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Dengue Fever: The Need of a Sustained and Integrated Epidemiological Surveillance Approach. Colombia, a New Perspective for Getting Back to Basics

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Abstract

This paper provides an updated review of the dengue situation in the Latin-American countries, focusing on Colombia as a highly and historically affected nation. In first instance, it presents a scientific overview about the biology, clinical progress, transmission mode and epidemiology of the disease. Secondly, it describes the different outbreaks in the region during the past five decades. Thirdly, as an illustration of historical trends in most provinces and Colombian territories, early detection and predictive value of a dengue epidemic is inadequate and how a surveillance system should work. Based on these, the document proposes to provide a framework for a pilot model of a sustained and integrated epidemiological surveillance system in Colombia, focused on early detection, prediction (turning point) of outbreaks and recommendation of a model to be implemented by the Colombian local health units of each affected territory.

It emphasizes that a vector-borne disease such as dengue must be addressed locally, having the individual, all the way through a primary health care and population-based approach, at the center of the system. It also highlights a new approach for returning to the basics in primary health attention in which the community health promoter be again one of the main participants. The paper concludes that without a primary health care approach, particularly under the existing decentralized local and regional governments, it will be so difficult to achieve real control over this kind of cyclical public health issues.

Keywords: Colombia, dengue, dengue outbreaks, dengue fever, dengue hemorrhagic fever, epidemiological surveillance system, active surveillance system, passive surveillance system, integrated epidemiological surveillance system, epidemics of dengue

Dengue: La necesidad de un enfoque sostenido e integrado de vigilancia epidemiológica. Colombia, una nueva mirada para retomar lo esencial

Resumen

Este documento proporciona una revisión actualizada de la situación del dengue en los países de América Latina, centrándose en Colombia como una nación alta e históricamente afectada. En primera instancia, proporciona una visión científica sobre la biología, evolución clínica, modo de transmisión y epidemiología de la enfermedad. En segundo lugar, describe los diferentes brotes de las últimas cinco décadas en la región. En tercer lugar, es un ilustrativo de las tendencias históricas, en la mayoría de las provincias y territorios colombianos, donde se evidencia que la detección temprana y el valor predictivo de una epidemia de dengue es inadecuado, mostrando la situación actual en Colombia y cómo debe funcionar realmente el sistema de vigilancia. Con base en estos aspectos, se pretende brindar un marco para un modelo piloto de un sistema de vigilancia epidemiológica sostenido e integrado para Colombia, orientado a la detección temprana y predicción (punto de inflexión) de los brotes de dengue. De esta forma el modelo se brinda como una recomendación para ser implementado por las unidades locales de salud en cada territorio afectado.

Al final, este artículo de revisión enfatiza que una enfermedad transmitida por vectores como el dengue debe ser abordada a nivel local, teniendo al individuo, a través de un enfoque de atención primaria de salud, en el centro del sistema. También destaca una nueva mirada para volver a las bases en la atención primaria de salud, en la que el promotor comunitario de salud vuelve a ser uno de los principales actores. De hecho, el documento concluye que, sin un enfoque de atención primaria de la salud, particularmente bajo los gobiernos locales y regionales descentralizados existentes, será muy difícil lograr un verdadero control de este tipo de problemática en salud pública.

Palabras Clave: Dengue, dengue hemorrágico, brotes epidémicos de dengue, sistemas de vigilancia, sistema activo de vigilancia epidemiológica, sistema pasivo de vigilancia epidemiológica, sistema integrado de vigilancia epidemiológica

Dengue: a necessidade de uma abordagem sustentada e integrada da vigilância epidemiológica. Colômbia, um novo visual para voltar ao essencial

Resumo

Este documento fornece uma revisão atualizada da situação da dengue nos países da América Latina, com foco na Colômbia como um país alto e historicamente afetado. Em primeira instância, fornece uma visão científica da biologia, curso clínico, modo de transmissão e epidemiologia da doença. Em segundo lugar, descreve os diferentes surtos das últimas cinco décadas na região. Em terceiro lugar, é ilustrativo de tendências históricas, na maioria das províncias e territórios colombianos, onde é evidente que a detecção precoce e o valor preditivo de uma epidemia de dengue são inadequados, mostrando a situação atual na Colômbia e como deve ser o sistema de vigilância para realmente funcionar . Com base nesses aspectos, pretende-se fornecer uma estrutura para um modelo piloto de um sistema de vigilância epidemiológica sustentado e integrado para a Colômbia, voltado para a detecção precoce e previsão (ponto de inflexão) de surtos de dengue. Dessa forma, o modelo é oferecido como recomendação a ser implementada pelas unidades locais de saúde de cada território afetado.

Ao final, este artigo de revisão enfatiza que uma doença transmitida por vetores como a dengue deve ser abordada no nível local, tendo o indivíduo, por meio de uma abordagem de atenção primária à saúde, no centro do sistema. Também destaca um novo olhar para o retorno ao básico na atenção primária à saúde, na qual o promotor comunitário de saúde é novamente um dos principais atores. De fato, o documento conclui que, sem uma abordagem de atenção primária à saúde, particularmente sob os atuais governos locais e regionais descentralizados, será muito difícil conseguir um verdadeiro controle desse tipo de problema de saúde pública.

Palavras-chave: Dengue, dengue hemorrágica, surtos epidêmicos de dengue, sistemas de vigilância, sistema de vigilância epidemiológica ativa, sistema de vigilância epidemiológica passiva, sistema integrado de vigilância epidemiológica.

Scientific Overview

Biology of the Organism and Clinical Course of the Disease

Dengue fever is an acute febrile viral disease caused by one of four antigenically related but distinct virus serotypes [1], subtypes belong to the *flaviviridae* family, consisting of 60 arthropod-borne viruses and virions contain a single-strand of RNA in an isometric nucleocapsid. Once infection is set in a human host, it can cause dengue fever (DF) or the more serious syndromes: dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). Infection occurs when an infected mosquito, most commonly the *Aedes aegypti* species, transmits the virus particles and infects a susceptible host. The virus attaches to and penetrates mononuclear phagocyte cells where it replicates itself and excises from the cell via exocytosis forming additional infectious virus particles [2].

