

Implementation of Malaria Dynamic Models in Municipality Level Early Warning Systems in Colombia. Part I: Description of Study Sites

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Abstract. As part of the Integrated National Adaptation Pilot project and the Integrated Surveillance and Control System, the Colombian National Institute of Health is working on the design and implementation of a Malaria Early Warning System framework, supported by seasonal climate forecasting capabilities, weather and environmental monitoring, and malaria statistical and dynamic models. In this report, we provide an overview of the local ecoepidemiologic settings where four malaria process-based mathematical models are currently being implemented at a municipal level. The description includes general characteristics, malaria situation (predominant type of infection, malaria-positive cases data, malaria incidence, and seasonality), entomologic conditions (primary and secondary vectors, mosquito densities, and feeding frequencies), climatic conditions (climatology and long-term trends), key drivers of epidemic outbreaks, and non-climatic factors (populations at risk, control campaigns, and socioeconomic conditions). Selected pilot sites exhibit different ecoepidemiologic settings that must be taken into account in the development of the integrated surveillance and control system.

INTRODUCTION

The malaria prevention and control community has supported the concept that in areas where malaria transmission is sensitive to climatic factors, historical, current, and forecasted climate information should be incorporated into routine surveillance and control activities to better predict patterns of malaria risks in time and space. Such information may also be used to improve malaria epidemic early warning and response.^{1–5} As part of the Integrated National Adaptation Pilot Project, the Colombian National Institute of Health (CNIH) is working on the design and implementation of a proactive, collaborative, multidisciplinary, integrated surveillance and control system (ISCS) for malaria.⁶ The aim of this initiative is to improve risk assessments of malaria transmission to facilitate effective allocation of health resources and more cost-effective preventive responses. One of the key components of the ISCS is a Malaria Early Warning System Framework,^{7–11} in which the CNIH is proposing several mathematical models as a means to predict changes in the risk of malaria in specified populations. Dynamic models (i.e., those that use the established biological mechanisms of the transmission cycle of malaria parasites)¹² are being used to integrate relevant climatic variables with demographic, epidemiologic, entomologic, and non-climatic factors to simulate malaria transmission dynamics. This report provides a description of the local ecoepidemiologic settings in Colombia where several malaria process-based mathematical models are currently being implemented. The practical implementation of such tools in operational surveillance is presented in

the second part of this study, where preliminary results using observed weather and seasonal climate forecasts are discussed in detail. The main goal of our activities is to provide a framework for the use of dynamic models in routine activities of state and municipal health services, and in a more general sense, for strengthening the institutional capacity of the malaria surveillance and control program in Colombia.

Colombia provides an excellent setting for testing the implementation of the ISCS in Latin America for the following reasons. First, *Plasmodium falciparum* and *P. vivax* malaria infections, which are responsible for 36% and 64% of the current national malaria burden, respectively, are still a major public health concern in the Americas because their official morbidity profiles account for almost 15% of the total primary cases observed in the region.⁵ A successful malaria surveillance and control campaign in a single country could thus have a significant regional-scale impact. Second, although nearly 85% of the rural territory in Colombia has environmental conditions suitable for malaria transmission, only 2 of 32 states have 50% of malaria cases, and 75% of the national reported cases occur in only 44 municipalities.¹³ Malaria interventions could then be targeted at those localities hardest-hit by malaria infections to control the nationwide disease burden. Third, malaria in Colombia has unstable/epidemic periods that have been strongly linked to the warm phase of the El Niño-Southern Oscillation, particularly in lowland regions along the Pacific and Atlantic coasts.^{8,13–16} The El Niño-Southern Oscillation, which is the most significant single driver of climatic events worldwide, is the basis for the development of seasonal climate forecasts. Such forecasts could be used to predict high-risk and low-risk years for malaria transmission with sufficient lead time to mobilize resources to reduce the impact of epidemics.¹⁴ Fourth, in its two official national communications to the United Nations Convention on Climate Change, the Colombian government has identified malaria as one of the two climate-sensitive diseases of primary concern.

