Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

State of the Art in the Prevention and Control of Dengue in the Americas

Meeting Report

28–29 May 2014 • Washington DC, USA

dengue

Summary

I. INTRODUCTION

Dengue is the most widespread vector-borne viral infection in the world, representing a severe public health problem[1]. The infection is caused by the dengue virus, of which four serotypes (Denv1, Denv2, Denv3 and Denv4) are known, and the main vector in the Americas is the *Aedes aegypti* mosquito[2]. This disease affects populations of all ages and socio-economic levels, with an estimated 2.5 billion people living in endemic countries at-risk and 50 to 100 million cases per year. The Region of the Americas is not an exception; dengue incidence has increased 30 times in the last fifty years, and between 2008 and 2012 more than 1.2 million cases of dengue were notified annually, including 28,233 severe cases and 1,000 deaths. Furthermore, 2013 had the highest burden of disease ever registered, with the largest epidemic in the history of the Americas, with a total of 2.3 million cases, 37,898 severe cases and 1,318 deaths[3]. This disease has a high social and economic impact, affecting not just the patient, but also families and the community as a whole. The estimated economic cost of the disease supersedes 2.1 billion US dollars per year[4].

PAHO/WHO, through the Dengue Regional Program, supports member states in the implementation of the Integrated Management Strategy for the Prevention and Control of dengue (IMS-Dengue) (Fig. 1). This strategy was adopted by the countries of the Americas through the Resolution of Governing Bodies CD44.R9 in 2003; since then, 22 countries of the Americas have developed national IMS-Dengue Prevention and Control Plans. In addition, 20 of the countries have completed an assessment of their IMS-Dengue strategy, with the support of experts from the International Technical Group on Dengue (ITG-Dengue), following the recommendations of Resolution CSP27.R15, adopted in 2007 by the 27th Pan American Health Organization Sanitary Conference.

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[1]WHO. Dengue hemorrhagic fever: Diagnosis, treatment, prevention and control. Geneva. World Health Organization, (1997): 12-23

[2]WHO. Strengthening Implementation of the Global Strategy for Dengue Fever and Dengue Hemorrhagic Fever, Prevention and Control. Report of the informal consultation, 18.20 October, 1999. Available at: http://www.who.int/csr/resources/publications/dengue/whocdsdenic20001.pdf. Accessed on June 5th, 2014.

[3]PAHO. Number of Reported Cases and Severe Dengue (SD) in the Americas, by Country. Available at: http://www.paho.org/dengue. Accessed on June 5th, 2014.

[4]Shepard, Donald S., Laurent Coudeville, Yara A. Halasa, Betzana Zambrano, and Gustavo H. Dayan. "Economic impact of dengue illness in the Americas. *"The American journal of tropical medicine and hygiene* 84, no. 2 (2011): 200-207.

Among the current efforts of the Regional Dengue Program are the following: **1) Strengthen epidemiological surveillance of dengue,** through the development of a generic model of an integrated epidemiological surveillance system, **2) Strengthen laboratory networks** in the management of effective practices in the diagnosis of dengue through the Dengue Laboratory Network of the Americas (**RELDA,** acronym is from the Spanish name of the network), **3) Strengthen vector monitoring and control** in entomology, integrated vector management, and monitoring of insecticide resistance, **4) Improve clinical management of patients,** through the adaptation for the Americas of the WHO clinical guidelines published in 2009; a second edition of which is currently in progress, and **5) Strengthen social communication** by use of communication planning methodologies to impact behaviors of populations facing the dengue problem, including political leaders, health officials, residents, and other stakeholders.

The Regional Dengue Program convened a meeting to examine achievements and challenges over the past 10 years of implementation of the IMS-Dengue strategy, and engage stakeholders in a discussion of future steps. Sessions on initiatives evolving in the Americas, including vaccines and vaccine development, the economic impact of dengue, and emerging technologies for vector control were also included. This report is a summary of the presentations, discussions and recommendations from the *Meeting on the State of the Art for the Prevention and Control of Dengue in the Americas,* held May 28-29, 2014 in Washington, D.C.

Figure 1. Integrated Management Strategy for the Prevention and Control of Dengue in the Americas (IMS-Dengue), PAHO/WHO (2014)

II. MEETING OBJECTIVES

1. Review the currently available knowledge of and experiences for surveillance, detection, diagnosis, management, treatment, and prevention of dengue.

2. Derive conclusions and recommendations that will help the Dengue Regional Program to modify and update its strategies and technical cooperation plans, as well as its role in the prevention and control of dengue in the Americas.

3. Learn from the experiences of countries in the Americas who have been focusing on generating knowledge through research and practice, of how to better approach dengue in the 21st century.

4. Review preliminary results of a systematic review of the published literature for each component of the IMS-Dengue strategy to identify research opportunities and gaps.

III. MEETING SESSIONS

1. Current dengue situation

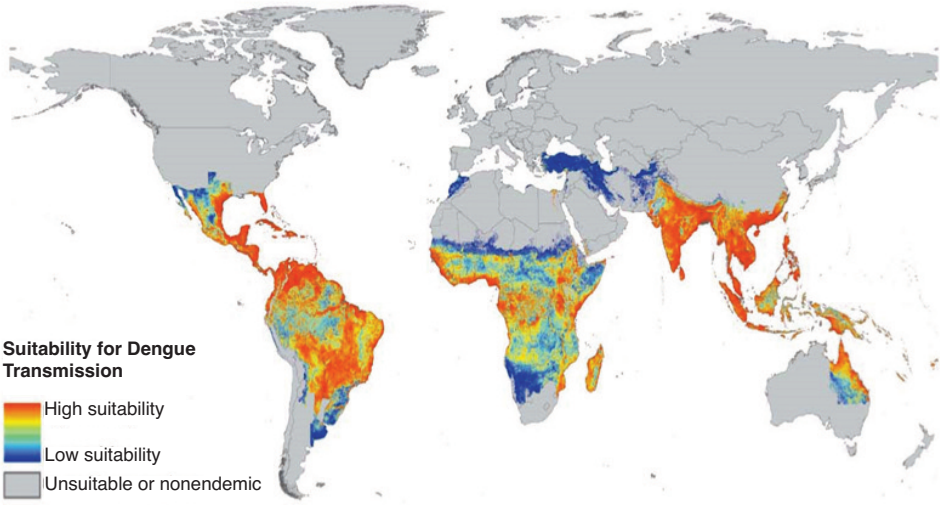
Facilitator: Dr. Luis Gerardo Castellanos, PAHO/WHO

Presentations on the global and regional dengue situation provided the overall context and background for the *Meeting on the State of the Art for the Prevention and Control of Dengue in the Americas*.

1.1. Global

Dr. Raman Velayudhan, Coordinator of the Vector Ecology and Management Unit in the Neglected Tropical Diseases Division of the World Health Organization in Geneva, Switzerland, presented information on the global risk for dengue across regions, the number of dengue cases reported to WHO by WHO regional offices, and the total number of deaths due to dengue (Figure 2). While the number of dengue cases continues to increase, mortality due to dengue has not risen as significantly. The greatest number of dengue cases is reported from the Americas, due in part to improved surveillance and reporting all forms of dengue cases, not just severe dengue. The African region continues to be an area of concern, with little data available outside of periodic outbreaks. The WHO *Global strategy for the prevention and control of dengue 2012-2020* was presented, the goal of which is to reduce the burden of dengue by reducing dengue mortality by 50% and morbidity by 25% by 2020. An immediate objective is to more accurately measure the burden of disease by 2015, currently underway by expanding earlier economic studies to estimate the full burden of disease.

Figure 2. Global dengue risk, 2014



Source: Simmons CP et al. N Engl J Med 2012; 366: 1423 - 1432

The Global Strategy is based on five technical elements intended to work together in an integrated fashion: *Diagnosis and case management; Integrated surveillance and outbreak preparedness*; Sustainable vector control; Future vaccine implementation; Basic operational and implementation research. The importance of five enabling factors for the successful implementation of the Global Strategy *(Advocacy and resource mobilization; Partnership, coordination and collaboration; Communication to achieve behavioral outcomes; Capacity building;* and *Monitoring and evaluation*) is highlighted in the document (Figure 3). Advances and challenges on a global level for each technical element and enabling factor were presented, with one of the weaker areas identified being the limited number of vector control tools, along with the urgent need to strengthen country capacity to monitor insecticide resistance. The recently established Vector Control Advisory Group (VCAG) is a response to this need, and serves as a WHO advisory group to provide recommendations on the use of new tools and technologies for vector control. The goal is to decrease duplication of efforts across the regions, and support increased research to help countries meet the global targets.

Figure 3. WHO Global Strategy implements needs

Source: WHO Global Strategy Plan

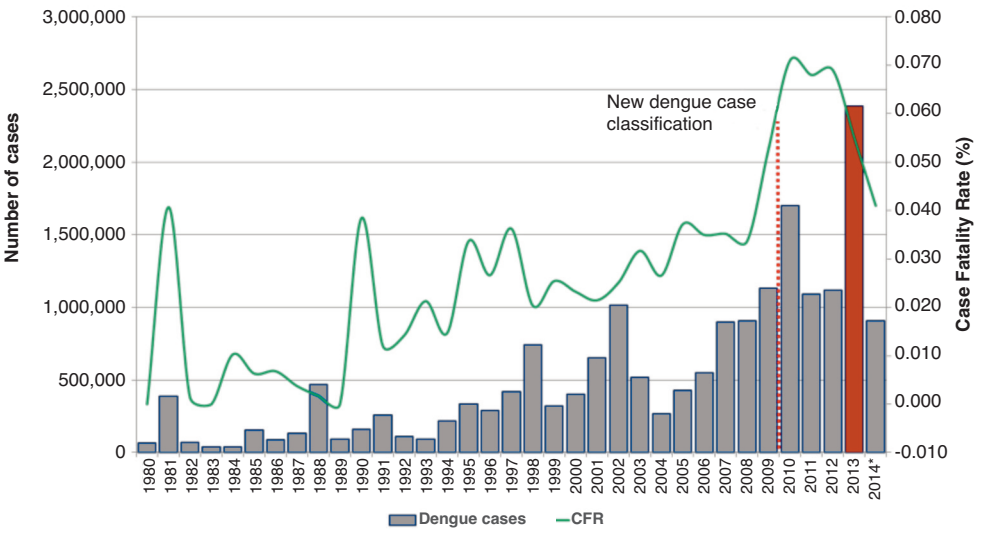
1.2. Region of the Americas

Dr. José Luis San Martín, Regional Advisor on Dengue, PAHO/WHO, presented data from the Americas showing the great majority of countries in the Region report circulation of all 4 dengue virus serotypes. Over 44 countries/territories reported 2.3 million dengue cases in 2013, the year with the greatest number of dengue cases reported in the history of the Americas. However, the case fatality rate (CFR) due to severe dengue has shown a decline in the Region over the past three years, and the region of the Americas has the lowest CFR of any WHO region (0.055%). This is attributable in part to use of the new dengue severity classification and intensive efforts to train physicians on the proper management of dengue cases (Figure 4). Data showing the widespread distribution of *Aedes aegypti* in the Region highlights the challenges facing vector control programs. An analysis of dengue cases and the social and economic determinants of health revealed that countries with higher levels of social inequality (Gini index), illiteracy, and populations living without access to water and sanitation services also had the highest prevalence of dengue.

The Integrated Management Strategy for the Prevention and Control of Dengue (IMS-Dengue) was developed to more effectively address the factors that influence the proliferation of the mosquito vector and facilitate disease transmission, through coordinated actions across the dengue program components of *Social communication, Environment, Laboratory, Patient care, Integrated vector* management, and Epidemiology (Figure 1). The IMS-Dengue has a conceptual and legal framework affirmed by the PAHO Directing Council over the past ten years, and the strategy has been implemented in the majority of the countries/territories of the Region, and evaluated in 22.

Evaluation results support the need for a strategic, multisectoral operational approach to strengthen the core capacity of national dengue programs, with a strong focus on health systems in order to reduce the dengue case fatality rate. This calls for: (1) strengthening of public policies for development and health, (2) an integrated and intersectoral response to outbreaks and epidemics that involves sectors other than health, such as water and sanitation, and (3) increased attention to actions at the household level such that greater responsibility for dengue breeding site control on household premises is assumed by householders.

Figure 4. Number and case fatality rate (CFR) of dengue in the Americas, 1980 – 2014*



* As at Epidemiological Week 25 – Updated July 8th, 2014
Source: Dengue report from countries PAHO/WHO

Conclusions

1. Dengue is a health problem that threatens and affects a significant number of people around the world. The highest number of cases is reported from the region of the Americas, constituting a public health priority for PAHO/WHO. In spite of this, this region also recorded the lowest dengue case fatality rate when compared to other WHO regions.

2. Data from the past 10 years and analysis of inequalities in health determinants show that dengue continues to create a significant health, economic and social burden in endemic countries of the Americas.

3. The general dengue trend shows a steady increase in the number of cases and the populations living in areas at risk, showing a geographical expansion of the vector in areas vulnerable to the occurrence of cases and outbreaks.

4. PAHO/WHO and the countries of the Americas should make an effort to establish an intersectoral approach on the social and economic determinants of health as dengue is not a problem exclusive to the health sector. These efforts should take into account issues of equity.

5. The IMS-Dengue has been adopted, adapted and implemented by the majority of countries in the Americas since 2003, and 22 countries have participated in an evaluation of the implementation process.

6. The new WHO Global Strategy and the PAHO/WHO IMS-Dengue regional strategy are aligned for the achievement of their respective goals and targets, utilizing technical elements that cover the same general program components and areas of strategic emphasis in each plan.

2. Implementation of the Integrated Management Strategy for Dengue Prevention and Control in the Americas (IMS-Dengue)

Facilitator: Dr. Jose Luis San Martín, PAHO/WHO

The Integrated Management Strategy for Dengue Prevention and Control in the Americas (IMS-Dengue) is the model for technical collaboration and integrated program management between the PAHO/WHO Regional Dengue Program and the countries of the Americas (Figure 1). It uses peer-to-peer technical support, with experts from countries throughout the Region, the International Technical Group-Dengue (ITG-Dengue), working as a team with national technical teams in the preparation of their national Integrated Management Strategy for Dengue Prevention and Control (national IMS-Dengue plan), provision of technical assistance during imple- mentation and evaluation of the plan, or during dengue outbreaks/ epidemics. Over the past 10 years, capacity building has been carried out with standardization of protocols, indicators and technical training taking place across the Americas, in each of the five IMS-Dengue components.

2.1. Social communication

Dr. Linda Lloyd, ITG-Dengue member, presented the achievements, strengths and challenges of the *Social communication and behavior change* component over the past 10 years, in addition to proposed next steps. She noted that the compoznent is rooted in the broader framework of health promotion, but that the term "Social communications" was selected as the name for the component due to the importance of communication across all of the IMS-Dengue components. The objective of the Social communications component is to strengthen country capacity for implementation of *social communications* interventions focused on changing targeted behaviors as part of an integrated dengue prevention and control program.