Dengue viruses have an incubation period of 3 to14 days (average is 5 to 8 days), after which symptoms begin to appear. This period also presents acute fever during which the virus circulates in the host's blood. If an uninfected mosquito bites the individual during this phase, the mosquito becomes infective and can pass the virus to others after an extrinsic incubation period within the vector of 8 to 12 days [3].

The symptoms of DF include abrupt fever, which can last 4 to 6 days, headache, myalgias, chills, aches, facial flushing and a transient macular rash, which may appear during the first 24 to 48 hours of the disease period. Subsequently, anorexia, nausea, vomiting, lymphadenopathy, and cutaneous hyperalgesia can develop during days 2 to 6. A secondary macropapular rash can occur towards the end of the disease period, along with itching, an increase in temperature and/or hemorrhagic lesions on the extremities. Children also frequently experience a sore throat and cough [4]. The disease course of DHF and DSS begin in a similar fashion to that of DF; however, patients with these more serious illnesses tend to deteriorate after 2 to 5 days, experiencing petechiae, bleeding, easy bruising, hepatomegaly, and eccymoses [5]. The World Health Organization (WHO) classification system of the range of severity of DHF is presented in Table 1.

Table 1. World Health Organization Criteria for Classification of DHF patients*.

Grade of Disease	Signs and Symptoms
1	Fever accompanied by non-specific constitutional symptoms with a positive tourniquet test as the only hemorrhagic manifestation
2	Same as grade 1, except with spontaneous hemorrhagic manifestations
3	Circulatory failure manifested by rapid, weak pulse with narrowing of the pulse pressure (<20mmHg) or hypotension
4	Profound shock with undetectable blood pressure and pulse

*(Henchal and Putnak, 1990)

The virulence of the virus depends on genotypic differences in the virus serotype; glycosylation of viral proteins; and the maturation state of the virus [4]. Individual genetic differences within the host may also affect infectivity [4]. Infection with one serotype of the dengue virus provides immunity against that same serotype; however, individuals remain susceptible to the other three serotypes. In fact, secondary infections with dengue sometime after a first infection of a different serotype can often result in an amplification of disease severity, a phenomenon described as antibody-dependant enhancement of viral infectivity [6]. This is due to a complex immunologic mechanism where the antibodies from a previous infection form a complex with the new virus, increasing the virus' infectivity of mononuclear phagocytes. Secondary infection is also a risk factor for DHF/DSS [4].

Modes of Transmission

Dengue is a vector-borne virus biologically transmitted to humans via a mosquito of the species *Aedes* and not person-to-person. *A. aegypti* tends to breed around standing water near domestic dwellings and feed during the day, becoming with the dengue virus 8 to12 days after biting an infected host. Peak biting happens early in the day, 2 to 3 hours after sunrise and again in the evening before dark and often does so from multiple host during one feed. If the mosquito is infective, this can result in multiple cases of dengue within one household or family. This makes *A.aegypti an* effective vector [7]. Although usually vector-borne, transmission of dengue can also occur in blood transfusions, organ transplants or from an infected mother to her fetus [8].

The only natural hosts for the dengue viruses are humans, primates and mosquitos, which act as the primary vector [9]. The enzootic transmission cycle involves the Aedes mosquitos and lower primates primarily in rainforest climates. Rural epidemic transmission cycles occur when the virus moves into inhabited areas and quickly infects all susceptible persons, leading eventually to herd immunity and reduced infectivity. Urban epidemic/endemic transmission cycles involve the sustainment of the virus within a mosquito-human-mosquito cycle and often involve multiple virus serotypes circulating at the same time, referred to as hyperendemicity [3]. Any environmental factor that affects A.aegyptisurvival or reproduction will have an effect on the transmission of dengue. For example, global temperature and rainfall changes have led to and increased geographical distribution and a denser population of A. aegypti [10]. Another factor implicated in the increment of incidence worldwide is increased air travel, which effectively spreads dengue across the world to places where it was not previously endemic [11].

Epidemiology

The World Health Organization calls dengue: "The most important mosquito-borne disease in the world". Globally, there are 400 million dengue infections per year with 500,000 cases of DHF and 22,000 deaths [12], being most prevalent in urban areas in the Americas, South-East Asia, the Eastern Mediterranean and the Western Pacific and rural Africa [13]. As documented, certain factors in developing countries in the tropics have contributed to the spread of dengue in said areas: "Rapid population growth, rural-urban migration, inadequate basic urban infrastructure (e.g., unreliable water provision, leading householders to store water in containers near to homes) and increase in volume of solid waste, such as discarded plastic containers and other abandoned items, which provide larval habitats in urban areas" [14]. Bite rates during dengue epidemics are usually 40% to 50% but can be as high as 80% to 90%. Without treatment, case fatality rates (CFR) for DHF often exceed 20%, but efficient, proper medical treatment can reduce the CFR to less than 1% [13]. From 1995 to 2020, the average incidence of DF in Colombia was 126.1 per 100,000 (range: 48 to 324/100,000), the average incidence of DHF was 7.5 per 100,000 (range: 0.5 to 20.8/100,000) and the average CFR was 0.09% (range: 0.015% to 0.18%). See Table 2 for detailed statistics over the past 25 years [15,16].

Dengue transmission in Colombia is endemic; seasonal increases frequently occur, especially during heavy and prolonged rainfall, as illustrated in Exhibit 3. As such, in 2010, Colombia experienced a fivefold increase in incident cases (at 345.3/100,000 or 157,152 new cases observed during that year), compared to previous years [16]. This increase was associated with the environmental changes brought about by the ENSO weather phenomenon, which produces excessive monsoon rainfall and increased humidity – both major factors in increased dengue transmission due to vector proliferation [17]. According to specific related research: "Even half a degree centigrade increase in temperature can translate into a 30% to 100% in mosquito vector proliferation, resulting in a higher disease burden for affected countries" [18].

Description of Past and Present Outbreaks

Dengue is now present in more than 30 Latin American countries. In 1977, serotype 1 caused a large-scale pandemic, which started in Jamaica, and quickly spread to other Caribbean, Central American and South American countries, reaching Colombia in 1978. A total of 702,000 cases were reported. In the 1980s, serotypes 2 and 4 were also implicated in small scale outbreaks in the region, resulting in the circulation of multiple serotypes of the dengue virus [19]. Periodic outbreaks are now common in Colombia, with the most notable outbreaks occurring in 1991, 1994, 1998, 2001, and 2010. The dengue serotype 3 had been absent from Colombia since the mid-1970s but reappeared in 2001 and is now circulating endemically [20]. In June of 2010 there was one of the country's major outbreaks with 90,360 reported cases by the National Institute of Health (83,508 were DF; 6,852 were DHF/DSS) and 99 deaths. [16,21].