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As a result of this political will, an adaptation research and implementation agenda plan has already been proposed in response to the recommendations of the Intergovernmental Panel on Climate Change.¹⁷ Fifth, in recent years many resources have been invested in strengthening the institutional arrangements of the national, state, and municipal health services in an attempt to build the capacity for a routine evaluation of the spatio-temporal risk of malaria infections and the implementation of locally adapted malaria control strategies.^{17,18} Sixth, the steep increasing trend in the overall malaria morbidity that was observed during 1960–1998 is now showing a moderate decrease.¹³ The overall malaria mortality, which reached approximately 130–150 deaths per year over the most recent decade, has also significantly decreased and the downward trend continues. Seventh, the global economic downturn of the past five years has focused the attention of the malaria control community on the better targeting of scarce resources.¹⁹ These characteristics suggest that an integrated approach to malaria control has the potential for success and that it may also be relevant to the development of an elimination strategy for the country and region.^{5,20}

STUDY SITES

Four malaria pilot sites distributed throughout the country (Figure 1) were selected through a multi-criteria analysis²¹ that considered, among other factors, the level of endemicity, primary and secondary mosquito vectors, sectorial and

territorial decentralization, easy access, and political will. Although these localities exhibit historical hypoendemic conditions according to world's malaria clinical endemicity profiles,²² they are the municipalities with the highest morbidity and transmission levels in Colombia. These municipalities include the localities of Montelíbano and Puerto Libertador, both are located in the Department of Córdoba, on the Caribbean Coast of Colombia, and have surface areas of 1,900 and 2,060 km², respectively. The municipality of San José del Guaviare in the Department of Guaviare is located in a transition region between the Colombian grassland plains to the northeast and the tropical rainforests of the Amazon to the south. San José has a total area of approximately 16,200 km², of which 84% is an indigenous reserve and protected forest. Also selected was the municipality of Buenaventura, the most important maritime port on the Colombian Pacific Coast. Buenaventura is located in the Department of Valle del Cauca and has a total area of 6,297 km². The Pacific Coast, an area of approximately 72,000 km² and with approximately 2.2 million inhabitants, is among the regions in Colombia with the highest transmission rates (51% of *P. falciparum* infections are reported in this region). All pilot sites are located at altitudes below 200 meters above sea level and have historical mean annual temperatures of 27–28°C. Their main natural resources include numerous water sources, highly diverse flora and fauna, vast savannahs, and gold, silver, platinum, coal, manganese, and copper reserves, as well as various pristine rainforests protected by law in several natural parks.