In 2003, WHO's Communication for Behavioural Impact (COMBI) planning methodology as selected as the tool for developing social mobilization and communications activities focused on behavior change by the PAHO/WHO Regional Dengue Program, and in 2004 the first

planning guide for dengue was published. Capacity building through train-the-trainer workshops (n=23) were held throughout the Region; an interactive video game that focuses on sanitation, vector-borne diseases, and community and intersectoral participation (*Pueblo Pitanga: Enemigos silenciosos* / *Pittsville Town: Silent Enemies*) developed by the Regional Dengue Program has been downloaded over 44,000 times; and two evaluations of the *Social communications* component were conducted in 2005 and 2009. As a result of the 2009 evaluation, the COMBI planning process was modified from 15 to 10 steps based upon the practical experiences and national program staff recommendations from the 15 countries participating in the evaluation.

Strengths noted include recognition of the value of social communications in dengue prevention and control, increased communications knowledge and practice, creation of multidisciplinary IMS-Dengue teams, use of data for decision-making regarding behaviors and identification of target audiences, and community empowerment at the community and Ministry of Health staff levels. Challenges included weaknesses in implementation of the COMBI planning methodology, lack of continuity due to staff turnover, a lack of validated behavior indicators that can be incorporated into routine dengue program monitoring, lack of support from ministries of health and local governments for sustained communications and behavior change interventions, and the ongoing belief that health and illness are the sole responsibility of the health sector. Proposed next steps are strengthening communication with policy makers for implementation of the IMS-Dengue strategy, supporting communications and behavior change capacity building within ministries of health, working with countries to strengthen risk and crisis communications for dengue outbreaks, and publishing an updated, revised edition of the COMBI planning guide using regional experiences.

2.2. Laboratory

Dr. Elizabeth Hunsperger, CDC Dengue Branch-Puerto Rico, RELDA member and ITG-Dengue member, presented a brief overview of the virus, antibody and antigen dynamics during primary and secondary dengue infections, and the Dengue Laboratory Network of the Americas (RELDA)-approved flowchart for laboratory confirmation of dengue infection.

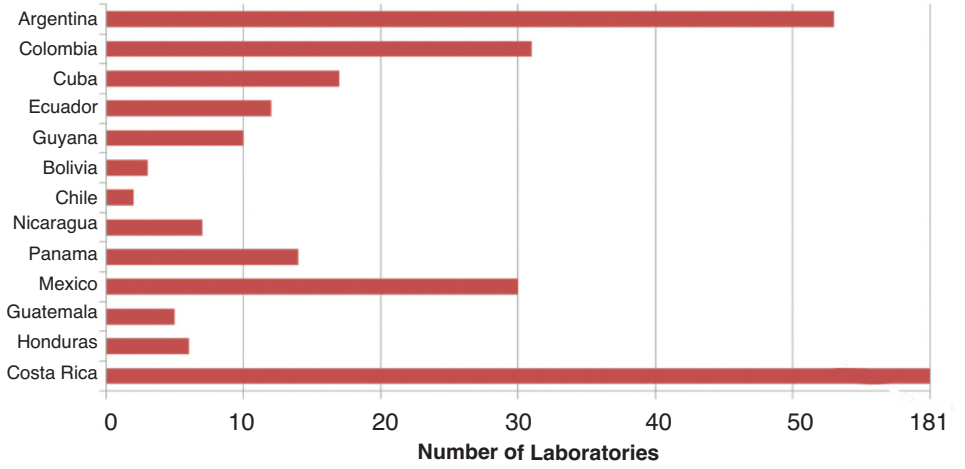
RELDA was established as part of the IMS-Dengue *Laboratory* component; it is coordinated through the Consultative Technical Committee with representation from five regional laboratories, four of which are Collaborating Centers. A total of 28 countries of the Region with their national reference laboratories are members of RELDA, all of them with dengue diagnostic capacity. RELDA's objectives are to integrate the scientific and technical capacity available in the Region to provide a systematic surveillance for dengue and respond to outbreaks and epidemics; strengthen the technical and scientific capacity of dengue laboratories in the Region; normalize laboratory protocols, evaluation of kits and diagnostic methods, and exchange of reference reagents; support the implementation of a quality control system in dengue laboratories; and implement a research agenda. Achievements to date include capacity building through training courses (4 completed and one planned for summer 2014), integrated laboratory response during outbreaks and epidemics, establishment of a system for exchange of reference reagents within the Region, and a quality control system that uses a proficiency panel specific to the Region managed by RELDA in collaboration with several laboratories of the Region.

In 2010, RELDA surveyed its member laboratories to determine regional capacity, laboratory methods used, laboratory networks, quality control, and diagnostic capacity for other flaviviruses (Figure 5). Information regarding facilities for dengue diagnostics and other arboviruses, staffing, biosecurity, reagents, quality management, training, proficiency, and research was also collected. Seven of 13 responding laboratories reported good levels of quality management with all noting conducting inventories of materials, quality control, and registry and reporting. Six laboratories reported monitoring and maintenance of equipment and pre- and post-analytic procedures, and four laboratories reported having staff for this task. With respect to the types of diagnostic tests used, all nine laboratories responding to this question reported capacity to isolate and type dengue viruses, use of MAC-ELISA, ELISA IgG, and RT-PCR; HI (78%), real-time PCR and antigen (67% each), hemagglutination assay (HI) and plaque reduction and neutralization test (PRNT) (56%), and immunohistochemistry (44%). Training in sequencing was requested by four laboratories, and three requested training in the areas of

phylogeny, laboratory administration and bioinformatics. There is good diagnostic capacity for other arboviruses, with eight national laboratories and CDC reporting capacity to diagnose yellow fever and West Nile virus, six to diagnose St. Louis encephalitis, five to diagnose Chikungunya, and five to diagnose equine encephalitis.

Challenges faced by the IMS-Dengue Laboratory surveillance component include the need to increase communication between national laboratories and the Collaborating Centers, problems obtaining permits and the mailing and receipt of serum panels by the countries, availability of reagents, financial resources, and cooperation between laboratories during an emergency. Future needs include development of a more concrete plan that reflects country realities and BSL3 laboratories for biosecurity.

Figure 5. Survey results in 13 countries of the Americas, 2010: Number of laboratories per country with dengue diagnostic capacity



Source: RELDA survey on 13 countries of the Americas, 2010 - PAHO/WHO Regional Dengue Program

2.3. Patient care

Dr. Ernesto Pleites, Ministry of Health-El Salvador, National Children's Hospital 'Benjamín Bloom' and ITG-Dengue member, noted the importance of considering dengue a single disease that ranges from 'asymptomatic' to and 'severe dengue.' The general objective of the IMS-Dengue *Patient care* component is to strengthen clinical case management of patients with dengue, with specific objectives being to reduce the number of severe dengue cases, reorganize health services during outbreaks or epidemics, implement an integrated emergency response plan, and develop and implement clinical research.

Great efforts have been made over the past ten years to train physicians in appropriate dengue case management. With publication of the 2009 WHO new dengue case classification and the 2010 PAHO/WHO guidelines for the new dengue case classification, efforts were redoubled to ensure that countries in the Region received training on the proper management of dengue cases (severe and not severe dengue) using the new severity classification and to update national dengue case management guidelines. Four sub-regional training courses were held, and ITG technical experts visited countries to provide targeted training to physicians as well as to members of national and regional medical and scientific associations. Training courses include a pre- and post-course test to assess changes in knowledge, a didactic session, analysis of dengue case studies, and hospital visits to observe patients with dengue.

The lack of continuing medical education requirements in many countries was identified as a challenge, along with the fact that copies of the new dengue case classification have not been provided to all primary care units, some intensive care units have not implemented the new guidelines, there is inconsistent clinical care provided during the different disease phases and in particular the critical phase, high turnover in medical staff, deficiencies in medical record charting and a lack of medical audits, and extemporaneous interpretation of laboratory results. Next steps for the Patient Care

component include modification of the ICD-10 so it reflects the new classification: A90.0 : Dengue without warning signs (classic dengue), A90.1 : Dengue with warning signs (DHF Grade I, Grade II) and A90.2 : Severe dengue (DHF Grade III, Grade IV). Other future activities will include ongoing capacity building of health staff, developing more robust monitoring and evaluation processes, developing operational clinical research to help improve clinical case management, and publication of the second edition of the new case classification for the Americas.

2.4. Integrated vector management

Dr. Haroldo Bezerra, Regional Advisor for Public Health Entomology, PAHO/WHO, presented a summary of the activities conducted through the IMS-Dengue *Integrated vector management* component. The objective of this component is to ensure that *A. aegypti* breeding sites are managed such that mosquito breeding does not take place and to reduce the adult mosquito population. This objective is achieved through strengthening entomological surveillance systems to guide vector control actions, incorporate families into the management of mosquito breeding sites in the domestic setting and instill an understanding of the entomological risk these sites represent, improve the quality and effectiveness of vector control actions, and conduct basic and operational research to improve feedback on vector control processes and decision-making. The integrated vector management (IVM) operational framework, defined as a rational decision-making process to optimize resources in vector control, requires that national dengue programs use data and evidence-based practices for determining the appropriate selection of vector control methods.

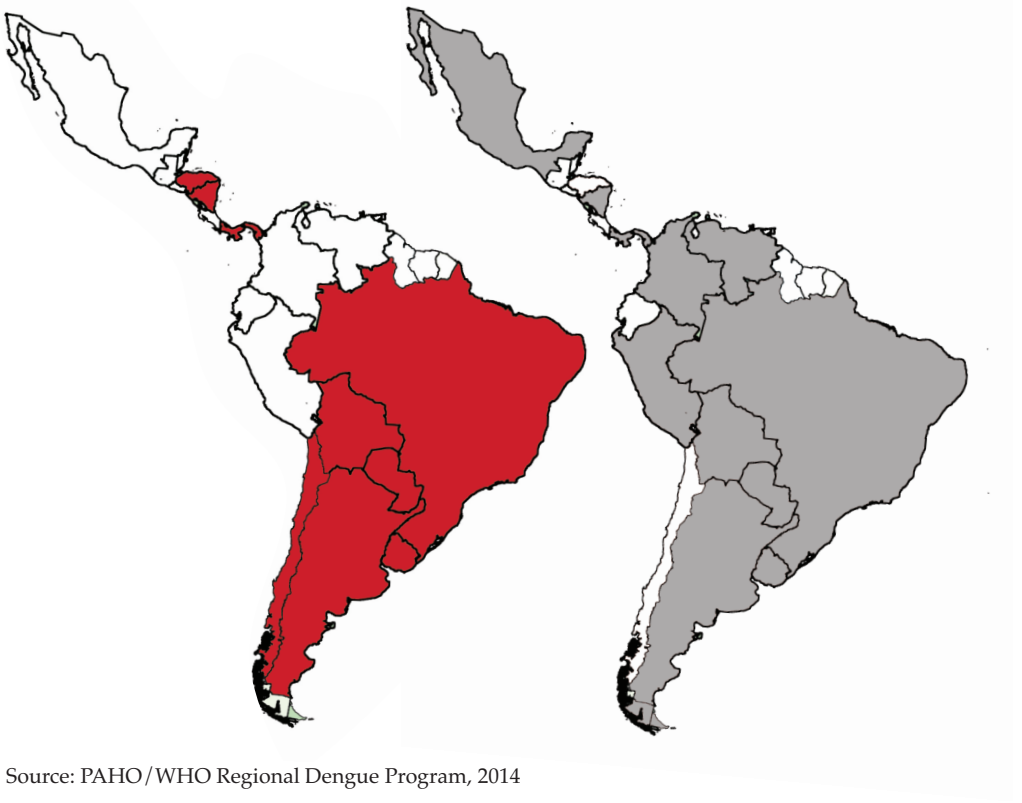
Some of the challenges noted with current vector control practices include a lack of entomological surveillance capacity which results in poor planning and evaluation of vector control actions; many countries do not use the entomological surveillance data they collect to determine appropriate vector control actions; lack of trained field and supervisory staff; insufficient human and financial resources for routine vector control actions; and a paternalistic program frame-

work that impedes assumption of responsibility by individuals and other sectors, for household vector control actions and basic sanitation services. Additionally, use of insecticides to interrupt dengue virus transmission is often done haphazardly, without a foundation in ento-epidemiological criteria to support the effective use of this control method, equipment for chemical control interventions receives inadequate or no maintenance and calibration, and assessments of vector susceptibility to the insecticide are not conducted. This is compounded by a lack of training in the proper handling of insecticides or the doses needed to ensure an impact on adult mosquito densities, of the individuals responsible for the management and implementation of these vector control tools. The slow transition of vector control programs to programs that work within an IVM framework means that national dengue programs often have little interaction with other areas that could support IVM actions, and thus allow dengue vector control efforts to be more focused.

In spite of these challenges, a standardized framework and technical guidelines for both regional and national levels were published and a new tool to efficiently generate good quality data on vector infestation levels in large urban areas, the Rapid Index Survey for *Aedes aegypti* (LIRAa), was tested and is use in several countries in the Region (Figure 6A). Technical capacity was strengthened by offering international courses on methods for evaluation of insecticide resistance in *A. aegypti* (2 courses) and train-the trainer courses for the application of insecticides and workplace safety (4 courses). An international workshop to define needs, analyze new vector control tools, identify gaps in knowledge, and propose new procedures to improve control of *A. aegypti* was held in November 2013. Next steps for the IMS-Dengue *Integrated vector management* component include recuperation of the knowledge and practice of entomology in the Region, strengthening monitoring of *A. aegypti* insecticide resistance and preparation for the introduction of a dengue vaccine as IVM will be key to its overall success. Several countries of the Americas have the technical capacity to detect *A. aegypti* insecticide resistance (Figure 6B) although not all of them conduct systematic resistance surveillance activities.

Figure 6A. Countries using the Rapid Index Survey for *A. aegypti* (LIRAa), 2014

Figure 6B. Countries with technical capacity to detect *A. aegypti* resistance to insecticides, 2014



Source: PAHO/WHO Regional Dengue Program, 2014

2.5. Epidemiology

Dr. Angel Alvarez, National Epidemiology Advisor, PAHO/WHO-Cuba and ITG-Dengue member, presented the summary of achievements, challenges and next steps for the IMS-Dengue *Epidemiology* component. Objectives of this component are to strengthen country capacity in integrated data analysis and early detection of and response to outbreaks; establish diagnostic definitions and classification of dengue cases; generate information for decision-making for dengue prevention and control actions; and define and evaluate the impact of vaccination strategies.

Dengue is a reportable disease under the 2005 International Health Regulations (IHR) and as such, outbreaks should be reported to the PAHO/WHO IHR office. An achievement of the *Epidemiology* component is the creation of a regional dengue surveillance system through which 46 countries/territories report dengue cases on a weekly basis. The system facilitates tracking of disease incidence as well as circulating viruses, detection of outbreaks, monitoring of case fatality rates, and contribution of data for decision-making for prevention and control actions in epidemic and non-epidemic periods. The PAHO/WHO Regional Dengue Program webpage integrates information from various sources and publishes program advances, scientific findings, epidemiological alerts, and other dengue-related information relevant to the Americas. Additionally, over 20 countries in the Region publish an epidemiological report on their ministry of health website, and most countries provide follow-up to outbreaks and epidemic transmission during the year. Of note are the integrated surveillance systems that provide real time data in El Salvador, Mexico and Brazil.