The last decade also had significant dengue epidemics in Colombian regions with more than 100,000 cases. During 2013 there were 126,425, 2016 with 101,016, and 2019 with 127,553 cases respectively, being approximately five to nine times higher than in other time periods. High number of dengue deaths were also reported in various zones [22]. Recently (January 2020), during the fifth epidemiological week, Colombia recorded one of the highest numbers of cases in history with spikes in several territories. Compared with the same date (epidemiological week) of 2019 (with 6,232 cases), there was an increase of 93.69% (12,071 cases) [15].

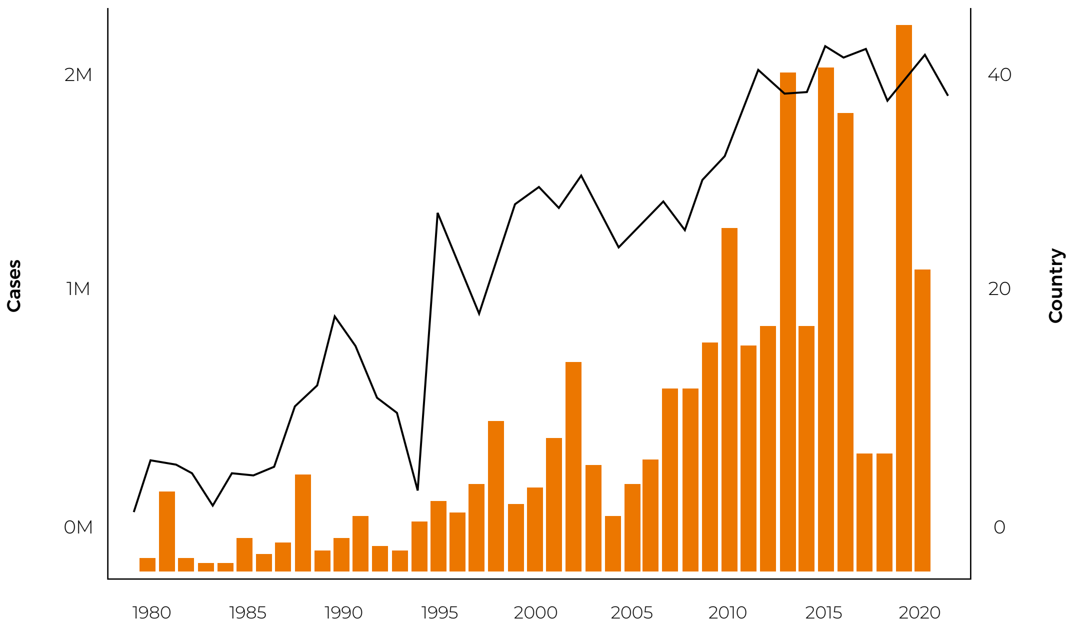
Dengue Surveillance System

Current Situation in Colombia

Despite being a notifiable disease and the presence of various levels of dengue fever surveillance in Latin American countries, it is evident that outbreaks of epidemic dengue fever caused by all four serotypes have expanded significantly since 1980. Most of these have been in Brazil, Colombia, and Peru, and to a lesser extent, in other countries [16, 4, also see Figure 2, 3]. Colombia has occupied the second place after Brazil, in new cases (incidence) and prevalence. Although there has been an increase in disease burden, dengue epidemics in Colombia and Latin America have not been well managed, as no strict control measures have been implemented in order to control the emerging trend [23 also see Figure 2, and Table 2].

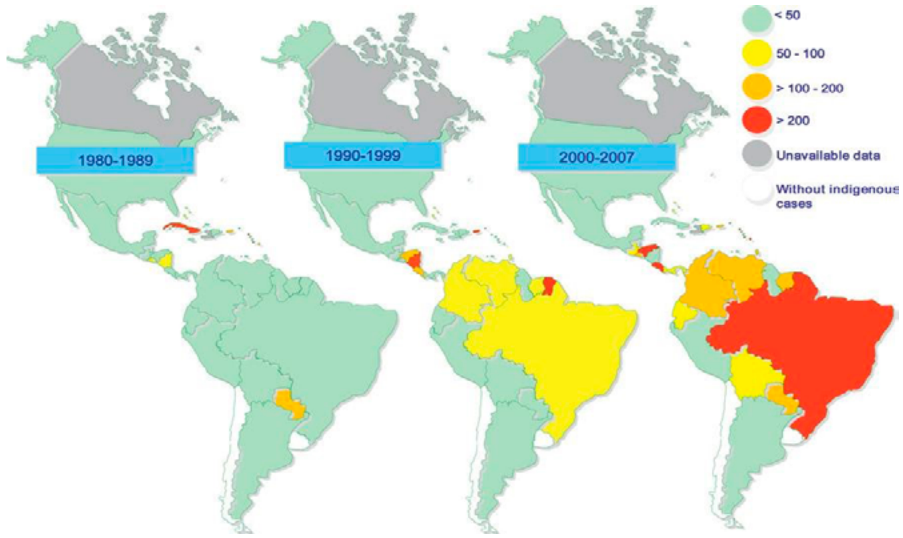
Figure 2: Number of DF cases and Affected Countries in the Americas from 1980 to 2020