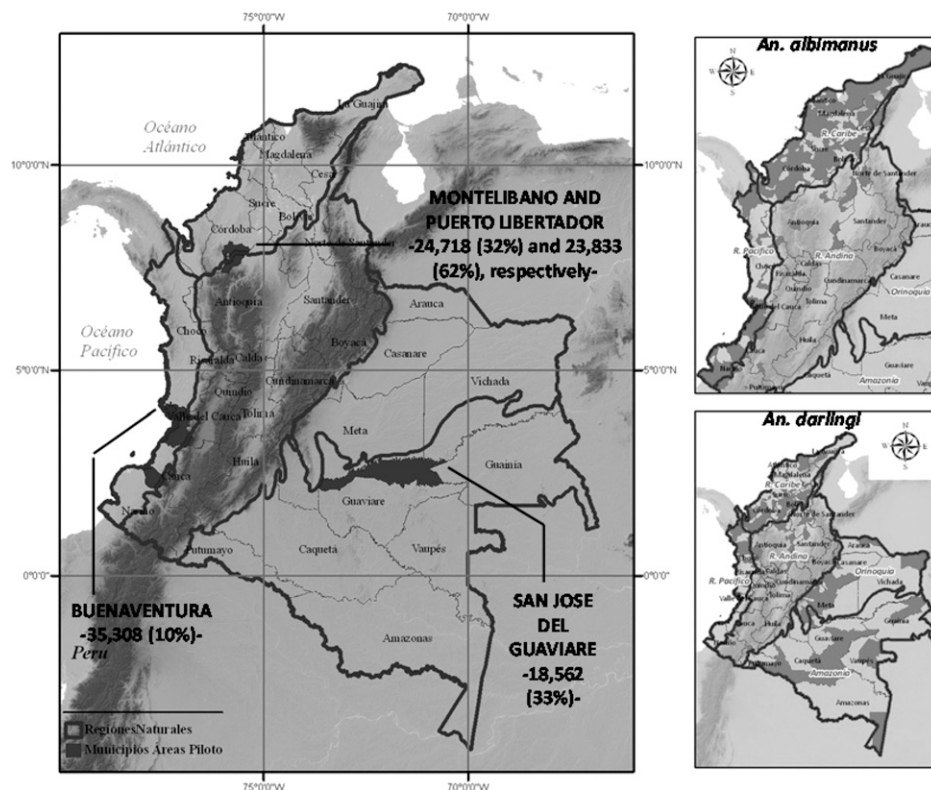


FIGURE 1. Pilot sites of the Integrated National Adaptation Pilot project (left panel) and spatial distributions of *Anopheles albimanus* and *An. darlingi* primary vectors (top and bottom right panels). Colombia. See also the total number of persons living in their rural areas as of 2008 and the proportions (in parentheses) with respect to the total number of persons living in the municipality. In top and bottom right panels, municipalities with reports of *Anopheles* are shaded.^{31,32}

MALARIA PROCESS-BASED MATHEMATICAL MODELS

Four malaria process-based models were used in this study: the model proposed by Ross²³ and Macdonald,²⁴ as well as those suggested by Martens,²⁵ Ruiz et al.,¹⁰ and Worrall, Connor, and Thomson.²⁶ These models were made available on a malaria multi-model ensemble platform created by using the modeling and simulation tool Powersim Constructor Version 2.51 (Powersim Corporation, Reston, VA). Detailed information regarding each model (their systems of ordinary differential equations, schematic diagrams,

stock-flow models, level and exogenous variables, as well as key simulation results) is provided in the supplementary material.

DATA

Malaria, entomologic, climatic, and socioeconomic data were gathered to characterize the malaria situation in each of the pilot sites and parameterize the process-based models (Table 1). Data from health facilities at each site included laboratory-confirmed malaria-positive cases and dominant associated malaria parasite (*P. falciparum* or *P. vivax*). In

TABLE 1
Summary of parameters of the implemented process-based models, Colombia*

	Parameter	MAC	MAR	SimulMal	WCT	Unit	Source	
Community-based	Total human population at risk			P_{hu}	d	Individuals	Demographic census	
	Per capita birth rate			R_{na}		/year	Demographic census	
	Natural per capita mortality rate		μ	R_{mo}		/year	Demographic census	
	Percentage coverage achieved by control campaigns				C	NA	Reports by health services	
	Proportion of cases reporting at health facilities				λ	NA	Not available	
Parasite	Number of degree days required for parasite development	n	D_m	D_m	f_N	°C/day	Literature	
	Minimum temperature required for parasite development		$T_{min,p}$	$T_{min,p}$	g_N	°C	Literature	
Human host	Duration of exo-erythrocytic schizogony			k_{in}	x	Days	Literature	
	Duration of erythrocytic schizogony	HD		k_{er}		Days	Literature	
	Host delay for immunity	WN	υ	υ		Days	Literature	
	Immunity window		τ	τ		Days	Literature	
	Susceptibility		b	b		NA	Literature	
	Recovery		c_i		r	1/day	Literature	
Mosquito	Rainfall to mosquito constant				μ	Mosquitoes/mm	Literature	
	Rate of oviposition			R_{po}		Eggs/batch	Literature	
	Eggs: becoming non-viable, mortality multiplier, and cycle duration to larva–first instar			$\mu_E, T_1, \text{ and } k_E$		NA, NA and days	Laboratory experiments	
	Larvae: becoming non-viable, mortality multiplier, and cycle duration to pupae			$\mu_L, T_2, \text{ and } k_L$		NA, NA and days	Laboratory experiments	
	Pupae: becoming non-viable, mortality multiplier, and cycle duration to imago stage			$\mu_{PU}, T_3, \text{ and } k_{em}$		NA, NA and days	Laboratory experiments	
	Daily survival probability or natural mortality	p	p	μ_m		NA	Literature and laboratory experiments	
	Probability of a vector surviving each gonotrophic cycle				α_w	NA	Literature and laboratory experiments	
	Induced mortality			α_m		Mosquitoes/day	Literature	
	Percentage of vectors surviving each feeding cycle in sprayed population				β	NA	Literature	
	Number of degree days required for the digestion of a portion of ingested blood	a	D_{bd}	D_{bd}	f_u		°C-days	Laboratory experiments
	Minimum temperature required for the digestion of a blood meal		$T_{min,bd}$	$T_{min,bd}$	g_u		°C	Laboratory experiments
	Human blood index		HBI	HBI	h		NA	Literature
Duration of the second and third phases of the gonotrophic cycle				v		Days	Literature	
Proportion of anophelines with sporozoites in salivary glands that are infective	b		SR			NA	Field entomologic collections and laboratory experiments	
Probability of becoming infected per infectious meal					k	NA	Literature	
Probability of becoming infectious after an infectious blood meal					v and S	NA	Literature	