Challenges faced by the *Epidemiology* component include: not all countries have updated national norms for dengue epidemiological surveillance; there is insufficient feedback from epidemiological surveillance departments to other areas within the country, including border zones that are at risk for dengue outbreaks; and a lack of implementation of situation rooms during dengue emergencies. Next steps include strengthening surveillance so that epidemiological, laboratory, entomological, and behavioral indicators are integrated into a single real-time surveillance system, improving quality control of the data being reported, developing analytic tools (e.g., predictive modeling, risk stratification) for integrated dengue surveillance, standardizing operational dengue case definitions, and harmonizing regional surveillance activities with those of the WHO Global Strategy.

An example of research facilitated through the *Epidemiology* component is the "Generic Protocol for Epidemiological Surveillance of Dengue" study, in which eight countries/territories from the Region will participate to determine whether a generic protocol allows for (1) early detection of cases and/or outbreaks, (2) improved description of trends and distribution of cases by time, place and circulating serotypes, and (3) detection of deaths due to severe dengue and unusual cases of dengue (Figure 7).

Figure 7. Countries with implementation of the Generic Protocol for Epidemiological Surveillance of Dengue, 2014

Source: PAHO/WHO Regional Dengue Program, 2014

2.6. Environment

The transmission dynamic of dengue depends on interactions between the environment, the virus, the host population and the vector, which coexist in a specific habitat.

Even when the environmental component is an important part of the IMS-Dengue, the complexity and the diversity of actors involved was a major challenge in addressing it as effectively as the other components, during this review of the *State of the Art in the Prevention and Control of dengue in the Americas*. However, the environment was considered on several presentations and discussions throughout the meeting particularly those that focus on socioeconomic and environmental aspects influencing the dengue transmission dynamic (Figure 8A and Figure 8B). The participants also noted the need for public health policies that facilitate actions on these environmental determinants and also, progressively reduce the risk of dengue transmission.

It is necessary that all countries establish a legal framework to have an impact in reducing the most common mosquito breeding sites which result from daily activities such as: construction areas, inadequate disposal of tires, uncovered barrels, and other uncovered household water containers which are used daily. Several experiences have already been generated in the Region (example; Brazil, Costa Rica, Cuba, El Salvador, Panama, Paraguay), effecting laws and regulations that favor the elimination of these breeding sites. However, in order to achieve a long term and sustainable elimination of these environmental risks, the highest political support and involvement of all possible actors, including the society, the family and the community are essential in addressing key elements and conditions, including the following: climate change, the inadequate disposal management, poor or the lack of water quality and supply, and uncontrolled or unplanned urbanization.

As mentioned previously, achieving the corresponding behavior change among affected or at risk families to eliminate mosquito breeding sites in their homes is an action that should not be postponed. It requires the participation of multidisciplinary and intersectoral teams that investigate the best methods according to the

Figure 8A. Dengue incidence in the Americas according to sanitation coverage, 2011 and 2013

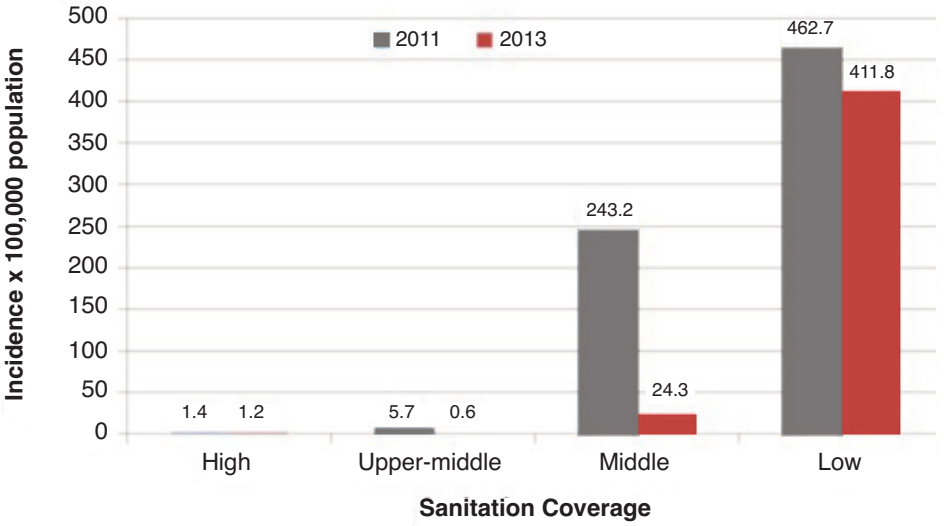
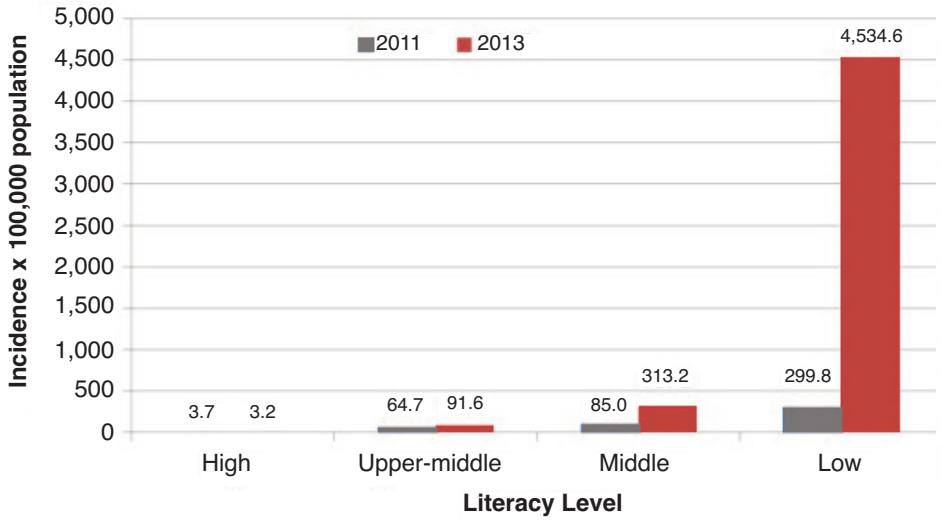


Figure 8B. Dengue incidence in the Americas according to literacy level, 2011 and 2013



Source: World Bank. Indicators. http://datos.bancomundial.org/indicador/SH.STA.ACSN.UR

culture and context of each area within each country. The construction and development of tools (as COMBI) that can be assimilated by the countries will continue and will be supported by ITG-Dengue.

Discussion

Meeting participants noted that the focus on continued capacity building of technical skills in each of the components is a key achievement of the IMS-Dengue, allowing countries to rebuild expertise in the technical elements required for successful implementation of an integrated national dengue program.

Another significant achievement is the reduction in the dengue case fatality rate in the Americas due to improved clinical case management and introduction of the new dengue case classification. It was noted that in the Americas the case fatality rate is calculated using a denominator of total dengue cases, not just severe dengue cases. Participants also shared their country experiences reorganizing health services to better manage clinical cases in line with the new case classification, although there is still a need for models that countries can adopt during dengue emergencies.

Participants shared diverse experiences with implementation of the IMS-Dengue in national and local contexts. In response to a question regarding how to sustain intersectoral collaboration with other ministries, an example was shared from El Salvador where social protection civil law was used to bring other sectors into the integrated dengue management strategy through participation on the Intersectoral Working Group on Dengue. Each member of the working group assumes responsibility for specific activities and reports to the working group on accomplishments as well as issues that require an intersectoral response. Stratifying areas by dengue risk has allowed the national program to maximize financial and intersectoral resources because intervention measures are better targeted to areas with high transmission. In Nicaragua community participation is coordinated by the Office of the President, which allows the national dengue program to prioritize dengue within intersectoral groups.

Several countries have modified the IMS-Dengue based on their experience implementing the strategy and to bring the specific IMS components into line with ministry of health technical areas. There was a general consensus of the importance of program management, and several countries have added *"Management"* as an IMS-Dengue component. In Colombia, *"Management"* and *"Knowledge management"* have been added, the *"Social communications"* component name has been changed to *"Health promotion"* with a strong focus on social mobilization and communication, and *"Epidemiology"* has been placed within *"Health intelligence."*

The need for operational research identified in each of the IMS-Dengue component presentations sparked significant discussion. The Sustainable Sciences Institute shared results from the "Camino Verde" intervention of community mobilization without use of chemical control methods, in Nicaragua and Mexico in which fewer dengue cases, lower entomological indices and reduced risk of dengue infection in children were reported; findings should be published in 2014. Dengue diagnosis, progress on new dengue diagnostic tests (e.g., NS1), development of indicators to measure the effectiveness of the new clinical guidelines, and harmonization of these indicators across countries in the Americas were also identified as important research issues for the Region. A suggestion was made to consider experiences from malaria control, such as the "Malaria Champions of the Americas" strategy which successfully raised the profile of the disease and the importance of its prevention and control.

Conclusions

General conclusions for the Integrated Management Strategy for Dengue Prevention and Control (IMS-Dengue):

2.0.1 The Integrated Management Strategy for Dengue Prevention and Control (IMS-Dengue), technically supported by PAHO/WHO, promotes a rational decision-making process for the optimal use of resources for vector control using an operational approach.

2.0.2 New components that address program management and intersectoral collaboration should be added to the IMS-Dengue.

IMS-Dengue conclusions by component

2.1 Social communication

2.1.1 Ways to ensure sustainability of communication and mobilization activities are needed given that social communication is a key component for the success of the IMS-Dengue.

2.1.2 While there have been advances in the past ten years, Social communication continues to be an area of great need with regards to funding, operational research and sustainability.

2.2 Laboratory

2.2.1 Despite challenges of dengue case detection, each country has trained staff and a strengthened laboratory network so that laboratory diagnosis of dengue is available in every country of the Region.

2.2.2 There is a lack of communication and case notification between the public health system and private laboratories.

2.2.3 In light of new challenges facing the Region, coordination between the Regional Dengue Program (RELDA Technical Secretary) and the RELDA Collaborating Centers needs to be strengthened to facilitate greater interaction, visibility, training, and improved approaches for addressing regional issues.

2.2.4 Development of a genomic map for dengue viruses in the Americas is an important next step.

2.3 Patient care

2.3.1 Patient care is one of the most developed and implemented components of the IMS-Dengue. Several studies have proven that the new dengue classification is better to properly identify severe dengue cases. However there are still gaps that need to be studied; more evidence is necessary to evaluate the impact and utility of the warning signs to prevent severe dengue and as well as a better dengue case definition.

2.3.2 There are opportunities to expand on successes in further reducing the dengue case fatality rates. Currently, most of dengue deaths are related to an improper clinical management and also to cases in which patients arrive (too) late to hospitals or primary health care units to receive treatment.

2.4 Integrated vector management

2.4.1 There is a progressive weakening of the entomological surveillance, with less ability to map, analyze data and assess the situation to support the decision making process by managers.

2.4.2 There is a lack of or a low integration and articulation between vector control actions and other important areas that are necessary to support these activities, such as: sanitation, environment, water supply, etc.

2.4.3 Many countries use the chemical control as their first alternative method for vector control.

2.4.4 The use of insecticides to control and / or interrupt transmission is often done haphazardly without entomologic/epidemiological criteria; with inadequate or no equipment maintenance and calibration; and without an assessment of the susceptibility of the vector.

2.4.5 More monitoring programs for vector resistance to insecticides are needed and a more effective response to the lack of human and material resources for vector control.

2.4.6 Integrated vector management continues to be more of a theoretical construct than a practical framework that can be applied in the field.

2.5 Epidemiology

2.5.1 Dengue surveillance in the Americas has improved. Not only are more countries reporting dengue, but the quality and detail of the data is significantly better, with countries and territories now

reporting; suspected dengue cases, laboratory confirmed cases, severe dengue cases, circulating dengue serotype, and deaths.

2.5.2 PAHO/WHO and national counterparts have developed a generic protocol for integrated dengue surveillance at the national level and at sentinel sites, thus ensuring that all countries use the same dengue case definition and severity classification. This is a step forward in the goal to develop integrated surveillance for dengue prevention and control.

2.6 Environment

2.6.1 Dengue transmission is strongly influenced by socioeconomic and environmental conditions. Illiteracy and poor sanitation coverage are just a few examples mentioned as determinants associated to dengue transmission.

2.6.2 Several countries and territories in the Americas have elaborated and implemented regulations that favor the elimination of the most common mosquito breeding sites in order to reduce dengue transmission.

3. Country experiences with the Integrated Management Strategy for Dengue Prevention and Control in the Americas (IMS-Dengue)

Facilitator: Dr. Franklin Hernández, PAHO/WHO

Integration of the IMS-Dengue into national dengue programs can be a challenging task as it calls for an integrated, multidisciplinary approach between groups and sectors that traditionally have not worked together in a sustained fashion. Examples from two countries illustrate how the strategy has been adapted to each country setting and implementation challenges the programs faced.

3.1. Brazil

Dr. Giovanini Coelho, Coordinator, National Dengue Control Program (PNCD), Secretary of Health Surveillance, Ministry of Health, Brazil provided a brief summary of the Brazilian health system,

noting that Brazil provides universal coverage through a public health system that is decentralized to the municipal level. The Ministry of Health transfers funds directly to states and municipalities, with municipalities responsible for management of local health services. For this reason, PNCD has made significant investments in training staff at the municipal and state levels. All municipalities report epidemiological and entomological surveillance data through the national surveillance information system, and dengue control actions are determined from an integrated analysis of the data. Dengue cases are monitored weekly by the MOH, and all deaths attributed to dengue are investigated using a standardized dengue death investigation form. In 2014 the surveillance reporting system was modified to reflect the new dengue case classification, new forms were developed and staff trained on the changes made to the surveillance system. These activities were held at the state and municipal levels (Figure 9).

Figure 9. Timeline of Brazilian National Dengue Control Program – PNCD, 2002 - 2014

Source: Secretariat of Health Surveillance of Brazil SVS – Ministry of Health, 2002 - 2014

Use of the integrated vector management approach provides a legal framework for field activities and dealing with closed or abandoned properties, or householder refusal to allow an inspection of their premises. Copies of the national guidelines are provided to local Health Secretariats for enforcement. There is an active monitoring system for insecticide resistance, and PNCD works with municipalities to manage insecticide use in areas with documented resistance. Given the seriousness of insecticide resistance, the MOH purchases and distributes insecticides to municipalities in order to properly manage their use. The Rapid Index Survey of *Aedes aegypti* (LIRAa) is a simplified method developed and validated by PNCD to determine the *A. aegypti* House Index and identify the principal mosquito breeding sites and critical areas for vector control intervention. The PNCD has a long history of working with mass media at the national, regional and local levels; for example, LIRAa survey data are provided to the media as a means to mobilize the community and increase program transparency. In addition, the COMBI planning methodology was tested in four municipalities.