Región	Total	Confirmed	Severe	Deaths
The Americas	1,419,899	560,402	3,183	473



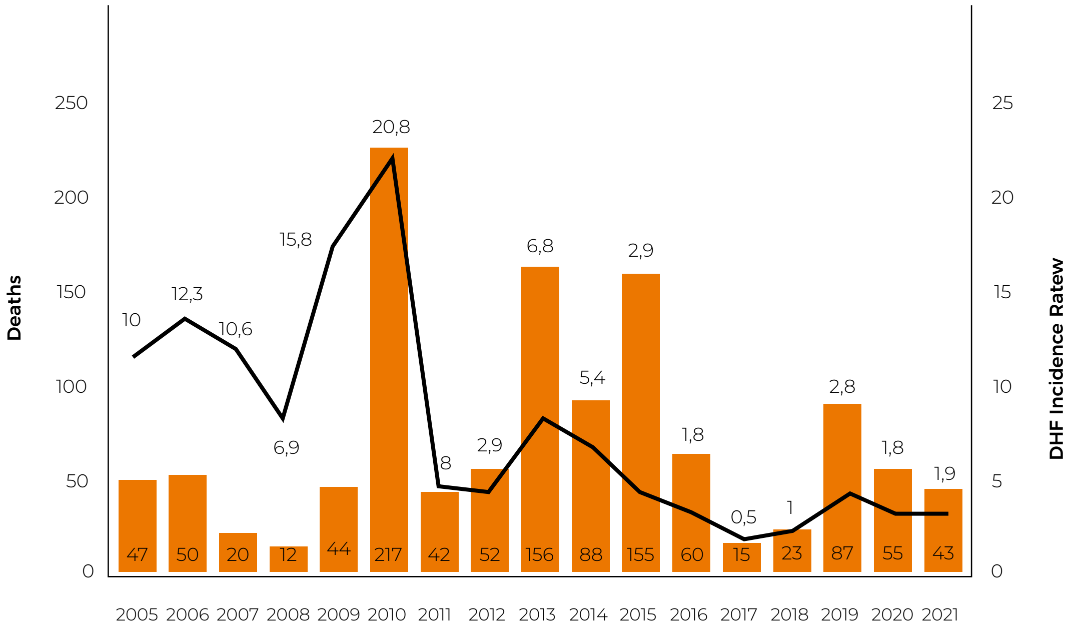
Retrieved from the Pan American Health Organization (PAHO) PLISA Health Information Platform for the Americas (2020), Dengue.

Figure 3: Average Dengue Incidence per 100,000 in Various Regions of the Americas from 1980 to 2007



Adapted and retrieved from: The Epidemiology of Dengue in the Americas Over the Last Three Decades: A Worrisome Reality. Jose Luis Martin et al. Am. J. Trop. Med. Hyg., 82(1), 2010, pp. 128–135

Figure 4: Number of Deaths and Incidence Rates /100.000 per DHF – Colombia, 2005 to 2020



Retrieved from the Pan American Health Organization (PAHO) PLISA Health Information Platform for the Americas (2020), Dengue.

Table 2. Number of DF and DHF Cases in Colombia from 1995 to 2021

Year	Population x 1,000	Total cases	DF Incidence rate x 100,000	DHF cases	DHF incidence rate x 100,000	% DHF cases	Deaths	CFR (%)
2021	51,266	53,334	104	958	1.9	1.79	43	0.081
2020	49,856	78,979	160	897	1.8	1.14	55	0.070
2019	49,465	127,553	255.8	1,406	2.8	1.10	87	0.068
2018	49,465	44,825	90.6	526	1.0	1.17	23	0.051
2017	49,068	25,284	51.5	236	0.5	0.93	15	0.059
2016	48,654	101,016	207.6	899	1.8	0.89	60	0.059
2015	48,229	96,444	200.0	1,421	2.9	1.47	155	0.161
2014	47,791	107,975	225.9	2,619	5.4	2.43	88	0.082
2013	47,343	126,425	267.0	3,197	6.8	2.53	156	0.123
2012	46,881	50,040	106.7	1,350	2.9	2.70	52	0.104
2011	46,404	31,819	68.6	1,388	3.0	4.36	42	0.132
2010	45,510	147,640	324.4	9,482	20.8	6.42	217	0.147
2009	44,979	44,412	98.7	7,131	15.8	16.06	44	0.099
2008	44,452	23,651	53.2	3,081	6.9	13.03	12	0.051
2007	43,927	38,562	87.8	4,665	10.6	12.10	20	0.052

Year	Population x 1,000	Total cases	DF Incidence rate x 100,000	DHF cases	DHF incidence rate x 100,000	% DHF cases	Deaths	CFR (%)
2006	43,406	31,092	71.6	5,379	12.3	17.30	50	0.161
2005	42,889	26,169	61.01	4,306	10.0	16.45	47	0.180
2004	42,368	24,708	58.3	2,815	6.6	11.39	20	0.081
2003	41,849	47,710	114.0	4,878	11.6	10.22	7	0.015
2002	41,329	71,727	173.6	5,269	12.7	7.35	27	0.038
2001	40,814	48,874	119.7	6,563	16.0	13.43	54	0.110
2000	40,293	20,956	52..0	1,819	4.5	8.68	19	0.091
1999	39,731	19,243	48.4	1,093	2.8	5.68	14	0.073
1998	39,184	58,011	148.1	5,171	13.2	8.91	63	0.109
1997	38,636	20,340	52.6	3,950	10.2	19.42	28	0.138
1996	38,069	31,398	82.5	1,757	4.6	5.60	11	0.035
1995	37,472	50,031	133.5	1,028	2.7	2.05	14	0.028

The threat of the disease has not been effectively evaluated and documented in Colombia, as demonstrated by current data and from the last fifteen years. Incidence and prevalence are rising in endemic areas in Colombia, resulting in an increased disease burden [15 see Colombia, and see also Table 2]. More than 100 deaths have been reported so far during the last two year and there were 993 during the last decade. Moreover, the incidence rates over the last five years averages at 136 /100 000 (see Table 2). Considering the gaps in various levels of disease surveillance and data collection, the statistics could be much worst. Other factors may contribute to an increased number of misdiagnosed and undiagnosed cases of DF in Colombia, such as regions where residents have difficulty accessing medical health services, there is a high pervasiveness of malaria, sika, other endemic diseases and a high proportion of dengue infections, which are sub-clinical or present like malaria [15, 24].

Additionally, The World Health Organization (WHO), through the Pan American Health Organization (PAHO), has recognized and documented that the increase in Colombia's disease burden due to dengue fever or dengue hemorrhagic fever can be attributed to an inoperative passive surveillance system, similar to that of many dengue-endemic countries. The current system relies mainly on reports from local healthcare providers who complete case reports on both ambulatory and hospitalized patients. The healthcare providers, in many cases, do not take into consideration dengue in their differential diagnosis and/or fail to report cases rapidly and regularly [25, 26 and see Table 3].