*MAC = Ross²³ and Macdonald;²⁴ MAR = Martens;²⁵ SimulMal = Ruiz et al.;¹⁰ WCT = Worrall, Connor, and Thomson;²⁶ NA = not applicable.

addition, relevant entomologic, environmental, and socio-economic data were obtained from a variety of sources along with information on key anti-malaria interventions undertaken in each locality. A brief description of the datasets used is presented below.

Malaria-positive case data. Colombia has had various major institutional health systems over the past five decades.^{13,27,28} Surveillance activities have shifted from state collective notification to locality-level individual report. These changes in malaria control policy and institutional arrangements play a role in changes in morbidity profiles observed over the long-term historical period (1960–present).¹³ To consider a single source of malaria cases data, *P. falciparum* and *P. vivax* malaria morbidity profiles reported by the Colombian passive Public Health Surveillance System were processed for each of the malaria pilot sites. A 540-epidemiologic week (EW) period, spanning from the first EW of 2000 through the eighteenth EW of 2010, was selected for the analysis. Each EW begins on a Sunday and ends on a Saturday. Case data are available as single data points for each EW, for each age class, and for each pilot site. There is no information available on the proportion of cases reporting at health facilities, and changes in the reporting rate may result in differences between sites, as well as changes in observed cases over time. Between 9% and 19% of the total number of EWs are blanks (either missing or null records) in the provided datasets. Also, historical data showed strong changes in the mean and various inconsistent records, particularly in the datasets of the municipalities of Puerto Libertador and San José del Guaviare.

Entomologic data. The variables required for an in-depth understanding of local entomologic conditions, such as mosquito density, species, birth rate, survivorship, feeding frequency, prevalence of infection, and susceptibility,²⁹ were

gathered from a number of sources, including the literature, field collections, and laboratory experiments. The international literature search resulted in the quantification of several mosquito exogenous variables, such as the rate of oviposition, the natural and induced (for instance, by insecticides) mortality rates, and the human blood index.^{22,30} Local literature search led to the analysis of secondary information previously documented by the Malaria Eradication Service of the Colombian Ministry of Health and published papers^{31,32} on the nationwide presence of *Anopheles* mosquito species (Figure 1). In addition, a series of field entomologic collections were performed during 2008–2011 at the different pilot sites, which resulted in the collection of more than 5,040 adult female mosquitoes and the analysis of primary and secondary vectors incriminated in malaria transmission locally, as well as in preliminary estimates of mosquito densities. A total number of 4,914 *Anopheles* mosquitoes were then processed for the assessment of natural prevalence of malaria infection. Last, experiments conducted under controlled laboratory conditions with more than 1,240 adult female mosquitoes resulted in the assessment of *Anopheles darlingi* feeding frequencies (Figure 2). It is worth noting that this is one of the first set of experiments designed to estimate the feeding frequency of this *Anopheles* species. We were unable to obtain satisfactory information on some exogenous variables, such as vector resistance against insecticides, seasonality of local breeding sites, and mosquito feeding and resting habits.