Another area of significant program effort has been in patient care. Guidelines for physicians and nurses were updated in accordance with the new dengue case classification, specialized guidelines for care of patients with other conditions (e.g., pregnant, social risk for dengue) were produced, and trainings on the new case classification were held throughout the country. An online course was created to reach physicians unable to participate in traditional in-person trainings while a shorter online session, "Dengue in 15 minutes," was designed to update health staff knowledge of dengue. Given Brazil's broad experience with dengue, the MOH has developed new strategies for the organization of health services during epidemic situations, such as the establishment of hydration tents and use of containers as temporary primary care units. There is an extensive laboratory network with 100% of states with IgM capacity, most states with virus isolation capacity, and approximately half of the states with PCR capabilities.

The PNCD added a *"Management"* component to the Brazil IMS-Dengue strategy and developed an international "Integrated Management Strategy for the Prevention and Control of Dengue" course that is in its 7th edition. The ministry has also released a call for training in integrated vector management that targets public health institutions. And finally, while not a formal component in PNCD's IMS-Dengue strategy, operational research is an important activity with six studies in epidemiology, laboratory surveillance and patient care having been funded thus far. PNCD collaborates with an array of research partners both national and international, such as the "Multicentre Retrospective Study for Alarm Signals for a Dengue Outbreak: Brazil, Mexico, Dominican Republic, Vietnam, and Malaysia" to be published in 2014; a phase 1 effectiveness study of *Wolbachia*-infected *A. aegypti* has been completed and the phase 2 field release of modified mosquitoes in four communities in Rio de Janeiro is scheduled for July 2014; and a study on the effectiveness of insecticide-treated window and door screens and targeted interventions is being conducted in over 56,000 households in two cities. Brazil will be involved with dengue vaccine implementation and a seroprevalence study with adults and children will start later this year in 63 cities across the country, a cellular immunity study is in the start-up phase, and a study on a mathematical model for dengue transmission is scheduled for 2015.

Dr. Coelho closed his presentation by noting that decentralization of the Brazilian health system allowed surveillance and vector control activities to be expanded across the country by working directly with municipal governments. However, dengue prevention and control strategies must be fairly simple and easy for a municipal government to manage; otherwise they won't use the tools. Supervision and evaluation methods to assess impact need to be improved, and new tools and strategies need to be scaled-up to demonstrate feasibility and cost effectiveness.

3.2. Mexico

Dr. Cuauhtémoc Mancha Moctezuma, Adjunct Director General for Prevention Programs, Secretaría de Salud, México, presented the general context for the national dengue program by noting there are 100 cities in the country with persistent dengue virus transmission, putting 25 million people at risk for dengue infection. The five key elements that support implementation of the Mexican IMS-Dengue strategy are advocacy, social mobilization and legislation; collaboration within the health sector and with other sectors; integrated disease control; evidence-based decision making (Figure 10); and capacity building. The national dengue program operates in states with an administrative structure that permits implementation of all seven IMS-Dengue components: Health promotion; Social, community, intra- and intersectoral participation; Epidemiological and entomological surveillance; Laboratory diagnosis by the state public health laboratory; Patient care; Control of health risks; and Chemical vector control. Operational decision making is based on state and local norms, with technical assistance, supervision and evaluation conducted by the federal program level.

Figure 10. Decision based on evidence: Entomology

Source: InDRE Mexico, 2012–2013

During dengue emergencies the federal government may also contribute extra-budgetary human and financial resources. Outbreak control is managed using risk stratification and integrated actions, including large-scale campaigns to eliminate breeding sites with community participation, targeted use of larvicides and indoor residual spraying, fogging in the early evening over four continuous weeks, calibration of insecticide application equipment, permanent supervision, monitoring and evaluation from the federal level, and daily correction of operational errors.

The federal government works closely with states and municipalities through a variety of programs, including *"Municipalities for health,"* which receives annual federal funding for dengue prevention and control; *"Recycle for your well-being,"* which encourages recycling and is managed by state governments; *"Municipal initiatives for dengue control using the legal system,"* which focuses on abandoned houses and homes where no one is available to permit entry and is managed by municipal governments; *"Legal initiative for housing construction,"* which has enacted new housing construction requirements such as installation of screens in new homes; and *"Verification for protection against health risks,"* which targets breeding sites found on the premises of service providers.

The national dengue program's integrated management focus includes environmental management achieved through the 'Scrub, Cover, Turn over, Throw away' communication strategy, breeding site elimination campaigns, individual and household behavior change, and personal protection messages; chemical control through the safe use of larvicides and adulticides, occupational protections, and a regional insecticide resistance monitoring plan; evidenced-based decision making using epidemiological, entomological, laboratory, and clinical case data which are used to create a "Risk indicator" and routine program monitoring and evaluation using standardized indicators; and incorporation of new technologies such as vaccines.

Discussion

The presentations from Brazil and Mexico generated a lively discussion and sharing of experiences by meeting participants. Participants appreciated the willingness of Drs. Coelho and Mancha to share not only the positive outcomes but also the challenges faced by the national programs of Brazil and Mexico. A question was asked whether participation of co-actors or other sectors was measured. Dr. Mancha noted that in Mexico participation is measured in different ways, depending upon the area and the actors involved. While it has been difficult to engage other sectors in large urban areas where there little pressure or motivation for them to participate in dengue prevention activities, the hotel industry has been a strong partner in areas where tourism is important.

A follow-up question concerned how they were able to bring in other sectors when ministries of health generally do not have the intersectoral convening capacity of ministries of finance or external relations. Dr. Coelho noted that it was, in fact, very difficult to convene other sectors outside of dengue emergencies due to a lack of interest. While the health sector generally accepts the importance of intersectoral articulation, this process is not clear and sustained intersectoral articulation remains a challenge. He suggested that ministries of health find indicators that will encourage and support enthusiasm for ongoing dengue prevention and control activities among non-health sectors.

Dr. Mancha noted that the health sector in Mexico is divided, with health programs in one area and health services in another, so intersectoral collaboration is essential. They have examples of successful intersectoral collaboration, such as during the cholera outbreaks of the 1990s when various sectors came together to eliminate cholera. The national dengue program has been able to convene committees at the local and state levels by using the *"Verification of protection from health risks"* law, similar to El Salvador's use of a social protection civil law.

A meeting participant noted that many countries in the Region share the challenge of working in communities with high levels of

violence, and asked how program field staff worked in those communities. In both countries, local program staff works with community leaders to identify the days, times and number of vector control staff allowed into the community to carry out household inspections. Dr. Mancha noted that in some areas they are not allowed into the community so they provide the materials to the community leaders in the hope that the vector control actions will be carried out.

In response to a question regarding the introduction of Bti (*Bacillus thuringiensis israelensis*) at the community level in Mexico, Dr. Mancha noted the greater challenge was convincing field staff, not the community. To address dengue program staff resistance, an internal educational process was carried out that addressed the benefits of Bti as a new tool for the prevention and control of dengue.

Questions were raised regarding innovations in clinical case management and training in Brazil, in particular the *Dengue in 15 minutes* educational video. The focus on shared case management responsibilities by doctors, nurses and other health professionals was appreciated, as in many countries dengue case management is primarily the responsibility of physicians. Other participants were surprised that dengue case management could be properly addressed in a 15-minute video, and many requested copies for possible use in their own countries. Dr. Coelho explained that the *Dengue in 15 minutes* video complements other traditional training formats, and was developed to address the low participation rates of physicians in the more traditional formats that take place over a period of several hours. Since all physicians in Brazil receive basic training on dengue clinical case management as part of their medical studies, the video only highlights specific clinical aspects. While they need to further evaluate the impact, initial results confirm improved knowledge. A participant was shared the importance of complete blood counts in clinical case management as this can help identify patients in shock without warning signs. Recent revisions to the WHO 2009 dengue clinical case management guidelines regarding intravenous fluid management were welcomed.

The need for a focus on behavior change and more effort devoted to sustained behavior change were brought up. Participants were interested in hearing how behavior change specialists worked within the national multidisciplinary teams mentioned in both presentations. Dr. Mancha responded that the need to bring new professions into dengue prevention and control was recognized so they incorporated a medical anthropologist into the dengue program team. Understanding and addressing intercultural aspects of dengue prevention ("to understand why people act the way they do") can provide the justification for hiring a social scientist (e.g., anthropologists, sociologists, etc.) as part of an integrated dengue prevention and control team.

Conclusions

1. The process of the implementation of the IMS-Dengue at national level has allowed that most of the countries and territories of the Region now have a solid instrument to prevent and control dengue.

2.The IMS-Dengue can be adapted to each country context. In Mexico the IMS-Dengue include seven components: 1) Health promotion; 2) Social, community, intra- and intersectoral participation; 3) Epidemiological and entomological surveillance; 4) Laboratory diagnosis by the state public health laboratory; 5) Patient care; 6) Control of health risks; and 7) Chemical vector control.

3. Decentralization of the Brazilian health system allowed surveillance and vector control activities to be expanded across the country.

4. Several countries in the Americas have implemented an outbreak control system that uses risk stratification and integrated actions to optimize the management of material and human resources in dengue prevention and control.

5. Inclusion of a medical anthropologist as a member of the national dengue prevention and control program team in Mexico helped with the development of an integrated approach that addresses cultural aspects that affect community participation.

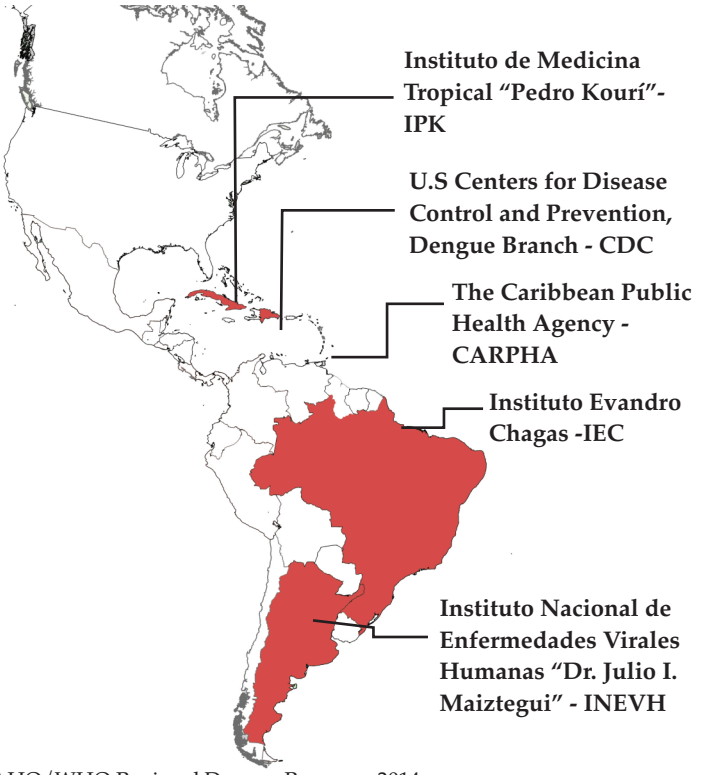
6. Interventions must be simple and easy to implement by municipal governments, otherwise they will not be adopted and dengue prevention efforts will continue to be insufficient.

4. PAHO/WHO Collaborating Centers for Dengue in Latin America and the Caribbean

Facilitator: Dr. Siripen Kalayanarooj, WHO Collaborating Centre on Dengue, Thailand

This session describes the activities of the PAHO/WHO Collaborating Centers for Dengue in Latin America and the Caribbean. Through the Dengue Laboratory Network of the Americas (RELDA), the Collaborating Centers provide technical assistance to strengthen regional capacity for best practices in laboratory diagnosis of dengue, clinical-epidemiological surveillance for dengue and incorporation of laboratory data for integrated dengue surveillance as part of the IMS-Dengue (Figure 11).

Figure 11. PAHO/WHO Dengue Collaborating Centers in the Americas, 2014



Source: PAHO/WHO Regional Dengue Program, 2014

4.1. Instituto de Medicina Tropical "Pedro Kourí," Havana, Cuba

Dr. Ángel Álvarez, Epidemiologist, PAHO/WHO-Cuba, presented the background and activities of the Instituto de Medicina Tropical "Pedro Kourí" (IPK), a PAHO/WHO Collaborating Center since 2005 that provides technical assistance on viral and communicable diseases and vector control. Its multidisciplinary team includes virologists, immunologists, molecular biologists, clinicians, epidemiologists, sociologists, entomologists, geographers, and mathematicians. The main activities include information dissemination; development of guidelines, training manuals, and protocols; and training and education. IPK provided technical cooperation in the following areas:

- "Impact Assessment of the New Clinical Classification" workshop
- Review of the revised PAHO clinical guidelines for the new dengue case classification
- Training on insecticide resistance
- Evaluation of participatory strategies for vector control
- Organize and offer the International Dengue Course (1987 to date)
- Training of laboratory technicians and graduate students
- Master's degrees offered in the areas of Virology, Entomology, Infectious Diseases, Epidemiology, and Environmental Health
- Development of PhD courses

4.2. U.S. Centers for Disease Control and Prevention, Dengue Branch, Puerto Rico

Dr. Harold Margolis, Director of the Dengue Branch of the U.S. Centers for Disease Control and Prevention (CDC), presented the background and six technical areas within the Dengue Branch: Epidemiology, Immunodiagnostics Laboratory, Molecular Diagnostics Laboratory, Entomology and Ecology, Public Health Management, and Communications. Its multidisciplinary team includes epidemiologists, entomologists, field biologists, virologists, statisticians, public health specialists, health educators, psychologists, and graduate students. The Dengue Branch provides technical assistance to countries through the following services: DENV strain collection, Diagnostic testing proficiency and quality assurance (provision of characterized materials), Evaluation of dengue diagnostic tests (commercial or laboratory developed), Provision of technical infor-

mation on dengue, Training in research methods (laboratory, epidemiologic, entomologic, and vector control), Outbreak response and investigation, and Research.

The Dengue Branch focuses on primary (vaccines and integrated vector control) and secondary prevention (diagnosis and case management), accompanied by surveillance and education activities. Research activities include the development of new tools for entomological surveillance and vector control such as the Sticky Autocidal Gravid Ovitrap as well as dengue diagnostics such as development of an improved NS1 antigen detection immunoassay and prognostic tests for severe dengue. Research is also conducted in the area of epidemiologic surveillance, such as the development and validation of serologic approaches for surveillance for incident DENV infections, validation of participatory surveillance for acute febrile illnesses and dengue, and development and validation of a protocol for enhanced surveillance for fatal dengue.

The CDC Dengue Branch provided technical cooperation in the following areas:

- Dengue Diagnostic Testing workshops
- Molecular epidemiology of dengue viruses
- Dengue Clinical Case Management courses, in classroom (with or without continuing medical education credit [CME] options) and online formats (non-CME option only)
- Epidemic response cooperation in the Americas as well as other regions

4.3. Instituto Evandro Chagas, Belém, Brazil

Dr. Pedro Vasconcelos, Director, Section for Arbovirology and Hemorrhagic Fevers of the Instituto Evandro Chagas (IEC), provided an overview of this research institute within the Secretary of Health Surveillance of the Brazilian Ministry of Health. The Section for Arbovirology and Hemorrhagic Fevers conducts surveys, assists with laboratory surveillance and provides laboratory materials. Staff includes researchers, PhD and master's students, and laboratory support staff. They work with a large number of viruses, including

dengue, and have technical capacity in virus isolation, molecular biology, serological techniques, HI, ELISA (IgM, IgG and antigen detection), FC and PRNT. IEC plays an important role in the detection of viruses associated with human disease and has created a detailed map of viral infections in the Brazilian Amazon. New dengue serotypes have been detected, and viral genotyping has shown where introduction points were and dispersion routes within Brazil.