Table 3. Characteristics of Dengue Surveillance Systems in Various Latin American Countries

Country	Population	Total cases year	Reported DF:DHF	DHF CFR	Surveillance Method	Source of cases*	Required Legal report	Vector surveillance
Argentina	38,592,150	34(2005) 181 (2006)	ND**	ND	Passive	OP, IP	Yes	Yes
Brazil	189,335,187	203,789 (2005) 346,550 (2006)	551:1	11%	Passive	OP, IP	Yes	Yes
Colombia	42,090,512	39,825 (2005) 38,271 (2006)	6:1	5%	Passive	OP, IP	Yes	NO***
Costa Rica	4,401,845	37,798 (2005) 12,052 (2006)	137:1	ND	Passive	OP, IP	Yes	Yes
Cuba	11,416,987	14,8883 (2001–2002)	178:1	4%	Active	OP, IP	Yes	Yes
Honduras	7,400,000	18,843 (2005) 7,800 (2006)	45:1 74:1	3%	Passive	OP, IP	Yes	Yes
Mexico	108,700,891	29,836 (2006) 16,862 (2005)	4.8:1	0.4%	Passive	OP, IP	Yes	Yes
Nicaragua	5,142,098	13,831 (2005) 10,073 (2006)	26:1	2%	Passive	IP	Yes	No
Puerto Rico	3,937,316	6,039 (2005) 3,286 (2006)	84:1	6%	Passive	OP, IP	Yes	No
United States^	11,000,000	28 (2005)	16:9	0	Passive	OP, IP	Yes	No
Venezuela	26,084,662	39,860 (2006) 42,198 (2005)	9:1	0.1%	Passive	OP, IP	Yes	No

Adapted from: Best Practices in Dengue Surveillance. A Report from the Asia-Pacific And Americas Dengue Prevention Boards. PLoS Neglected Tropical Diseases. Nov 2010, vol 4, Issue 11. *Source or location where cases are detected: OP = Outpatient clinics; IP = Inpatient or hospitalized. **ND = No data ^ USA-Mexico border only. ***Despite Colombia having a recent entomological guide for supporting dengue control, it is just a rhetorical document, relying on non-existent (or weakened) community and primary health care-oriented system.

Colombia, through the National Institute of Health (NIH), has a centralized data collection system, which generates a morbidity and mortality report on a weekly basis (NIH-SIVIGILA). Local hospitals report periodically to the provincial level (Departments), which in turn reports to the central level. A major limitation is that the information is rarely used locally; data are forwarded to the central ministry offices (NIH) for official evaluation and consolidation, which significantly obstructs the opportunity for a timely local response. Another limitation of the current system is the lack of funding for laboratory confirmation of cases and laboratory facilities are available only at the central (national) level [27].

Moreover, although a country like Colombia has updated framework documents and surveillance protocols about dengue, these guidelines are only in written paper, very far from the current regional and national reality. As such, The Colombian National Institute of Health (INS) recently revised a guideline stating that: “Surveillance and responsibility strategies by levels of care, emphasizing broadly on active surveillance, and active community searches in outbreak situations and new sources of transmission” [21]. Unfortunately, the fact is that administrative and decentralized local and regional government bodies (in charge of the active surveillance) steer in totally different directions. Little by little, during the last two decades, the decentralization process has transferred the responsibility of community health to the local level, profoundly affecting primary health care as well as active community surveillance, and negatively affecting population health outcomes [28].

Nowadays, the truth is that almost all primary health attention under local government responsibility is highly transformed and vital services severely restricted. As a result, in vulnerable areas (primarily rural places) several community health centers (puestos y centros de salud) have been closed, implying also that community health promoter or community health worker positions have been cut [29]. Community health workers (CHW), for whom one of the main duties is active seeking of febrile cases, represents the effective bridge between health care services providers and the community. Thus, without such a health promoter, particularly for vector-borne diseases, it is very difficult to carry out active surveillance within the community. The CHW is a vital support at the local regions for management of the epidemiological scenario as to provide necessary control, as well as virological and entomological surveillance actions [30].

Public Health Surveillance Protocols by the INS (including early detection and reporting) will not be carried out properly since one of the main components for its development is missing. Communities, therefore, will have the historical risk of seeing an epidemic pass, along with all the morbidity and mortality that this entails, without the timely intervention or mitigation. Under these circumstances, the main concern is that the peaks of the 2010, 2013, 2015 and 2019 years will be repeated; time periods in which Colombia reported one of the worst mortality, incidence and prevalence rates in Latin America [31, see also Figure 4].