Climate data. Historical records of daily minimum, mean, and maximum temperatures, total daily rainfall, and mean daily relative humidity, which were provided by the Colombian Institute of Hydrology, Meteorology and Environmental Studies through the CNIH, were processed for each of the pilot sites. One nearby weather station per municipality chosen among moderately dense hydrometeorologic networks was

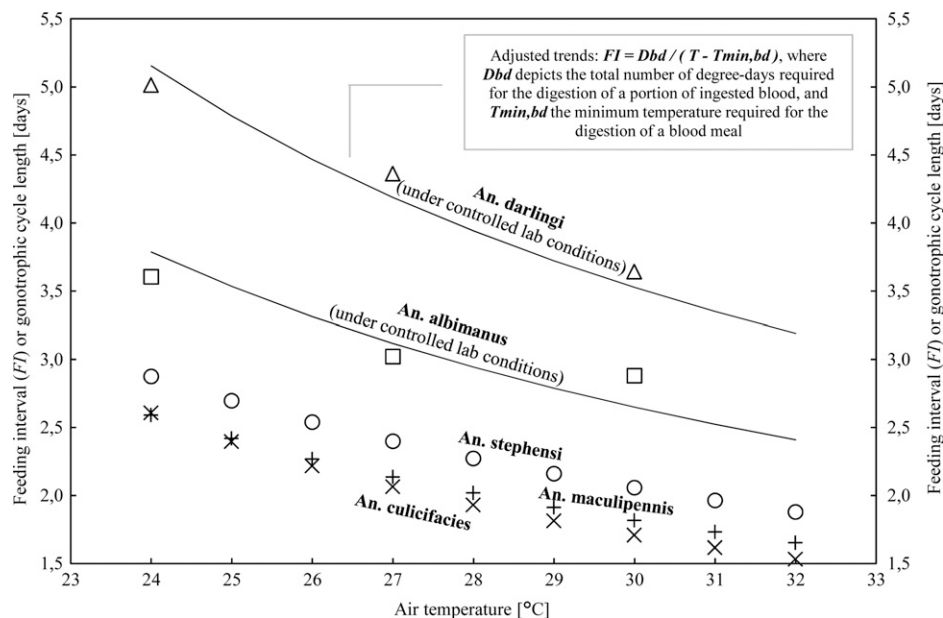


FIGURE 2. Gonotrophic cycle lengths of primary malaria vectors, *Anopheles darlingi* and *An. albimanus*, compared with feeding intervals of *An. stephensi*, *An. maculipennis*, and *An. culicifacies* mosquito vectors, Colombia. Feeding intervals of vectors from Africa are based on scientific literature. The following sample sizes were used to assess the gonotrophic cycle length of *An. darlingi*: $n = 66$ at 24°C; $n = 170$ at 27°C; and $n = 87$ at 30°C. The duration of gonotrophic cycle of *An. albimanus* was estimated under controlled laboratory conditions during previous research projects conducted in Colombia.^{37,39}

TABLE 2
Weather stations available for analysis of local climatic conditions in the INAP malaria pilot sites, Colombia*