Through their research activities, IEC has developed molecular diagnostic tools (Rapid MAC-ELISA, SYBR qRT-PCR and RT-PCR Semi-Nested), contributed to field research in support of surveillance activities, and contributed biological reagents (antigens and antisera) for detection of dengue, yellow fever and other arboviruses.

IEC provided technical cooperation in the following areas:

- Training of laboratory staff in dengue and Chikungunya diagnosis (serology and RT-PCR)
- Active participation in regional technical meetings
- Collaboration in research and diagnostic clarification
- Collaboration in scientific events in the Americas

4.4. Instituto Nacional de Enfermedades Virales Humanas "Dr. Julio I. Maiztegui," Pergamino, Argentina

Dr. Delia Enria, Director of the Instituto Nacional de Enfermedades Virales Humanas "Dr. Julio I. Maiztegui" (INEVH), Argentina noted that INEVH has been a PAHO/WHO Collaborating Center since 1987 and it serves on RELDA's Consultative Technical Committee. INEVH works closely with the national dengue program as part of the integrated surveillance system for dengue. Laboratory surveillance is conducted through a national laboratory network (SIVILA) following standardized protocols developed by INEVH. INEVH has technical capacity in serological (MAC-ELISA, IHA, ELISA IgG, PRNT, blocking ELISA, ELISA NS1) and virological and molecular techniques (viral isolation C6/36 VERO mice, IFD and IFA, Mabs, RT-PCR specific and general primers, RT-qPCR, sequencing, and phylogenetic analysis); production and provision of diagnostic reagents (antigens [sucrose acetone, cell lysates, eluted supernatant,

antisera]); lyophilization; supply management; and distribution of commercial reagents. INEVH has recently completed a new BSL3 laboratory. The Institute plays a key role in quality control for the national laboratory network in Argentina as well as for RELDA members. They are currently working with PAHO on the creation of a training program for the development of quality control systems for dengue laboratories.

INEVH provided technical cooperation in the following areas:

- Capacity building in laboratory surveillance for pathogens often confused with dengue
- Promotion of decentralization of national laboratory networks for the diagnosis of dengue
- Development and conduct of operational research as well as participation in research studies in collaboration with national and international agencies.

Discussion

The role of the PAHO/WHO Collaborating Centers in providing support to countries and their relationship with ministries of health and academia was the primary point of discussion. The session presenters noted that their institutions are part of ministries of health (Argentina, Brazil, Cuba) or the federal department of health (CDC Dengue Branch). Thus, each of them play a key role in the provision of technical support to the national laboratory network of their own country. Through technical cooperation agreements, the Collaboration Centers also work with other countries in the Region in the areas of operational research, surveillance, vector control and clinical case management.

A question was asked about how the Collaborating Centers collaborate with each other, and the importance of integration of the work of the centers. PAHO/WHO responded that one of the goals of this session was to show how the Collaborating Centers work in collaboration with each other as well as the types of technical assistance they provide internally in their own country and to countries in the Region.

Capacity for Chikungunya testing was noted and participants inquired about it. PAHO clarified that the Organization is already collaborating with the countries and specific institutions to expedite laboratory and case management capacity through the Region. It is still pending to see how this new effort will be operationally integrated with dengue efforts and infrastructure already in place.

Conclusions

1. The PAHO/WHO Collaborating Centers on Dengue are fundamental and indispensable institutions that support countries in the Region with state-of-the-art technology to ensure proper management, control and prevention of the disease. Coordination with PAHO/WHO is an opportunity to share responsibilities and tasks that allow for a more efficient and harmonized technical collaboration for the benefit of the national dengue prevention and control programs in the countries of the Americas.

2. The PAHO/WHO Collaborating Centers on Dengue contribute to the advancement of scientific knowledge in the field of dengue research.

3. RELDA will be a key partner for expanding laboratory diagnostic capacity for other diseases such as Chikungunya.

5. Economics of Dengue in the Americas

Facilitator: Dr. Angel Alvarez, PAHO/WHO-Cuba

5.1. Economic impact of dengue and dengue hemorrhagic fever in Zulia, Venezuela (1997 – 2003)

Dr. Germán Añez, currently with the U.S. Food and Drug Administration (FDA), presented a study conducted while he was a researcher at the University of Zulia of the direct and indirect costs associated with medical care of patients with dengue fever and dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) in the state of Zulia, Venezuela. During the seven-year study period (1997 – 2003), over 12% of all dengue cases in Venezuela were

reported in Zulia. Dengue continues to be a significant problem in Venezuela, reporting the third highest number of dengue cases (over 120,000) and the second highest number of cases of severe dengue (over 10,000) in the Americas in 2010.

The research team surveyed hospitals in order to calculate direct costs per patient in the outpatient emergency and inpatient settings. Direct costs for dengue fever and DHF/DSS cases seen in the emergency outpatient clinic were calculated at US $3.90/outpatient, while direct costs per patient with DHF/DSS per day per hospital bed (US $7.30 a day/bed) were calculated, along with clinical tests (US $5.60/patient) and serological diagnosis (US $4.60/patient). An average stay of 7 days was used to calculate total inpatient direct costs, excluding hospital staff salaries, of US $94.90 per hospitalized patient with DHF/DSS.

Indirect costs of dengue were calculated by estimating lost wages due to hospitalization (DHF/DSS cases) and convalescence (dengue fever and DHF/DSS cases). Lost wages were calculated using the national minimum wage and an estimate of 7 days of lost work for dengue fever patients and 14 days of lost work for DHF/DSS patients. Women caring for patients less than 15 years of age and male and female patients over 15 years of age, adjusted for national employment rates by age group, were included in the indirect cost calculations.

Total direct and indirect costs due to dengue fever in the state of Zulia over the seven-year period were US $1,348,077, with indirect costs accounting for the majority (65%) of the total costs. These findings support data from other economic studies of the high impact of dengue fever on the health sector as well as the individual and family levels. In particular, the research team noted the impact of dengue fever on families due to lost income and the general workforce due to work absenteeism, which could significantly impact regional and national economic development. Future studies should include costs which were not part of this study such as the cost of items not

produced due to absenteeism and additional wages paid to health staff during dengue epidemics, as well as use of objective indicators such as the Disability Adjusted Life Years (DALYs) to better capture and define the true economic and social burden of dengue fever.

5.2. Socioeconomic burden of dengue: studies from the Universidad de los Andes, Bogota, Colombia

Dr. Raul Castro, Associate Professor at the Universidad de los Andes, presented a study of the socio-economic burden of dengue fever at the government, health system, patient, and household levels and a retrospective study of the burden of disease during endemic and epidemic years. To determine the burden of disease during a dengue endemic period, the period 1998 to 2012 was selected and years in which epidemics were recorded (1998, 2001, 2002, 2005, 2009 and 2010) were excluded. The research team selected 2010 to determine the burden of disease during an epidemic due to the size of the epidemic that year: over 108,000 outpatient visits due to dengue, 36,404 hospitalizations, and 9,745 severe dengue cases. Dr. Castro noted that approximately 3,990 Disability Adjusted Life Years (DALYs), or 83.88 DALYs per one million population, are lost in Colombia during an endemic year, as compared to 57,017 DALYs (1,198.73 DALYs per one million population) during a major epidemic year. Men between the ages of 15 to 44 suffered the highest number of DALYs followed by women in the same age range.

The direct and indirect costs of dengue fever were calculated for outpatient, hospitalized, and severe dengue cases across a three-year period (2010 – 2012). Data from the health sector were used to calculate government and health system costs while patient and household costs were calculated using data from a survey of representative households. Prevention / health promotion, vector control and surveillance, outbreak control, and "other" costs were included as government costs; costs associated with dengue fever treatment and "other" illness-related costs were included as health system costs; out-of-pocket illness-related expenses such as transportation, medical tests, purchase of medications, etc. were included as direct patient costs; loss of income due to premature death, lost productiv-

ity, loss of well-being, and other illness-related costs were included as indirect patient costs; and lost productivity of the caregiver (time spent caring for the patient, loss of well-being, other caregiver costs) were included as household costs.

The average treatment cost per dengue event (health system, individual and household direct and indirect costs) in Colombia in 2010 was US $292 for an outpatient case of dengue, US $600 per hospitalized case of dengue and US $1,975 per severe dengue case. In 2010, total direct costs to the health system were US $28,972,157 while total costs to patients and households were US $16,865,592 ($3,248,754 direct patient medical costs + $5,486,770 indirect patient medical costs + $8,130,068 lost productivity). Although these costs were lower during endemic years (in 2012, US $9,637,084 and US $6,494,974 [$1,314,804 + $2,133,440 + $3,046,730], respectively), millions of dollars are spent every year by central and local governments, and by patients and households for the care and treatment of dengue fever, not to mention millions of dollars in lost productivity.

The research team calculated an average annual household out-of-pocket expenditure for dengue prevention activities (e.g., purchase of insecticides, repellents, mosquito nets) of US $11.09 for households in low transmission areas and US $13.27 for those in high transmission areas. After including the costs of prevention activities from the central and local government levels, the total cost for prevention per household in high transmission areas was US $16.38. A comparison of two mathematical models to estimate the amount a household would be willing to spend annually to avoid a case of dengue revealed similar results, with households willing to spend US $55.57 using the cost of treatment method and US $55.45 using the contingent valuation method. These data were used to calculate an annual national household prevention cost of US $266,706,556 to prevent dengue fever.

The total cost of dengue fever to Colombia was calculated by summing the total (1) direct and indirect medical costs, (2) lost wages due to premature deaths, (3) costs of prevention/health promo-

tion/vector control/surveillance, and (4) annual national household prevention costs. In 2010, the dengue epidemic cost Colombia an estimated US $357,189,668 while in 2012, a dengue endemic year, total socio-economic costs of dengue were US $313,437,342. Finally, when one examines the cost of dengue for the nation as a whole, in 2012 dengue represented 0.036% of Colombia's gross domestic product (GDP), 0.03% of the national general budget and 0.0385% of the national health budget.

5.3. An evaluation of the economic impact of dengue in Mexico

Dr. Adriana Zubieta Zavala, a researcher with the Department of Public Health at the School of Medicine of the Universidad Nacional Autónoma de México (UNAM), presented a study of the economic impact of dengue in Mexico. The research team used a micro-costing methodology (PAATI) to examine differences between normative costs and what was actually spent on dengue, and to estimate future expenses related to dengue. Sixteen states participated in the study, and data were collected from the Secretary of Health (SS) and the Mexican Social Security Institute (IMSS), including review of electronic/paper health records, interviews with patients in the outpatient, hospital or household settings, verbal autopsies with a family member of patients who died due to dengue, key medical staff, and public health officials responsible for the dengue program.

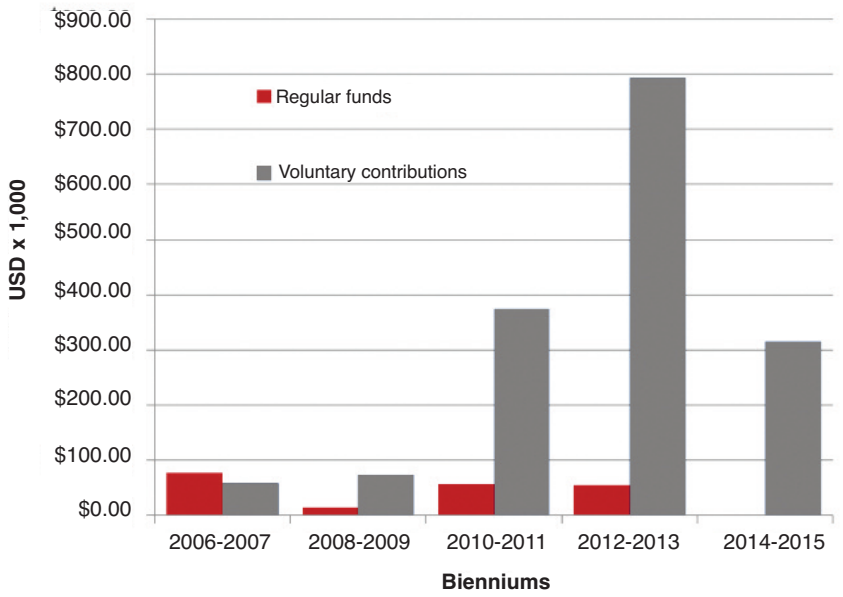
Normative and estimated real costs were calculated for dengue patients seen in the outpatient, inpatient and intensive care unit (ICU) settings as well as for patients seen in all three settings in the SS, IMSS and private sector health systems. Normative costs across the four scenarios were lowest for the SS, with costs per patient at US $164.57 in the outpatient setting, US $587.77 per hospitalized patient, US $6,786.19 per patient in the ICU, and US $7,538.54 for a patient seen in all three settings; IMSS costs were US $336.97, US $2,042.54, US $23,452.63, and US $25,832.14, respectively while in the private sector costs were US $487.39, US $4,077.81, US $23,753.19, and US $28,318.40, respectively. However, when real costs were calculated for the SS and IMSS using PAATI, per patient costs were lower for both health systems across the three settings as well as for patients seen in all three settings, although costs in the SS system were still lower than IMSS.

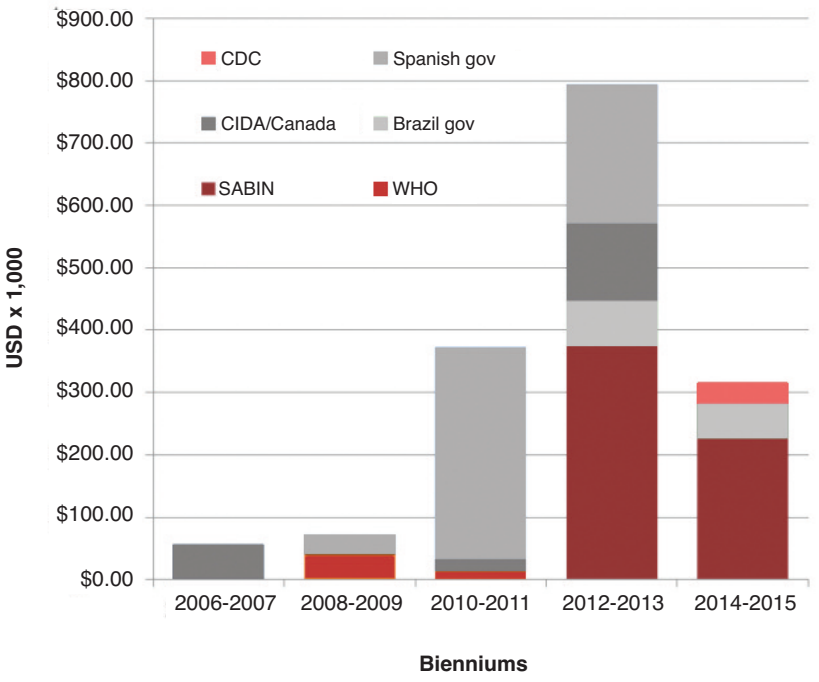
By comparing the PAATI estimated total normative program costs (US $11,766.55/10,000 pop.) with the total budgeted dengue program costs for 2011 (US $7,794.28/10,000 pop) and 2012 (US $6,422.30/10,000 pop), it is evident that programs funds were insufficient to meet expected demands. Total 2011 program (including direct and indirect clinical case management, family out-of-pocket expenses, and prevention and control costs) normative costs were calculated to have been US $128,769,620, compared to 2011 total program actual costs of US $113,648,671, showing that what is actually spent may be less than what has been budgeted. There are many reasons for why actual expenses may be less than budgeted expenses, but monitoring actual spending versus budgeted expenses will provide more information for use in decision making. The research team then used a mathematical model to determine future costs based upon previous years cases and projected population increases, estimating that dengue will cost the country in excess of US $238 million by 2022.