Proposed Surveillance System

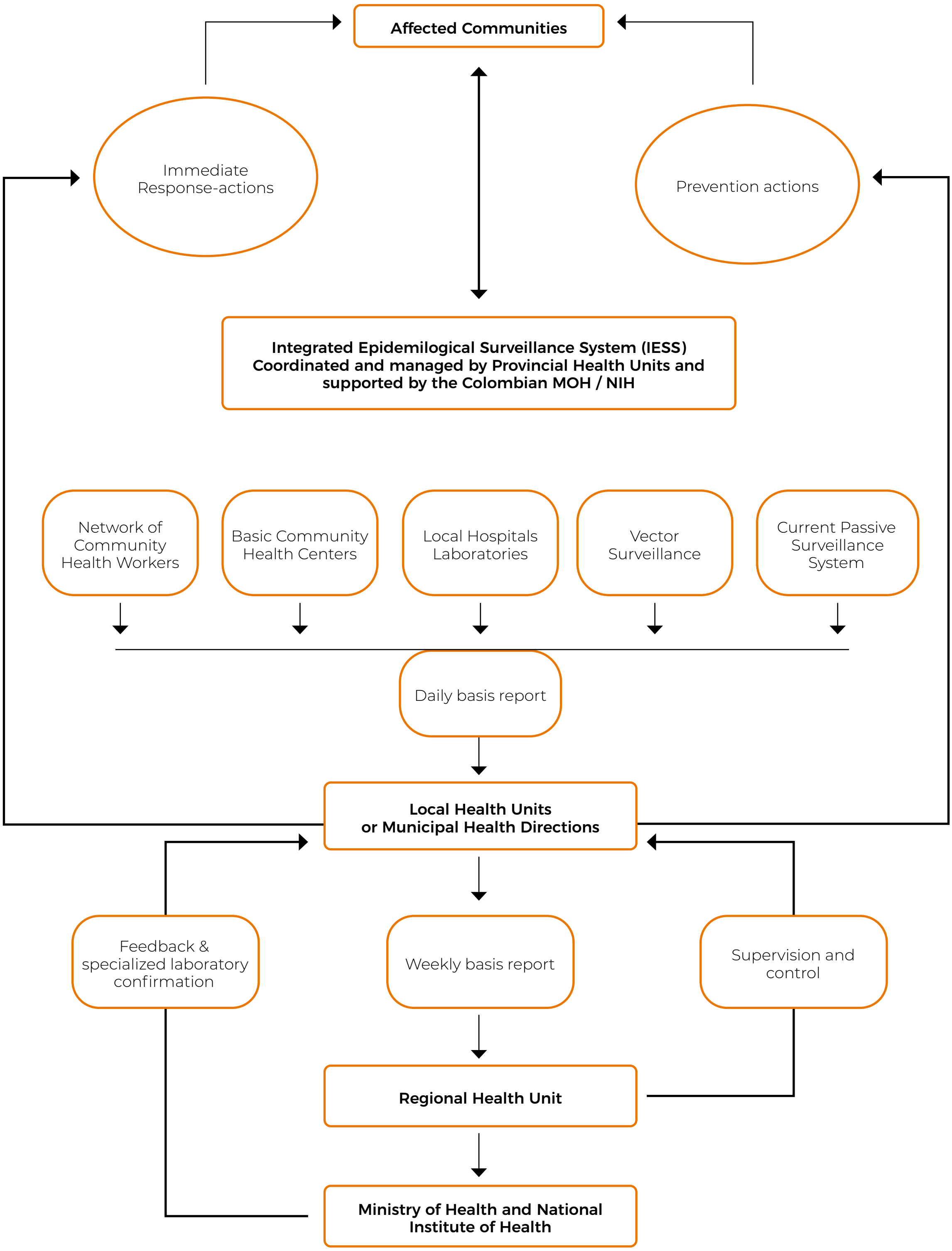
Integrated Epidemiological Surveillance System (IESS)

Most tropical countries, including Colombia, are in need of an integrated epidemiological surveillance system. In fact, at present, in most provincial territories (Departments), Colombia has a passive surveillance (PS) system which may be inadequate in its detection and predictive value of dengue epidemics, particularly under the existing decentralized local and regional governments. In addition to PS, an integrated epidemiological surveillance system (IESS) incorporates an active surveillance component. Then, since it is difficult to clinically differentiate dengue from illnesses caused by other viruses, bacteria, or protozoa, an IESS for dengue fever or dengue hemorrhagic fever (DF/DHF) must also include laboratory-based confirmation. Consequently, added into the current passive surveillance activities, the IESS proposed model is recommended to be implemented by the Colombian Regional Health Units of each affected territory. Although a few provincial health units have been trying to put in place some of the IESS framework, there is not a widespread approach as a National Health Policy implemented [28].

That is, in Colombia, as well as in most Latin America countries, given the type of information needed for effective and time sensitive dengue surveillance, it is obvious that passive surveillance alone will not generate sufficient information for the prediction and control of outbreaks [32]. An active, laboratory-based surveillance system, supported from both a clinical and entomological perspective is needed. This could be effectively implemented by the Ministries of Health with support from the regional offices of PAHO in each country of the region. The proposal in this paper is considered a pilot project for Colombia, in which Provincial Health Units in conjunction the National Institute of Health and the Ministry of Health (MOH) implements a new approachable dengue surveillance system in Colombia.

This paper, therefore, provides a framework for a pilot model of a sustained and integrated epidemiological surveillance system for Colombia, based on the issues above-mentioned, focusing on the early detection and prediction (turning point) of dengue outbreaks, described fully in the following paragraphs and laid out schematically in Figure 1. If implemented, it could have a significant effect on timely disease recognition and control. It has been designed to work with Colombian's existing health infrastructure and is specific to country's needs and context. In addition to early detection of DF/DHF cases, the IESS might also support the early detection of other tropical febrile syndromes such as malaria or sika, which are present simultaneously with dengue fever and can also be found in various regions of developing tropical countries.

Figure 1: Framework of a New Approach to an IESS for DF and DHF



As mentioned, Colombia has a decentralized administrative government model for the provision of public health services, which are organized by local agencies known as the Health Unit Municipalities [33], which are assigned to the specific provision of public health services. The MOH and NIH must keep working and supporting the Provincial Health Unit and Municipalities, as much as possible, because these have the responsibility and obligation of providing and coordinating services related to public health risks. In order to implement the new system, the MOH would work with established stakeholders and institutions in each local-municipal health unit, providing optimal conditions for the organization and implantation of this new integrated approach. These stakeholders must include a hired organized network of community health workers (CHWs or *promotores de salud*), distributed throughout the country. Also, a second hired group of community health workers must work specifically to identify and treat of malaria in endemic zones. The third set of stakeholders must include a well-ordered network of community health centers (CHC or *puestos and centros de salud*), reopened and located in urban and rural areas. An additional element of support, which could be implemented in high-need areas and in the search of febrile cases, would involve setting up localized sentinel sites through the community health centers. Provincial Health Units along with the NIH/MOH will work to integrate the new IESS with current infrastructure, stakeholders, and institutions. The system will have the following components: (see also Figure 1)

- Passive surveillance system: This would involve integrating sentinel sites with the IESS
- Active Surveillance System in which the following stakeholders and institutions would establish this: a network of community health workers, basic community health centers, local clinics, laboratories and hospitals, local medical offices, and private networks of medical services providers. The main activities would include:
  - » Organizing an active surveillance system based on an early warning system, event-based surveillance, and case-based surveillance (proactive searches for febrile cases).
  - » Supporting the search process with basic laboratory testing.
- Entomological or vector surveillance
- Specialized laboratory confirmation

Active Surveillance: Objectives and performance indicators

According to the WHO (dengue guidelines): "The objective of an active, laboratory-based surveillance system is to provide early and precise information to local public health authorities on four aspects of dengue activity: time, location, disease severity and virus serotype" [34]. This proactive, febrile illness surveillance system, headed by local health units from each municipality, would provide information on early detection and confirmation of dengue infection cases and will thus improve the capability of local health authorities to prevent and control dengue proliferation. Among its characteristics is its predictive capability, including analysis of trends of reported cases, establishment of sentinel centers, support for dengue cases (especially DHF) by basic laboratory reports, and in selected cases, the confirmation and identification of virus serotypes of dengue by a specialized laboratory. All of these components will provide the necessary information to predict dengue transmission and guide implementation of control measures well in advance of peak transmission. This system must be linked to entomological surveillance in order to be able to identify dengue transmission in time and place [32,35].