Identification no.	Type	Name (municipality)	Latitude north	Longitude west	Altitude (meters)	Climatic variable	Available period (monthly timescale)	Statistically significant long-term trend in annual time series
2502516	CO	Cuba Hda (Montelíbano and Puerto Libertador)	08°00'	75°25'	50	R	5/1973–11/2009	+6.9%/decade
						MinT†	1/1978–11/2009	+0.2°C/decade
						MaxT†	1/1978–11/2009	–
						MeanT†	1/1978–11/2009	–
3101501	CO	Trueno El (San José del Guaviare)	02°24'	72°43'	150	RH	1/1978–09/2006	NA
						R	8/1982–12/2009	–
						MinT‡	8/1982–12/2009	+0.4°C/decade
						MaxT‡	8/1982–12/2009	–
5311501	SP	Apto Buenav (Buenaventura)	03°51'	76°58'	14	MeanT‡	12/1982–12/2009	–
						R	1/1946–10/2010	+3.4%/decade
						MinT§	4/1983–10/2010	–
						MaxT§	4/1983–10/2010	–
						MeanT§	4/1983–10/2010	–

*INAP = Integrated National Adaptation Pilot; CO = ordinary climatological weather station; R = total monthly rainfall (in mm); MinT = minimum monthly temperature in °C; MaxT = maximum monthly temperature in °C; MeanT = mean monthly temperature in °C; RH = mean monthly relative humidity (%); NA = not available; SP = primary synoptic weather station.

†Daily minimum temperatures obtained at the weather station in Cuba Hda had a historical mean (SD) of 22.4°C (1.3°C). Only three potential outlying records > 26°C were deleted from climatic datasets. Daily maximum temperatures had a historical mean (SD) of 33.1°C (1.5°C). Two records > 39.0°C and one record < 25°C were considered true outliers. Daily mean temperatures had a mean (SD) of ≈ 27.2°C (1.1°C). Three daily temperatures of ≈ 22.1–22.5°C, one record of 6.5°C, and two records > 32.0°C were deleted from historical datasets.

‡Daily minimum temperatures obtained at the weather station in Trueno El had a historical mean (SD) of 21.1°C (1.4°C). Four records of ≥ 25°C and seven records < 15°C were deleted from climatic datasets. Daily maximum temperatures had a historical mean (SD) of 31.4°C (2.2°C). Two records > 38.0°C were considered true outliers. Daily mean temperatures had a mean (SD) of ≈ 25.2°C (1.4°C). Five daily temperatures > 30.5°C were deleted from historical datasets.

§Daily minimum temperatures obtained at the weather station in Apto Buenaventura had a historical mean (SD) of 22.8°C (0.9°C). Only one potential outlying record of 16.9°C was deleted from the available dataset. Daily maximum temperatures had a historical mean (SD) of 30.4°C (1.7°C). Only one record of 24.0°C was considered a true outlier. Daily mean temperatures had a mean (SD) of ≈ 26.0°C (0.9°C). Three daily temperatures > 29.0°C and two observations of ≈ 22.7°C were deleted from historical datasets.

selected for the analysis (Table 2). Criteria included records availability, observational periods, and quality and homogeneity of historical records. Selected weather stations are manually operated and have long, although discontinuous (at a daily timescale, climate variables have numerous missing records), historical climatic datasets. The longest historical time period spans back almost 65 years (January 1946–October 2010), and the shortest dataset covers the period December 1982–December 2009.²⁹

Non-climatic factors. For a partial level of understanding of malaria transmission,²⁹ non-climatic exogenous variables included 1) total human populations at risk (only rural communities) and their population growth rates, all based on previous demographic census and projections published online at <http://www.dane.gov.co/> by the Colombian National Administrative Department of Statistics; 2) descriptions of spray programs, activities blocking adult female–human host interactions, activities controlling immature mosquitoes, and environmental interventions, all based on reports of intervention campaigns conducted by state and municipal health services;³³ and 3) description of socioeconomic conditions prevailing in the communities at risk, particularly economic quantitative variables, cultural quantitative factors, and cultural qualitative potential drivers, taking into account 39 non-published local reports and datasets provided (physically or digitally) by the state health services: 13 files in total for the municipalities of Montelíbano and Puerto Libertador, and 15 and 11 files for the municipalities of San José del Guaviare and Buenaventura, respectively.

METHODS

Malaria-positive cases. *Plasmodium falciparum* and *P. vivax* malaria-positive cases were aggregated to obtain data points for each municipality and for each EP, which comprises four EWs. Malaria incidence per EP and per type of infection were calculated with the historical total human populations at risk, and then compared with the annual cycles of climatic variables.