5.4. Financial resources for the prevention and control of dengue in the Americas - PAHO/WHO

Dr. Luis Gerardo Castellanos, Senior Advisor for the Prevention and Control of Communicable Diseases, PAHO/WHO, presented total annual funding for the PAHO/WHO Regional Dengue Program, including both internal and external funding. Since fiscal year 2006-2007, the great majority of program funds have been external contributions, ranging from 43% to 100% of total program funds (Figure 12A). External contributors to the Regional Dengue Program include the US CDC, the Government of Spain, the Canadian International Development Agency, the Government of Brazil, the Sabin Vaccine Institute, and WHO (Figure 12B). He emphasized the advisory role that PAHO/WHO plays, and that national governments, not external funding, provide the vast majority of funds for dengue prevention and control in the Region, ranging from US $1.27 million (US $0.24 per capita) to $800 million (US $4.18 per capita) annually.

Figure 12. PAHO/WHO Regional Dengue Program Budget and voluntary contributions, 2006 - 2015





Source: PAHO/WHO Regional Dengue Program

Discussion

The presentations elicited a robust discussion regarding the elements included in the analyses, and suggestions regarding additional elements that should be considered in future studies on the burden of dengue. A question was asked regarding where vector control costs were included in the economic impact studies. It was noted that in the study of the socio-economic costs of dengue in Colombia, vector control costs were included but not broken out as a separate line item while in the study of costs in Mexico normative costs, but not actual expenses, were included. While the program budget did not vary from year to year in Venezuela, the budget line item for "actual costs", included as an "other" cost in the study, reflected costs incurred during outbreaks. It was generally agreed that vector control costs, which are substantial in most countries, should be included as a separate expense in economic impact studies of the cost of dengue fever.

A suggestion was made to examine the impact of dengue on health systems, not just the cost of dengue to the health sector. For example, how were unplanned costs such as those associated with a dengue epidemic addressed? Did other health programs suffer cuts as a result of the extra-budgetary costs associated with the dengue epidemic? The study in Colombia was noted for including expenses for non-traditional doctors; however, it was not clear why these expenses were categorized as "non-medical costs." Dr. Castro responded that the ministry of health does not include this group within its legal framework and thus the costs have to be classified as "non-medical." In response to a follow-up question regarding whether the researchers had examined the benefits of investing in strengthening medical care over preventive actions, he noted that it is likely that expenses are underestimated, but that if there is better dengue case management savings would be seen in DALYs and medical expenses. They have not conducted an analysis of how public policy can impact the cost of prevention efforts at the public and household levels as that was not part of the original study objective, but he agreed that it was a good idea. In response to a question regarding studies on families' "willingness

to pay" for a vaccine,several individuals noted that there were some studies currently addressing this issue.

Several meeting participants shared other burden of disease studies currently underway or in the process of being published. The availability of different methods for estimating costs, key papers that examine these methodologies, and the need for "benchmarks" were noted. The benchmarks in particular would allow for the true cost of a dengue case, an intervention, or an outbreak/epidemic to be placed in relation to a country's GDP, as seen in the presentation from Colombia. The importance of cost impact analyses was also highlighted as a step toward determining the cost effectiveness of the various interventions or components of an integrated program, which would be helpful to dengue program managers and policy makers. In the experience of a meeting participant, ministers of health and finance are more concerned with the impact of dengue prevention and control efforts on a country level, which calls for strengthening integrated approaches and going above and beyond activities such as integrated surveillance systems to including communications and other interventions that are part of an integrated program.

The challenge of distinguishing program costs between dengue and other vector-borne diseases such as malaria was raised, as the same staff may work in both programs. However, separating the costs is important and necessary in order to budget and appropriately plan program interventions.

A point of much discussion was how to use findings from studies like these to advocate for sustained or increased funding for dengue prevention programs, especially in light of a "so what" attitude among policymakers. Several meeting participants suggested bringing ministries of finance into program funding discussions much earlier, and looking for opportunities to present burden of disease study findings not only to ministers of finance but to policy makers and other strategic partners. It was suggested that discussions be

held with economists and experts in this area of study to identify the types of information needed to strengthen advocacy efforts and how this information can be effectively used with policy makers.

A meeting participant noted that governments will not invest in dengue programs if the impact of program interventions cannot be demonstrated, regardless of the data from burden of disease studies. Others agreed, and noted that greater effort is needed to evaluate the impact of new tools being deployed in order to identify the array of tools that improve program results. The ongoing challenge of the dengue, sanitation and water nexus was noted in light of the discussion, and concerns expressed that if the lack of water and sanitation in the communities most affected by dengue fever are not addressed, it will be impossible to control the disease. Given the significant costs spent by governments during outbreaks and epidemics, decision-makers in ministries of finance may decide prevention efforts are not worth the current investment as the programs have not been successful, to date, at reducing epidemics.

The representatives from Colombia and Mexico were asked whether they had seen the findings from the studies presented in the session. The study of costs in Mexico had not been presented to the national program staff while some data but not the entire study had been provided to the national program staff in Colombia. Findings from the Venezuela study were provided to the ministry of health but their impact on program funding was not known. The lack of integration of research and dengue program operations was discussed, due in part to insufficient resources both financial and human to coordinate between academia and ministries of health.

It was noted that in addition to the Regional Dengue Program, PAHO country offices often contribute directly to dengue prevention and control costs and that these costs vary from year to year. For example, the PAHO office in Nicaragua contributed $280,000 during the recent epidemic in that country.

Conclusions

1. Given the high social and financial costs of dengue, the possibility to include analysis of the "economic impact" of dengue into the health systems and services as an active element of the IMS-Dengue should be explored. This would allow programs to address questions such as "How much does prevention and control cost," "How much could be saved by sustained governmental investment in dengue prevention," and "What is the true financial and human impact of dengue in our communities?"
2. Financial indicators should be included in an integrated dengue prevention and control database such as the integrated surveillance system which combines epidemiological, entomological and laboratory indicators.
3. Most of the financial funds of the PAHO/WHO Regional Dengue Program are from external voluntary contributions. The participants expressed their astonishment and noted the efforts made by the PAHO/WHO Regional Dengue Program to take a lot of work with few resources.
4. In collaboration with PAHO, WHO is developing studies that will contribute towards a better understanding of the dengue burden and its economic impact in some countries of the Americas. This -is part of a global initiative of the WHO Global Strategy.

6. Dengue Research

Facilitator: Dr. Zaida Yadón, PAHO/WHO-TDR Liaison

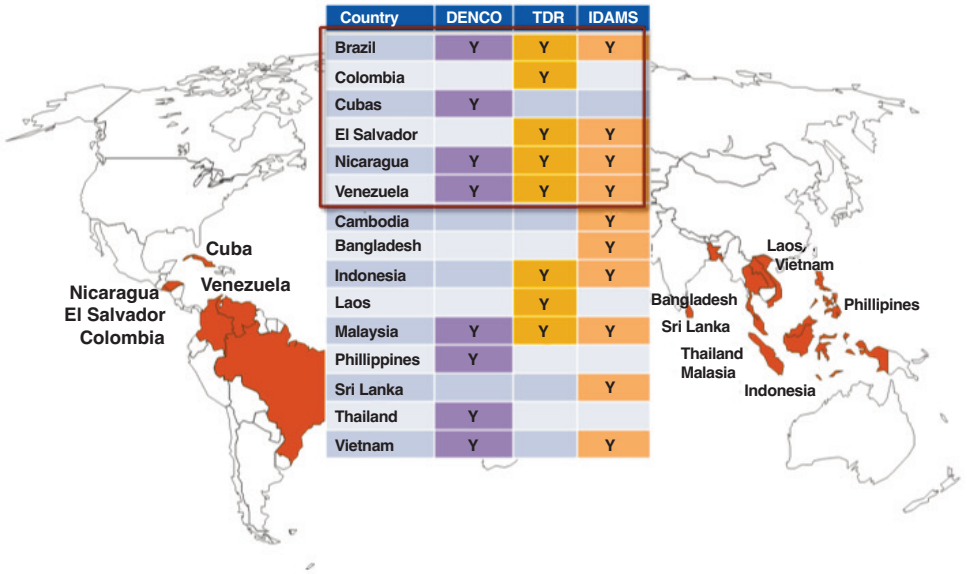
6.1. Priority Needs for Dengue Research: a WHO/TDR perspective

Dr. Piero Luigi Olliaro, Team Leader for Implementation and Intervention Research, TDR/WHO, presented TDR/WHO's dengue research priorities, which are based upon the premise that with new knowledge, new and improved tools can be developed that will lead to new and improved interventions, strategies and policies. There are three areas of focus:

(1) Dengue case management: The goal is to improve case management with high quality diagnostics. This has been accomplished by

development of the new dengue case classification (18 countries participated in this phase); validation and determination of the predictive value of dengue warning signs (8 countries participating as part of IDAMS, the International Research Consortium on Dengue Risk Assessment, Management and Surveillance); development of a new ICD web version to allow reporting in the old or new dengue case classification; and evaluation of performance of dengue diagnostics (Figure 13).

Figure 13. Countries included in TDR/WHO warning signs studies, 2014.



Country	DENCO	TDR	IDAMS
Brazil	Y	Y	Y
Colombia		Y	
Cubas	Y		
El Salvador		Y	Y
Nicaragua	Y	Y	Y
Venezuela	Y	Y	Y
Cambodia			Y
Bangladesh			Y
Indonesia		Y	Y
Laos		Y	
Malaysia	Y	Y	Y
Phillippines	Y		
Sri Lanka			Y
Thailand	Y		
Vietnam	Y		Y

Source: TDR/WHO, 2014

(2) Vector control: The goal is the development of new vector control strategies; improved knowledge of how to deliver dengue services through comprehensive approaches such as the eco-bio-social approach; and creation of a new research activity entitled "Social Enterprise Innovation and Social Entrepreneurship" to support innovation in research and development of dengue drugs, health services delivery, community-based vector control, and "green" technologies such as production of curtains by residents in the neighborhoods where they are being promoted.

(3) Outbreak detection and response: The goal is to identify new ways to gather evidence for the detection of dengue outbreak warning signs and through a prospective study; and the development of common indicators and terms for outbreak detection.

6.2. Preliminary results of a systematic review of the literature on dengue (2009 – 2013)

Dr. Gamaliel Gutiérrez Castillo, Epidemiologist, Regional Dengue Program, PAHO/WHO, presented the objectives of the systematic review of the literature on dengue being conducted in collaboration with the Milkin Institute School of Public Health at George Washington University: (1) Identify gaps in research for epidemiologic and vector control surveillance as described by the Integrated Management Strategy-Dengue (IMS-Dengue), (2) Determine acceptance and use of the new dengue case classification, (3) Determine use of laboratory tests and their contribution to dengue epidemiological surveillance, and (4) To assess the use of behavior change through the social communication component for the prevention and control of dengue. Standardized key words and terms are being used to search the Lilacs, Embase, Medline, and Scopus databases for publications in English, Spanish and Portuguese between 2009 and 2013.

The goal of the systematic review is to identify lessons learned from implementation of the individual components of the IMS-Dengue over the last 5 years. Implementation status of each component will be determined using the list of activities and proposed results described by San Martin and Brathwaite[5].

To date, 4,323 publications have been identified and 392 have been reviewed. Of the reviewed articles, the majority have been in the social sciences (271), followed by laboratory (56), integrated vector management (52), clinical case management (47), and surveillance (20). However, more articles meeting review criteria have been found in clinical case management and integrated vector management than in the remaining three components. The systematic review is still underway but preliminary findings from the 392 articles reveal:

[1]San Martin JL and Brathwaite O (2007). The Integrated Management Strategy for the Prevention and Control of Dengue in the Region of the Americas. Rev Panam Salud Publica/Pan Am J Public Health 21(1), pp. 55-63.

1. Dengue notification is mandatory in all countries of the region of the Americas.
2. Most countries in the Region rely on passive dengue surveillance through reporting of inpatient and outpatient dengue cases.
3. Use of mobile technologies can improve surveillance systems by increasing case capture and reducing reporting time.
4. There are few published studies on dengue warning signs and the new dengue case classification.
5. The new WHO case classification for dengue has been found to be:
   - More sensitive for capturing severe dengue cases
   - More user friendly for physicians, especially in epidemic situations.
6. There is evidence of new diagnostic capabilities (e.g., use of rapid tests) which can strengthen surveillance systems, but they are expensive.
7. Use of the COMBI planning methodology in its early stages showed a reduction of peridomestic mosquito breeding sites, but behavior change rates over the long-term were not sustained.
8. There are *A. aegypti* mosquito populations resistant to insecticides.
9. There is a lack of new molecules for *A. aegypti* control.

Next steps include completing the identification and review of articles which meet inclusion criteria (3,900 pending articles) and analyze findings from the review. It is hoped that the findings will support advocacy efforts for additional research on the effectiveness of the implementation of the IMS-Dengue strategy as a whole and not as stand-alone components.

6.3. The role of technologies developed with US government funding in the advancement of biomedical science, and

6.4. National Institute for Allergy and Infectious Diseases (NIAID) resources for dengue research

Dr. Cristina Cassetti, Dengue Program Officer for Extramural Dengue Research, NIAID, NIH presented the role NIH plays in the development of new technologies and a summary of NIAID's dengue research focus. The US government supports the translation of basic science research findings into the development of new tech-

nologies such as vaccines, drugs, and disease diagnostics, among others. One example is the dengue vaccine work conducted by the CDC, which has been licensed to several biotechnology companies. In addition, NIAID funds have supported the biotechnology company Takeda in the development of DenVax, including initial vaccine clinical trials.