Colombia during the last five years has an average of 65,995 cases of DF, with an incidence rate of 132.5/100,000, which it has been overshadowing by the covid-19 pandemic. As well, during the same period, has an average of 804 DHF with an incidence rate of 1.7/100,000 (see Table 2); therefore, the final goal of this integrated surveillance system is a 50% reduction in the number of incident cases during the first year of the program implementation, with a further 30% reduction during the second year. This means to have just about 15,804 new cases (incidence rates of 31.4 /100,000) at the end of the second year, meaning a total reduction of 80%. Additionally, it is expected that the case fatality rate will be reduced by more than 80% by the end of the second year (in 2021 the case fatality rate was 0.081%) yielding a CFR around of 0.015.

Case Definition and Clinical Alertness Criteria among Stakeholders and Sentinel Sites

As stated by the WHO guidelines, active dengue surveillance should rely on identifying and investigating clusters of non-specific febrile illnesses or viral syndromes with methods such as the fever alert (preparedness and actions carried out after searching and reporting of confirmed cluster of febrile cases) [36]. Thus, the case definition for DF/DHF as provided by WHO and PAHO is recommended to be used by all stakeholders and institutions with a standardized set of criteria. Cases of DF or dengue-like illness are characterized primarily by fever (the criteria for inclusion being an axillary temperature of more than 38 °C). The inclusion criteria for DF are fever without respiratory symptoms and at least two other symptoms: headache, arthralgia, myalgia-like backache, skin rash, retro-orbital pain, hemorrhagic manifestation (or incipient bleeding signs, characterized by the manifestation of at least one of the following: a positive tourniquet test, petechiae, ecchymoses, or purpura; or bleeding from the mucosa, digestive tract, injection sites, or others), and leucopenia (or abnormal reduction in the number of white cells in the blood). Cases of DHF are characterized by four clinical and blood test manifestations which must be present: (1) fever or recent history of acute fever (more than 38 ºC), (2) hemorrhagic phenomena as indicated above, (3) thrombocytopenia (a platelets count of 100,000 mm3 or less) and (4) plasma leakage due to increased capillary permeability manifested by a ≥ 20% rising hematocrit value (hemoconcentration) or by a decreasing similar value after intravenous fluid replacement [37,38]. Thus, trends in rates of febrile illness (oral or axillar temperature ≥ 38 ºC) are monitored as a crude indicator of possible dengue activity. The participants of the IESS should report the total number of febrile cases to the local health unit on a daily basis. The local health unit will in turn update the members of the IESS with incidence summaries according to their respective zones. As soon as a significant increase in febrile illness or viral syndrome is noted, the respective local health authorities should immediately investigate the associated cluster and blood samples should be taken for a simple hemogram. Although currently in Colombia most of the affected areas represent zones with high endemicity [39], the threshold for alert and response will differ according to the specific location of the outbreak (whether the affected area is considered an endemic/epidemic area or the area is at risk of dengue introduction). Generally, for locally endemic areas, a single suspected DHF case may trigger action. Additionally, clusters of ten dispersed daily cases, or more than two cases of dengue-like illness inside a family group should be investigated immediately. Early detection of DF/DFH, and the subsequent contact tracing and quarantine activity that will result from this detection may prevent widespread local and regional outbreaks with the catastrophic consequences that are often taking place nowadays [40].

Support of the IESS with Basic Laboratory Tests

A predetermined number of blood samples - simple procedure, available in most local laboratories found in any Colombian municipality - should be taken daily to support the search for febrile cases, especially in patients who display symptoms associated with dengue, or patients at risk of DHF. Along with the basic clinical diagnosis, basic laboratory tests represent a major component for improving the sensitivity, specificity and predictive values in this integrated surveillance system. The Colombian NIH/MOH should fund local-level laboratories with the materials and staff required to confirm dengue cases and relay that information quickly and accurately both back to local-level and national-level health authorities. Financial support for laboratory reagents and expenses will be provided by the MOH as part of the IESS budget. Data collected from the hemogram must include platelet count (to rule out thrombocytopenia), lowest and highest hematocrit value (to rule out hemoconcentration) and coagulation test with prothrombine time and partial thromboplastin time. The MOH will provide specialized laboratory training for CHWs, sentinel sites, and personnel from CHC (in places where there are no specialized personnel like general physicians) so that they may recognize and identify moderate thrombocytopenia (100,000 mm3 or less) and a rising hematocrit count (concurrent hemoconcentration) as the distinctive clinical laboratory finding of DHF. These findings help determine the severity of disease in DHF and differentiate it from DF. Finally, in regions also endemic to malaria, along with the hemogram, the careful examination of thin and thick blood films will allow for a differential diagnosis, distinguishing dengue fever from this other quite common tropical disease. Clinical suspected cases of DHF should have a complete hemogram that including a platelet count, lowest and highest hematocrit value (to measure hemoconcentration), results of a tourniquet test, investigation of any hemorrhagic manifestations, a chest x-ray (for pleural effusion), blood pressure, hepatomegaly screening, coagulation tests (phrotrombine time and partial thromboplastine time), liver enzymes, and a blood film [41].

Specialized Laboratory Support and Confirmation

Laboratory diagnosis is an essential part of an IESS. Laboratory testing and confirmation allows public health authorities to detect the presence of circulating dengue viruses, and allow them to better implement dengue control measures [42]. The specialized laboratory support for the proposed system will include the confirmation of cases, mostly DHF, through the national dengue diagnostic laboratory from the NIH. All patients hospitalized with hemorrhagic disease, viral encephalitis and aseptic meningitis, who experience a fatal outcome following a viral prodrome regardless of diagnosis, should have blood and tissue samples submitted to central reference laboratories to ascertain serological or virological confirmation [43].