Vector species, mosquito densities, prevalence of infection, and feeding frequencies. To define primary and secondary vectors in each malaria pilot site, maps of historical spatial distributions (presence/absence) of *Anopheles albimanus*, *An. darlingi*, *An. nuneztovari*, *An. punctimacula*, *An. pseudopunctipennis*, *An. neivai*, and *An. pholidotus* (as *An. lepidotus*) in Colombia were generated on a geographic information system platform (Figure 1). To confirm primary vector species at a local level, adult mosquitoes were collected in the study sites by using the human landing capture technique. Mosquito species were identified by morphologic characteristics; *An. nuneztovari* mosquitoes were confirmed by a polymerase chain reaction–restriction fragment length polymorphism assay. Indoor and outdoor mosquito densities were estimated through human biting rates (HBRs) during dry and wet seasons. Natural prevalence of infection was assessed through detection of *P. falciparum*, *P. vivax* VK 210, and *P. vivax* VK 247 circumsporozoite proteins in *Anopheles* heads and thorax by using an enzyme-linked immunosorbent assay kit, according to the standard protocol proposed by the U.S. Centers for Disease Control and Prevention. Field activities did not include tests to assess blood preference of mosquitoes (anthropophilic versus zoophilic mosquitoes). Last, the duration of the gonotrophic cycle of *An. darlingi* mosquitoes was estimated at the Entomology Laboratory of the CNIH, under controlled temperatures of 24, 27, and 30°C, controlled relative humidity > 80%, and a constant 12-hour photoperiod (Figure 2).

Climate variables. Climatic records were organized in Microsoft (Redmond, WA) Office Excel 2007 spreadsheets and shared with municipal health authorities, and were also posted on the Data Library of the International Research Institute for Climate and Society (<http://iridl.ldeo.columbia.edu/index.html>). Last and Kandel,³⁴ Grubbs,³⁵ and normal range statistical tests were initially implemented to detect inconsistencies and anomalous records in daily minimum, mean, and maximum temperatures. Outlying observations (i.e., those outside the expected range for the particular climatic variable, were deleted from climatic datasets before

calculating monthly values (Table 2). Annual cycles of temperature, rainfall, and relative humidity were then calculated and compared with the historical annual distributions of malaria incidence (Figure 3). Mean annual values of temperature and relative humidity, total annual rainfall, and their 95% confidence intervals were also calculated. Exploratory analysis, including time series and box plots, were performed to detect changes in the mean, changes in the variance and long-term linear trends in annual (free of seasonality) historical time series (Table 2). The t-test for detection of linear trends and the Hotelling-Pabst, Mann-Kendall and Sen hypothesis tests were applied to assess the statistical significance ($\alpha = 0.05$) of observed long-term linear trends. Slope parameters, calculated by the method of least squares, were determined for those historical time series showing statistically significant trends in the mean and were used to define future medium-term changing climate scenarios. Upper and lower confidence limits were also assessed for simple linear regression models.

Non-climatic factors. To quantify cultural quantitative and qualitative non-climatic factors, an analysis of critical conditions was performed at a local level for specific counties within three of the pilot sites: the counties of No Hay Como Dios and Alcides Fernández in Montelíbano; the county of Juan José in the municipality of Puerto Libertador; and the counties of Citronela and Zacarías in Buenaventura (Figure 4). This criticality analysis was conducted by using structured surveys applied to a representative sample of households in each area. Non-climatic factors were assembled into six representative groups (Figure 4): 1) variables related to the level of immunity of human populations, such as previous malaria infections, the proportion of the population under five years of age and the proportion of women of child-bearing age that were pregnant; 2) variables related to the risk of contact between mosquito populations and human hosts: age, sex, occupation, household structure including presence of walls, ceiling, windows and screens, doors and screens (and their materials), dominant crop type at the household level, sanitary services and their location; 3) variables related to local capacity: participation in malaria control programs, and education level of head of household; 4) variables representative of disease knowledge, attitudes, customs, practices, and beliefs, in particular those related to malaria symptoms, malaria treatment, infection with malaria parasites, auto-medication, self-protection, mosquitoes breeding sites, timing of malaria outbreaks, communication and education; 5) variables describing the access to health services: health insurance and access to malaria treatment; and 6) variables related to interventions: bed net use and mosquito larvicide and adulticide spraying frequency.