The vast majority of NIAID's US$47 M dengue research budget (90%) supports extramural research; 50% of these research projects are for basic science, 20% are vaccine research, and there is a small amount supporting diagnostics research. Some of the basic research is focused on vector biology and mechanisms of insecticide resistance, dengue virus replication, and the development of animal models to evaluate dengue vaccine candidates and drugs, as well as epidemiological studies to identify immunological correlates of protection and biomarkers for serial dengue disease. NIAID is interested in funding operational and interdisciplinary research that includes social scientists and international collaborations. Dr. Cassetti noted that NIAID has several mechanisms for supporting research conducted internationally, including the following:

- *International Research in Infectious Diseases, including AIDS:* This funding mechanism targets low and middle income countries.
- *Biodefense and Emerging Infections Research Resources Repository (BEI):* This funding mechanism provides reagents for free, but the researcher must cover the shipping costs.
- Contracts to provide direct services to researchers. Examples include placement of dengue virus genomes in VIPER and development of a new mouse model for vaccine and drug testing (AG129 mouse model) by the University of Texas Medical Branch at Galveston (UTMB).
- Vaccine and pre-clinical services: This is an NIAID incubator service.

Discussion

There was general consensus that capacity for operational research that responds to the needs of the Region is critical as evidence-based decision making for effective interventions relies upon access to good quality information from operational research. It was suggested that documentation of operational research needs and identification of collaborating centers and research institutes that could conduct the research would be a next step after the meeting. A cautionary observation was offered regarding development of a long list of research topics that is not transformed into an action plan that research groups can carry out. It was noted that while priority research areas were clearly presented by TDR/WHO and NIAID, there is a need to look at multiple funding sources to deal with the general lack of research funds for dengue; one such opportunity is working with the newly reorganized PAHO Foundation to identify funding for specific, well developed research projects.

A potential area of operational research could be an examination of the aggregated value of using global themes such as 'Healthy households' or 'Healthy communities', to measure the impact of dengue on households with good sanitation conditions (i.e., mosquito breeding sites are properly managed) versus households without adequate sanitation over time. This could help respond to questions regarding whether communication and behavior change interventions are working, and how effective these interventions are within an IMS-Dengue framework. Most countries do not monitor or evaluate this program component due to a lack of technical capacity and a lack of funds.

Two suggestions were made regarding inclusion of topics in the systematic review of the literature: (1) social science disciplines that could expand understanding why people 'do one thing, and not another' in spite of knowledge regarding the benefits or dangers of the behavior and (2) vaccine development. It was noted that vaccine development has not been included because the review is examining implementation of the IMS-Dengue components, and vaccines are not yet an intervention.

It was suggested that other vector control programs be reviewed for lessons learned. For example, treated curtains are an extension of bed nets so what can be learned from the malaria program? Given that indoor residual spraying has proven to be effective in Australia, are there areas in the Americas where this strategy might be appropriate and if so how could it be deployed? There is a need to work on design issues such as how to design user-friendly covers for different types of water storage containers, which calls for research in collaboration with industrial design specialists or perhaps engineers. Research on use of impregnated curtains currently underway in Yucatán, Mexico and Mexican regulatory mechanisms requiring screening in new housing construction were noted as an example of the need for stronger connections between research and public policy.

Discussion on monitoring and evaluation of vector control interventions centered on the Region's general weakness in this area. While insecticide resistance is very important for any country using insecticides, many do not monitor for resistance so this could be an opportunity for country partners to test diagnostics for *Aedes* resistance. In fact, the topic of insecticides is an area where there are many gaps for evidence-based decision making, beginning with a lack of uniformity on what insecticide resistance is. Additionally, there is conflicting information in the published literature that needs to be resolved so countries can make appropriate decisions regarding inclusion of insecticides as a program tool.

Another area of research is whether the current prevention and control model is sufficient, or do we need a new one that includes new interventions such as the dengue vaccine? This is especially relevant for monitoring and evaluation, as new tools may be needed to assess overall program effectiveness. For example, will the current breeding site survey form used by most countries be sufficient once vaccination is part of an integrated dengue prevention and control program, or is something else needed for monitoring mosquito breeding?

It was noted that greater information dissemination is needed as countries do not always know about tools that have been developed, tested and are in use in other countries. For example, a smoke-releasing tablet for community-based vector control during outbreaks was developed and tested for efficacy in Venezuela. Based on study results that showed community use of the tablet resulted in the same high efficacy as when placed in the household by vector control staff, these tablets are now available for purchase during dengue outbreaks.

A meeting participant noted that one of the priorities of their biotechnology company is to close the critical diagnostic window between days 4 and 7 of dengue infection by combining NS1 with IgA antibody to increase sensitivity to detect dengue infection, and that preliminary data are promising.

Conclusions

1. Even when research is not the primary objective of PAHO/WHO in the Americas, the organization does use and promote research (operative research, mainly) to support the countries and their ministries of health to answer questions that will facilitate immediate solutions to the problems that programs face in their fight to prevent and control dengue.
2. Effective coordination and communication between institutions and researchers is necessary in order to merge efforts and avoid unnecessary costs in material or human resources, and duplication of information.
3. Better integration of academia, research centers and institutes, and national dengue programs is a priority in order to meet the operational research needs of countries in the Region.
4. New or improved sustainable vector control strategies continue to be a priority for the IMS-Dengue.
5. Translation of research into local level interventions is the step that is often missed in many research projects.

7. Update on the development of new technologies in dengue prevention and control

Facilitator: Dr. José Luis San Martín, PAHO/WHO

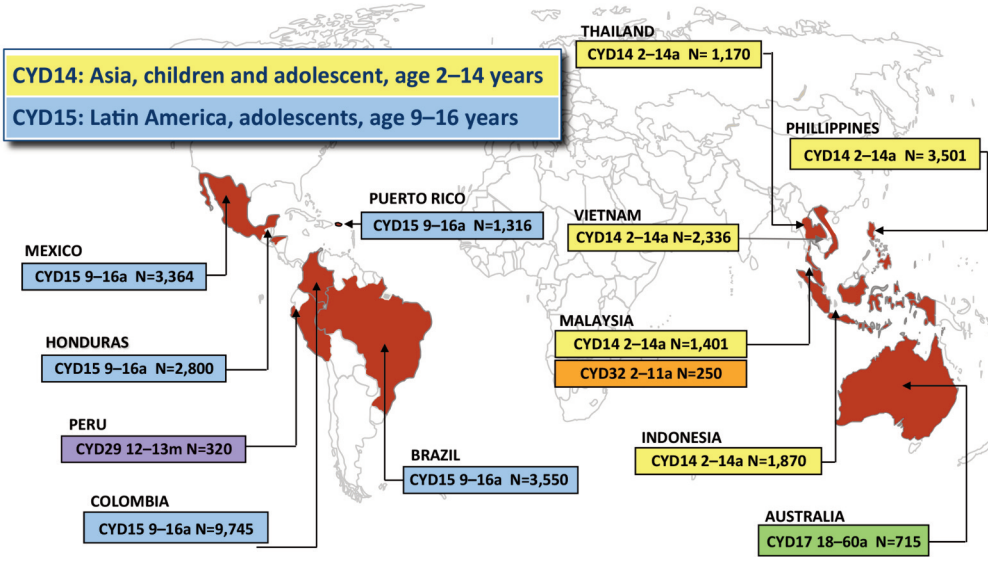
7.1. Vaccines and drugs

Dr. Andrea Vicari, Regional Advisor for Vaccines, Comprehensive Family Immunization Unit, PAHO/WHO-Costa Rica, presented a short summary of the status of dengue drug and vaccine development. To date there is no evidence that currently available drugs help prevent or reduce dengue disease or disease severity. Therapeutic approaches include (1) direct-acting antiviral drugs that target virally encoded functions, (2) drugs that target host functions essential for viral replication, (3) drugs that target dengue-associated pathology, such as vascular leakage, and (4) monoclonal antibodies against structural viral epitopes. Should drugs become available, how they would be used in the diverse settings of disease incidence is the next important issue to be addressed.

With respect to the status of a dengue vaccine, there are more than 20 in clinical development, three of which are in phase I clinical trials (to determine safety), two in phase II (to determine immunogenicity); and one in phase III (to determine efficacy). An unexpected result in the only efficacy study conducted to date, the Sanofi Pasteur phase llb study in Thailand with 4,000 healthy school children 4 to 11 years, was the limited protection for DENV2. Reasons for this may be interference between viruses contained in the vaccine and incomplete immune protection. Results from the Sanofi Pasteur phase lll trials taking place in several countries should help researchers better understand the Thailand study data (Figure 14).

Other issues to be considered are cost and cost-effectiveness of the vaccine, and community acceptance. While efficacy is important, other aspects such as the actual impact of the vaccine on the disease and changes in disease incidence are important considerations. Until the cost of the vaccine is known, impact cannot be determined or even modeled as cost may affect distribution as well as the number

Figure 14. CYD-TDV: Countries with clinical trials phase III, 2014.



Source: Adapted from http://clinicaltrials.gov

of doses of vaccine available. This information is critical for the definition of vaccination strategies, along with standardized data, in particular disease severity and patient age, and reliable monitoring systems.

As for community acceptance, there may be high community demand and not enough doses to meet the demand, or people may reject the vaccine for reasons that may not be well understood. In summary, there are high expectations for a vaccine in spite of the fact that it is not clear how well a vaccine will perform in real life settings.

7.2. Other technologies in the control of *Aedes aegypti*

Dr. Haroldo Bezerra, Regional Advisor for Public Health Entomology, PAHO/WHO, presented advances in the development of new, cost effective technologies for *A. aegypti* control. He noted that the vector control strategies being used today are the same as those used decades ago. While these strategies are effective when properly implemented, a major challenge has been the lack of proper and consistent implementation of control actions. In addition, many programs for preven-

tion and control of vector-borne diseases are based on existing malaria and yellow fever eradication programs, which may not be an appropriate model; chemical control is the primary strategy; and space applications and larviciding are not sufficiently evaluated. However, increased resistance to insecticides and the limited number of new products coming on market endanger the effectiveness of routine mosquito monitoring and outbreak/epidemic control. Calculation of entomological indices is essential to effective planning, yet it is labor intensive and therefore expensive. This has led to research on new strategies for the rapid assessment of entomological indices, such as LIRAa and the pupal index.

A significant amount of research has been carried out on the development of new tools for not only the collection of adult mosquitoes to calculate the adult mosquito index, but also to reduce adult densities such as lethal ovitraps, sticky traps (MosquiTRAPTM), autocidal gravid ovitraps, the Biogents® Sentinel (BGS) trap, the AdulTRAP®, and D-VAC insect collectors. Another innovation is use of technology to facilitate immediate responses to specific local conditions such as improved vector surveillance by electronic submission of results directly from the field using apps, and integrated data analysis of entomological and GIS mapping data.

Other technologies such as covers for water storage containers have been tested and evaluated; while there is evidence that these covers are effective in reducing dengue, consistent and correct use as well as degradation of the cover over time continue to be challenges. Ongoing development of community-based vector control tools include new ways to use insecticide-treated materials such as impregnated curtains for windows and doors as well as wall coverings. Studies have shown that impregnated curtains can reduce dengue rates if there is high use in the targeted area; if coverage is low, the effect disappears. These studies have also shown that while there may be high initial coverage, declines in use are seen over time due to lack of advocacy and communication strategies to promote continued use of the curtains. Other community-based tools include biological control methods such as copepods (*Mesocyclops*), fish or

bioinsecticides such as Bti (*Bacillus thuringiensis israelensis*) and spinosad to eliminate the aquatic phases of *A. aegypti*. Monomolecular films which cover water surfaces using a non-toxic substance, such as Aquatain MF® (mosquito formulation), are also useful at the household and community levels.

Genetic modification of mosquitoes to reduce adult mosquito densities is a growing area of research. One approach is genetic modification of males by inserting a lethal gene (RIDL, release of insects containing a dominant lethal) which doesn't allow the males to survive. Other genetic modifications include the sterile insect t echnique (SIT), which involves release of sterile males that breed with wild females whose progeny do not survive. A third approach involves inserting the bacteria *Wolbachia* into *A. aegypti* mosquitoes to reduce their ability to transmit the dengue viruses or to shorten the lifespan of the mosquito. It is expected there will be less dengue virus transmission with a greater proportion of *A. aegypti* infected with *Wolbachia*. Study data on the impact of genetically modified mosquitoes on disease transmission is not conclusive so more operational research in this area is needed.

The Vector Control Advisory Group (VCAG) on new tools, established in 2013, is a WHO advisory body on new forms of vector control for malaria and other vector-borne diseases. It has been tasked with:

- Reviewing and assessing the public health value, "proof of principle" (epidemiological impact), of new tools, approaches and technologies; and
- Making recommendations on the use of these new tools for vector control within the context of integrated vector management in multi-disease settings.

Dr. Bezerra closed the presentation noting that insecticides are still an effective and necessary mosquito control tool when properly used within an integrated framework, larval and pupal indices continue to be useful for entomological surveillance, and new monitoring and control alternatives should be further studied for their effectiveness, sustainability and costs.

7.3. Modeling in dengue control

Dr. Andrea Vicari, Regional Advisor for Vaccines, Comprehensive Family Immunization Unit, PAHO/WHO-Costa Rica, noted that modeling can provide key inputs for structured decision making. The five stages of a policy decision provide opportunities to identify the problem (Agenda setting), propose (Policy formulation) and select (Decision making) the solution, put the solution into practice (Policy implementation), and monitor results (Policy evaluation). Using a decision-making flowchart (Clemen and Reilly, 2002) can help determine whether the model is working properly for decision making.

An infectious disease model should help understand the driving forces of disease ecology and epidemiology, measure epidemiological parameters that cannot be directly measured, make predictions of disease incidence under specific conditions, and forecast the impact of prevention and control measures. To ensure the correct factors are measured or taken into consideration in the model, broader involvement of individuals in the dengue modeling process is needed so diverse perspectives are included, not just that of the modeling experts. He emphasized that modeling results are not as important as the inputs into the model, as the quality of the data and how well the inputs reflect disease transmission are key to obtaining useful outputs. The Ross-McDonald model for malaria transmission, a mathematical model and one of the first models for vector-borne diseases, has served as a basis for examining methods, defining what should be included, and building new models of mosquito-borne disease transmission. When compared to the classic malaria model, the dengue model is more complex because it needs to take into account both human and vector movement.

In a systematic review of dengue deterministic transmission models published between 1992 and 2011, 42 out of 389 articles were analyzed. It is notable that since 2002, there has been at least one publication every year and since 2005, several publications a year on dengue transmission models. The Vaccine Modeling Initiative (VMI), working in collaboration with WHO, was established to generate new computational models and simulations to improve decision making in

vaccine research and development and epidemic control policies. The Dengue Vaccine Initiative (DVI) has also been working on modeling the impact of vaccines on dengue transmission and incidence.

Modeling is important because the positive impact of vaccination can be measured, as well as details such as the number of cases averted due to specific vaccination coverage levels and the impact of a combination of vaccine strategies; thus providing key input to structured decision making. A gap in current efforts is that decision makers are not involved in the modeling process and thus inputs needed for decision making on vaccine implementation may not be included in the model.

VMI-WHO plans for 2014 include organizing a consensus meeting on dengue impact modeling to share best practices in vaccine and vector control models and to establish a consensus on key parameters, assumptions and public health outcomes. A comparative review of dengue impact models is on hold because most of the modeling groups are associated with only one vaccine developer.