Based on WHO published best practices, a national dengue diagnostic laboratory would provide the following functions within this system: detection of the introduction of dengue in an area; detection of a rise or fall in number of cases; confirmation of cases as support for clinical diagnoses; provision of training and supplies to laboratories (throughout Colombia) and informing control measures or interventions [44].

The main dengue-specific diagnostic test that the laboratories will perform is the ELISA test for IgM antibodies because these are present six days after infection and remain for one month making them good indicators. The other key test required from the laboratories is virus isolation from blood samples to determine its serotype. This can be done by inoculation of tissue culture and the national dengue laboratory will need to be equipped for this procedure [43]. The materials and reagents required for these tests can be prepared by the Colombian NIH central laboratory.

Entomological Surveillance

Surveillance activities focused on the vector, mainly A. aegypti, can help to effectively monitor and prevent potential outbreaks. Entomological surveillance, as part of the IESS, would benefit the system in terms of early prediction, geographical distribution, and evaluation of control programs [36]. Surveillance methods will include regularly monitoring the house index (the percentage of houses infested with larvae); the container index (the percentage of water-holding containers infested with larvae); and the Breteau index (the number of positive containers per 100 houses) [36]. These indexes are useful for estimating and monitoring the adult mosquito population in relation to human habitations. IESS entomologic surveillance would also include monitoring insecticide resistance in order to implement the most effective interventions possible.

Vector control is a main output of the entomological surveillance system. It involves: "Planning, organization, carrying out and monitoring activities for the modification or manipulation of environmental factors with a view to preventing or reducing vector propagation and human-vector-pathogen contact" [36]. IESS environmental vector control measures will include permanent environmental modification of vector habitats, temporary environmental manipulation and/or modification of human habitation and behavior, with the goal of inhibiting or reducing vector breeding. Comprehensive vector surveillance can help inform intervention methodology [36]. and an integrated vector control is recommended in dengue outbreak situations, for it involves implementation of a combination of various types of control efforts simultaneously in safe, reasonable doses in order to have the maximum protective impact with the fewest harmful consequences (such as environmental or economic consequences). An example of an integrated vector control system would be the simultaneous reduction of still water, introduction of insecticides, and information campaigns for individual protection.

Non-Entomological Surveillance

In order for a surveillance system to be comprehensive, surveillance activities need to move beyond a focus on solely the disease vector. Non-entomological surveillance takes a broader look at society and seeks to support the surveillance process through the development of an ecological profile. This ecological profile would aid in disease management activities and intervention processes in the face of an epidemic. A key aspect of IESS non-entomological surveillance would involve an assessment of Colombia's population distribution and density, because it would have a significant influence on the speed at which the disease is spread, and the effectiveness of intervention measures. Densely populated areas will require more sensitive surveillance practices, as well as the allocation of more resources such as early detection along with effective intervention, which will help reduce the disease burden in these high-risk areas [45].

The presence and reliability of basic public utilities such as the provision of water, electricity and solid waste disposal services are also essential elements to be taken into consideration in disease management. In the absence of these, there is also an increased need for health promotion and education activities that would aid in educating the population on the dangers of various practices that promote disease spread, while increasing their knowledge of safer practices. The lack of a reliable running water source, for example, increases the need for water storage which in the case of dengue can significantly affect disease vector proliferation [46]. The proposed IESS non-entomological intervention would increase the population's knowledge of poor practices as well as foster awareness of alternatives in the absences of government interventions.

Meteorological data collection is the final aspect of the implementation of this IESS. Year-round monitoring of meteorological conditions, with an emphasis on rainfall patterns and conditions associated with the ENSO phenomenon, will be of significant predictive value in the fight against dengue [47]. This will be required in order to establish a pattern of meteorological activity, which will serve to support the IESS' early warning system of a possible increase in disease burden. This would in turn trigger an increase in screening procedures in an effort to increase the chances of detecting increased infection levels.

Finally, it is important to mention that despite having a comprehensive health care routes for vector-borne diseases in Colombia [48], in addition to an entomological guide for supporting dengue control [49], they are just rhetorical documents, based on non-existent (or weakened) community and primary health care. In fact, basic public health measures, such as community health promotion and disease prevention are missing altogether in most of the endemic-vulnerable territories around the country [50,51].

Conclusion

A couple of decades ago, Colombia had a better-intergraded system for vector-borne diseases, primarily for dengue and malaria monitoring. Based on groups of community health workers, they constantly looked out for fever cases in their communities, resembling a search for active cases. However, the current administrative and decentralized model left the basic well-being and crucial primary health care services as a local government responsibility. In most of the territories, several factors such as lack of political will, incapability, corruption, lack of commitment and appropriate planning process (among others) have abolished almost all previous and scarce preventive population-based health systems. As a result, most territories, particularly rural and vulnerable (endemic) areas, a big chank of primary health care services (provided across community health centers and staffed by community health promoters such as vector-borne disease community workers, as well as some nursing assistants) have been little by little reduced or shut down. Thus, making the active vector-borne surveillance task very difficult to carry out properly. Additionally, Colombia has made progress in updating frameworks for dengue surveillance protocols as per the MOH and NIH. These frameworks, rhetoric on paper, appeared to be the ideal foundation for a unique and equitable surveillance system; but in practice, it has been deficient and proved so in discordant with the current decentralized administrative governments at the local and regional level.

For partially addressing these issues, the present paper described the components and implementation for an IESS in Colombia, under the current administratively decentralized local governments where regular dengue outbreaks and a sustained level of endemic infections have been significantly increasing the burden of disease. The proposed IESS incorporates the current passive surveillance system used in Colombia, a real and approachable active surveillance system, a laboratory-testing component, as well as entomological and non-entomological support systems. All measures are aimed at enhancing the current capability, and support for other critical factors like tools improvements and community engagement, which are critical aspects for improving dengue prevention, mitigation, and control. Partially, this proposal could be a return to the previous people-center care and community surveillance, carried out by health workers searching for febrile cases. In addition, it is a call for supporting true possibilities within the decentralization process in local affected territories, in which people, endorsed by primary health care, must be at the center of the system.

Adapting similar IESS in other developing Latin American countries or regions might follow suit. In case of not following this integrated approach, epidemics will continue to reach or pass their peak long before being recognized or identified; and thus, opportunities for control of morbidity or mortality will be late or missed altogether.

Conflictos de interés

There is no potential competing interests.

Declaraciones del autor

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