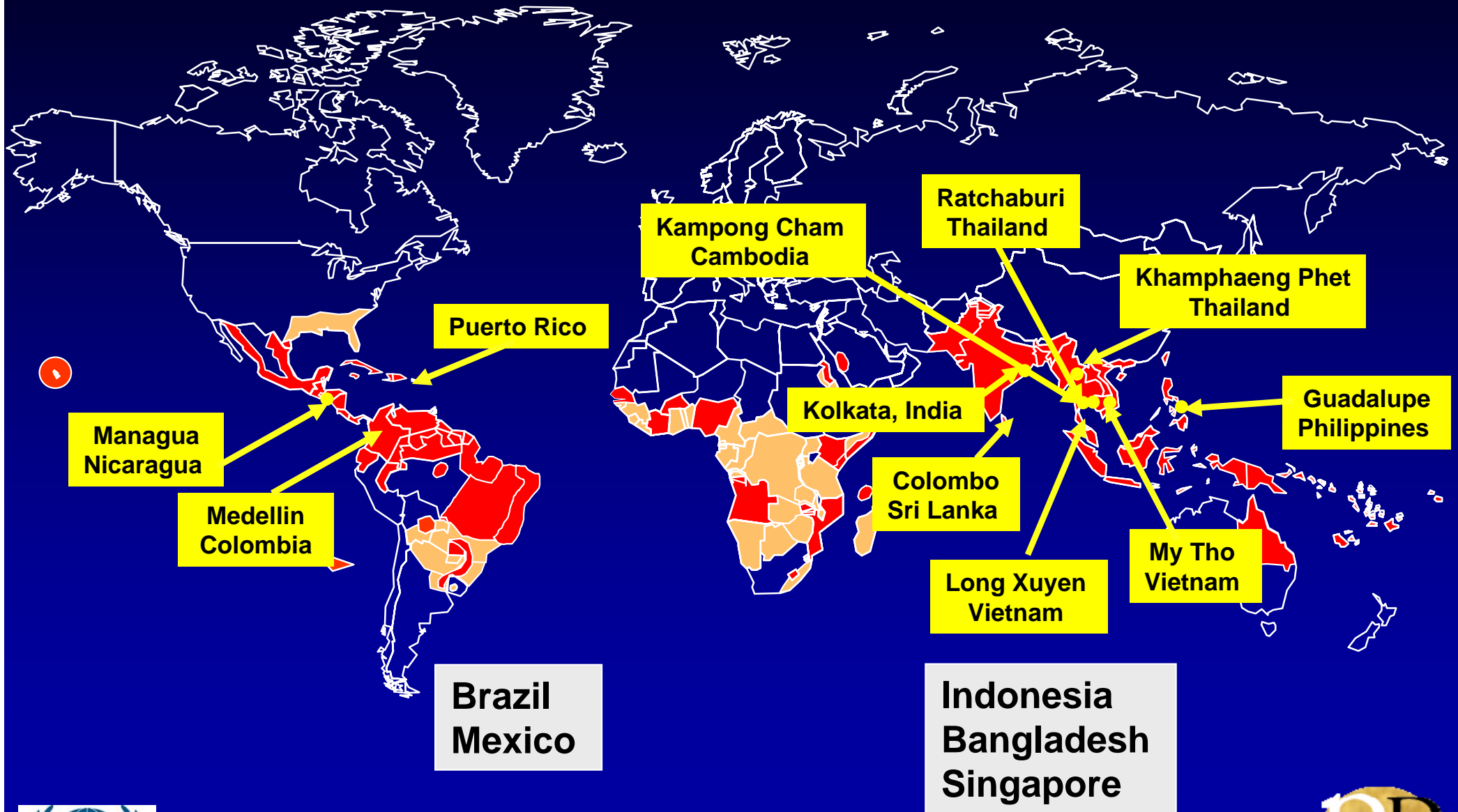


The PDVI *Field Site Consortium*

- **Multiple sites** – Asia and Americas
- **Multiple partners** – academia, NGOs, governments
- **Networked** – case definitions, proficiency testing, data sharing, pooled data analysis
- **PDVI Support** – epidemiologic, data management, laboratory proficiency
- **Governance** – access to specimens, access to sites for clinical trials



Field Site Consortium, 2007



Vaccine Access



Vaccine Access

The Gaps - 2003

- **Lack of regulatory pathways in developing countries to approve dengue clinical trials and vaccines**
- **No organized advocacy for dengue vaccines among endemic countries or the “vaccine community”**
- **No provisional Dengue Vaccine Investment Case**



Vaccine Access

- **Better information**
 - **Epidemiologic - surveillance, burden of disease**
 - **Economic**
 - **Costs of dengue and vector control**
 - **Comparative economic studies**
 - **Vaccine markets**
 - **Models**
 - **Effects of immunization**
- **Prepare for vaccine introduction**
 - **Advocacy - regional networks of experts (“dengue prevention boards”)**
 - **Capacity building among developing country vaccine regulators**
 - **Mechanisms to sustain vaccine access**

Dengue Prevention Boards

- **Asia – Pacific Dengue Prevention Board**
 - Inaugural meeting December 9-11, 2006
 - 2nd meeting: Dengue Surveillance June 21-23, 2007
Colombo, Sri Lanka
- **Americas Dengue Prevention Board**
 - Inaugural meeting July 23-25, 2007 Managua, Nicaragua



Dengue Prevention Boards

Contribute to and encourage actions to improve prevention and control of dengue virus infection in the region, particularly as they relate to the anticipated availability of dengue vaccines.



The Future



Near-term (2008 – 2015)

- **Create an enabling environment**
 - Facilitate and collaborate in Phase 3 trials
 - Improve diagnostics / validate assays for vaccine correlates of protection
 - Develop new assays to identify breakthrough infections/disease in vaccinated persons
 - Guide vaccine registration in developing countries
 - Expand field sites and lead post-Phase 3 vaccine trials / studies



Longer-term (2012 – 2020)

■ Achieve the Public Health Outcome

- Enable availability of dengue vaccine for developing countries - the dengue vaccine investment case
- Guide introduction of dengue vaccine, including safety monitoring, into national immunization programs of dengue endemic countries
- Monitor effectiveness of vaccine introduction through national dengue surveillance programs



Discussion