Discussion

Ensuring that evaluations of any new technology, be it vaccines or vector control, are conducted at the neighborhood level is essential as this is where the impact of the tools is targeted. It was suggested that decentralizing testing to local neighborhood settings to determine cost and effectiveness of the various interventions should be considered.

With respect to a dengue vaccine, it was noted that we generally do not know or understand what public health officials' expectations are for the vaccine, for example, do they expect it to reduce the number of cases of severe dengue, hospitalization of dengue cases, or the number of dengue cases? For example, the rotovirus vaccine was 90% effective for reducing hospitalizations and severe rotavirus but only 60% effective at reducing the number of cases. These are important differences that need to be understood prior to introduction of a vaccine. Additionally, three important points for the dengue vaccine need to be better understood: first is safety, not just reactive

but vaccination should not increase the number of cases of dengue; second is efficacy, with the highest possible efficacy for all four serotypes and a measurable decrease in mortality; and third is affordability and access, which includes production of enough vaccine to provide it to everyone who wants to be vaccinated or at minimum enough to make a difference in dengue case fatality rates. A final point was made that vaccine protection needs to be at least 10 years, with a minimum number of boosters. With respect to affordability and access, vaccine pricing is based on sustainability so an assessment of the resources available in light of introduction of a vaccine in the next year or two should be a part of the dialogue between national program directors and policy makers.

The point was made that there will never be a "perfect" vaccine, but that we should not lose sight of the important impact of vaccination on public health. Also, the funds being invested in vaccine development and testing are providing returns through discussions that have allowed for improved decision making. For example, it is now clear that effective dengue prevention and control will require both a vaccine and ongoing vector control. However, policy makers will be looking for data and cost analyses of the various options as a way to perhaps reduce dengue program costs. It was suggested that this is an area where PAHO/WHO could be influential by initiating conversations with policy makers across the Region so the impact of the vaccine on dengue programming is placed within the proper context. This context includes not just vaccine cost-effectiveness but logistics of implementation of the vaccine such as refrigeration, number of doses, boosters, whether to incorporate it into the national expanded program on immunizations, and distribution points, among others. Part of the discussion with policy makers should also include the issue of vaccine efficacy as even with 50% effectiveness in reducing cases, countries will still need to sustain all the other control measures.

A question regarding modeling dengue transmission and vaccination was raised, as useful information relevant to policy makers could be obtained. Examples were given of the utility of a model developed in Colombia to predict dengue outbreaks in the military

and the work being done by the modeling consortium supported by the Gates Foundation. A suggestion was made to include in the research agenda a study of what existing dengue models can contribute to decision making around vaccine implementation and disease transmission.

Several participants emphasized that it is not "if there is a vaccine" but "when the vaccine is introduced." This means countries need to start preparing for its introduction now by making adjustments to their epidemiological surveillance systems and vector control strategies. A meeting participant predicted that even if the vaccine only reduces dengue cases by 50%, there will be great demand for vaccination due to the heavy burden of the disease on communities. Preparation for communication with the population groups initially targeted for vaccination is important so the communication strategy can be implemented when the vaccine is available.

Public health entities such as PAHO and WHO are often called upon to comment on results from vaccine trials or studies of new vector control tools, at times without advance notice of the release of study findings. An example of a positive collaboration between industry and WHO was the sharing of a press release regarding vaccine trial results in advance of its official release, which allowed WHO to prepare for media inquiries. Collaboration between academia, industry, and WHO/PAHO can help reduce conflicting messages and streamline decision making.

An ongoing challenge noted by several participants is that despite documented high levels of knowledge about dengue, community practices have not changed much. Where are the models for impacting community behavior and how do they work? It was noted that as seen in the other IMS-Dengue components, there is no single model that will be effective for everything that is encompassed in the broad concept of "community behavior change." This requires different models for different stages of behavior change and perhaps also different target groups. It was noted that "behavior change" in dengue means millions of people

changing their behavior, so the scale of behavior change is significant. To effect this level of change requires changes in social norms, which occur over many years and through a combination of integrated approaches, such as mass media linked to school-based educational efforts and locally-focused interventions, targeted legal interventions, and sustained messaging about the positive community and social outcomes of the behavior change. This approach takes a large effort and significantly more funding that what has been allocated for social mobilization and communication for dengue. The reality is that most countries cannot manage large-scale, integrated communications interventions due to a lack of skilled staff and funding. A second aspect to community behavior change is the issue of access to reliable and good quality water and sanitation services, the lack of which leads to the behaviors that promote mosquito breeding. The behaviors to prevent mosquito breeding in water storage containers are often onerous and not feasible for the majority of residents. This combined with community resentment that the government has not provided basic services leads to community rejection of dengue prevention messages. Thus, sustained behavior change requires persistence and greater involvement of the other IMS-Dengue components, in particular integrated vector management.

Conclusions

1. Currently, several dengue vaccines are in development and there is a high possibility to obtain one of them in the next decade.
2. Dengue vaccines efficacy / impact, cost / affordability and number of doses available per country are critical data to define vaccination strategies. For this reason, it is important to bring policy makers into discussions regarding vaccine implementation, elements that should be included in modeling dengue transmission, and the integration of vaccination and vector control in national dengue programs.
3. The chemical control, used properly, is still necessary to control dengue transmission, but only into the IMS-Dengue framework. Existing vector control tools are effective in elimination of the *A. aegypti* mosquito, although questions on their sustainability and appropriateness for community-based use remain.

4. More solid evidence about the efficacy and impact (socioeconomic and ecologic) of new technologies (transgenic mosquitoes, Wolbachia, *Betta splendes* fish) is necessary to recommend them as vector control methods for dengue transmission. The VCAG mechanism from WHO is an available and recommended alternative to achieve this objective
5. Behavior change approaches for dengue prevention and control need to be conducted on a larger scale than what is currently seen, and with a corresponding investment in communications and social mobilization.
6. The main purposes of infectious diseases modeling include; to understand fundamental driving forces of disease ecology and epidemiology, measure epidemiological parameters, make predictions of disease incidence and forecast impact of different prevention/control measure.
7. Modeling can be a key input to structured decision making, especially on dengue vaccine (several vaccine initiatives on dengue modeling are ongoing).
8. The process of introducing new technologies to prevent and control dengue must undergo careful review to guarantee the proper use of these technologies by the countries.

IV. RECOMMENDATIONS

A draft set of recommendations was developed based upon the discussions from each plenary session. The recommendations directed toward PAHO/WHO or the PAHO/WHO Regional Dengue Program were categorized as "general recommendations"; while those for specific IMS-Dengue components were categorized as "IMS-Dengue component-specific recommendations." These recommendations will help the PAHO/WHO Regional Dengue Program in its review of the "state-of-the-art" in dengue prevention and control as well as to provide guidance for revisions and updates to the Integrated Management Strategy for Dengue Prevention and Control.

1.1 General recommendations:

1. To have a sustained impact on the prevention and control of dengue it is essential to have an inter and intrasectoral approach to enable action on the social and economic determinants of health.
2. PAHO/WHO, in coordination with national dengue programs, is responsible for facilitating compliance with the mandates and resolutions signed by the Ministers of Health in relation to the prevention and control of dengue in the Americas.
3. The PAHO/WHO Regional Dengue Program should prompt the evaluation of and revisions to each of the IMS-Dengue components, prioritizing those with less progress (i.e., Environment, Integrated Vector Management and Social Communication).
4. The PAHO/WHO Regional Dengue Program should review and update the IMS-Dengue components according to the needs and challenges presented by the countries in the Americas (e.g., Management, Financing, Vaccines).

5. PAHO/WHO should promote cooperation between countries to address common challenges such as the presence of dengue in border areas, and among mobile populations, marginalized and underserved populations in urban and peri-urban centers, and communities affected by social violence.
6. The PAHO/WHO Regional Program on Dengue should coordinate efforts with countries and other key stakeholders so that the information from studies of the economic impact caused by dengue is used by governments and decision makers.
7. The PAHO/WHO Regional Program on Dengue should work with the PAHO Foundation to provide necessary information and project and research proposals on the issue of dengue in order to form alliances and capture the interest of stakeholders and donors.
8. With the presence of Chikungunya in the Region, PAHO/WHO should support interventions and operational research to facilitate an efficient and effective approach to dengue and Chikungunya in all its components, mainly, using the IMS-Dengue as the platform to operate integrated action to prevent and control both diseases.
9. The launch of any vaccine in the Americas must be within the framework of the recommendations found in *Introduction of New Vaccines* established by PAHO/WHO.
10. PAHO/WHO should support the countries in the Region in decision making for the use of new technologies for the prevention and control of dengue following protocols for their introduction that meet the needs of national dengue programs.
11. PAHO/WHO should facilitate coordination between donors and national dengue programs to develop the research skills that generate evidence, through operational research developed by stakeholders, academia and specialized research agencies.
12. The PAHO/WHO Regional Dengue Program should work with countries in the development of multicenter research projects to address common problems that face national dengue programs.

1.2 IMS-Dengue component-specific recommendations

Laboratory

1. PAHO/WHO should facilitate the regular updating and adaptation of laboratory procedures, technology, work plans and proposals of the Collaborating Centers based on the identified needs of countries.
2. The elaboration of the Genomic map of dengue virus in the Region should be developed. This would allow a better understanding of the dynamic in dengue transmission and also would be an important tool in surveillance and interventions based on risk and evidence.

Epidemiology

1. PAHO/WHO should support the strengthening of surveillance systems (epidemiological, entomological, clinical, and social) within countries to generate information that is both timely and of high quality in accordance with the recommended standardized indicators and goals to facilitate decision-making.
2. The generic protocol for the integrated epidemiological surveillance is a necessary tool that will allow the standardization of dengue case reports, using the same case definition and severity classification in all countries. This integrated surveillance should be implemented in all countries once is available.

V. ANNEXES

1. Agenda

Wednesday, May 28, Room B
Coordinator: Dr. Tamara Mancero, PAHO/WHO

Time	Content	Participants
8:30 – 9:00 am	Opening Remarks	Dr. Francisco Becerra Assistant Director, PAHO/WHO
9:00 - 9:20 am	Participant introductions, review of agenda and introduction	Dr. Luis G. Castellanos Unit Chief, Neglected, Tropical and Vector Borne Diseases, PAHO/WHO
Session 1 Facilitator: Dr. Luis Gerardo Castellanos, PAHO/WHO		
9:20 - 9:40 am	Dengue situation in the world; the WHO perspective	Dr. Raman Velayudhan Coordinator , Vector Ecology and Management HTM/NTD, WHO Geneva
9:40 – 10:00 am	Dengue situation in the Americas; the PAHO perspective	Dr. José Luis San Martín Regional Dengue Advisor PAHO/WHO
10:00 – 10:15 am	Plenary Session 1	
10:15 –10:30 am	**Coffee break**	
Session 2 Facilitator: Dr. José Luis San Martín, PAHO/WHO		
10:30 – 11:45 am	Round table: Implementation of the IMS-Dengue in Latin America and the Caribbean. (15 minutes per presentation) • Communication • Laboratory surveillance • Care for patients • Integrated vector management • Epidemiology	GT-Dengue*: Dr. Linda Lloyd Dr. Elizabeth Hunsperger Dr. Ernesto Pleités Dr. Haroldo Bezerra Dr. Ángel Álvarez
11:45 -12:30 pm	Plenary Session 2	
12:30 – 2:00 pm	**Lunch**	

Time	Content	Participants
Session 3 Facilitator: Dr. Franklin Hernández, PAHO/WHO		
2:00 - 2:40 pm	Experience of Brazil and Mexico in the IMS–Dengue (20 min per presentation)	Dr. Giovanini Coelho (Brazil) Dr. Cuauhtémoc Mancha (Mexico)
2:40 – 3:25 pm	Plenary Session 3	
3:25 – 3:40 pm	**Coffee break**	
Session 4 Facilitator: Dr. Siripen Kalayanarooj, WHO collaborating center Thailand		
3:40 – 4: 40 pm	Round table: The work of the PAHO/WHO collaborating centers in Latin America and the Caribbean (15 min per presentation) • IPK (Cuba) • CDC (USA) • Evandro Chagas Institute (Brazil) • National Institute of Human Viral Diseases (Argentina)	Collaborators: Dr. Maria G. Guzmán Dr. Harold Margolis Dr. Pedro Vasconcelos Dr. Delia Enria
4:40 – 5:25 pm	Plenary Session 4	
5:25 – 5:40 pm	Closing Remarks	Dr. José Luis San Martín, PAHO/WHO

*GT-Dengue: International Dengue Task Force.

Thursday, May 29, Room B
Coordinator: Dr. Aída Soto, PAHO/WHO

Time	Content	Participants
Session 5 Facilitator: Dr. Angel Alvarez, PAHO/WHO		
8:30 – 8:50 am	Economic impact of dengue and dengue hemorrhagic fever in Zulia, Venezuela	Dr. Germán Añez, Researcher
8:50 – 9:30 am	Studies on the socioeconomic burden of dengue. (20 min per presentation). • Andes University, Bogota-Colombia • National Autonomous University of Mexico	Speakers: Raul Castro, Associated Professor Dr. Adriana Zubieta Zavala

Time	Content	Participants
9:30 – 9:45 am	Financial resources for the prevention and control of dengue in the Americas - PAHO/WHO	Dr. Luis G. Castellanos PAHO/WHO
9:45 – 10:30 am	Plenary Session 5	
10:30 – 10:50 am	Group picture (Room A)	
10:50 – 11:05 am	**Coffee break**	
Session 6 Facilitator: Dr. Zaida Yadón, PAHO/WHO		
11:05am–12:15 pm	Research on dengue: • Dengue Research and Capacity Strengthening: An Overview of Activities at the Special Program for Research and Training in Tropical Diseases (TDR), with Focus on the Americas (20 min) • Preliminary results of a systematic review on dengue during the last 5 years (20min) • The role of USG technologies in the advancement of biomedical science (15 min) • NIAID resources for dengue research (15min)	Speakers: Dr. Piero Luigi Olliaro - TDR/WHO Dr. Gamaliel Gutiérrez - PAHO/WHO Dr. Margarita Ossorio - NIH Dr. Cristina Cassetti - NIH
12:15 – 1:00 pm	Plenary Session 6	
1:00 – 2:30 pm	**Lunch**	
Session 7 Facilitator: Dr. José Luis San Martín, PAHO/WHO		
2:30 – 3:30 pm	Round table: Update and development of new technologies in dengue control and prevention (20 min per presentation) • Vaccines and drugs • Other technologies in the control of *A. Aegypti* • Modeling in dengue control	Dr. Andrea Vicari – PAHO/WHO Dr. Haroldo Bezerra - PAHO/WHO Dr. Andrea Vicari - PAHO/WHO
3:30 – 4:25 pm	Plenary Session 7	
4:25 – 4:40 pm	**Coffee break**	
4:40 – 5:10 pm	Closing Remarks Conclusions and recommendations	Dr. Luis Gerardo Castellanos PAHO/WHO

2. List of participants

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Dr. Yadón, Zaida
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Dr. Zubieta, Adriana
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3. Group photograph: State of the Art in Prevention and Control of dengue in the Americas meeting.

Lugar: Sala A de la sede de la OPS/OMS, Washington, D.C., EUA.