Last, to ground the effort at the scale of actual decision-making, an assessment of local capacity in state health authorities (to implement malaria dynamic models) was conducted (Figure 5). The assessment included six workforce-related aspects such as entomologic surveillance, epidemiologic surveillance, vector-borne diseases coordination, decision-making planning, social expertise, and collaborative/cooperative efforts, as well as six installed/available tools-related aspects: continuous AC power supply, computer access, Internet access, text editor software, at least Microsoft Office Excel, and simulation software such as Powersim Constructor Version 2.51 or Powersim Studio 8 Academic. Various in-person and online

workshops on the development and implementation of dynamic models were then held at state and municipal health services. Concepts of general systems theory, process-based (biological) modeling, malaria dynamic modeling, experimentation-validation-analysis processes, and malaria integrated surveillance and control activities were discussed with public health and tropical medicine experts. Lectures were supported on a recently created online course entitled “Simulating Malaria Transmission Dynamics,” which now includes two major sessions: a six-module conceptual session and a five-module practical simulation experiment.

RESULTS

Total primary cases, malaria incidence, and seasonality. Total *P. falciparum* and *P. vivax* malaria primary cases observed in the pilot sites over the historical period 2000–2010 are shown in Table 3. The total number of *P. falciparum* malaria infections reported annually ranged from 700 positive cases in San José del Guaviare to approximately 1,800 cases in the municipalities of Montelíbano and Buenaventura. *Plasmodium vivax* malaria infections showed average annual values in the range from 1,200 positive cases in San José del Guaviare to approximately 4,000 primary cases in Montelíbano and Puerto Libertador. A maximum number of approximately 730 cases per epidemiologic period of *P. falciparum* malaria were reported in Buenaventura in 2004, and more than 950 positive cases of *P. vivax* malaria were observed in Puerto Libertador in 2007. Available malaria records also suggest that infections tend to affect persons 15–44 years of age.

Plasmodium falciparum and *P. vivax* malaria incidence and seasonality for each of the pilot sites are shown in Figure 3. *Plasmodium falciparum* malaria in the municipality of Montelíbano (not the predominant type of infection) reached an average incidence of 4 positive cases per 1,000 inhabitants and shown to be stable year round (incidence ranges = 3–6 positive cases per 1,000 inhabitants). *Plasmodium vivax* malaria, the predominant infection, reached an average incidence of 15 positive cases per 1,000 inhabitants and also shown to be stable year round. In the municipality of Puerto Libertador located in the same region, *P. falciparum* malaria incidence reached 4 positive cases per 1,000 inhabitants and showed peaks in February and June of 6 and 8 positive cases, respectively. *Plasmodium vivax* malaria reached approximately 17 positive cases but shows a bimodal intraannual distribution with minimum and maximum values of approximately 7 and 23 positive cases in December and July, respectively. Mean temperatures in these two pilot sites and their surroundings are favorable for mosquito survival and successful incubation of malaria parasites (i.e., $> 21.5^{\circ}\text{C}$) year round. Monthly rainfall is suitable for breeding sites productivity (i.e., > 100 mm/month) only over the period April–November.

Comparisons of malaria incidence with intraannual cycles of climatic variables suggest that in the municipality of Montelíbano, *P. falciparum* and *P. vivax* malaria incidence followed, although not closely, the annual cycle of mean temperature (Figure 3). *Plasmodium vivax* infection, the predominant type of infection, showed a peak in its incidence during December–March. A 0-month lag and a 4-month lag with respect to monthly peaks in temperature and rainfall were observed in the annual cycles of malaria incidence.

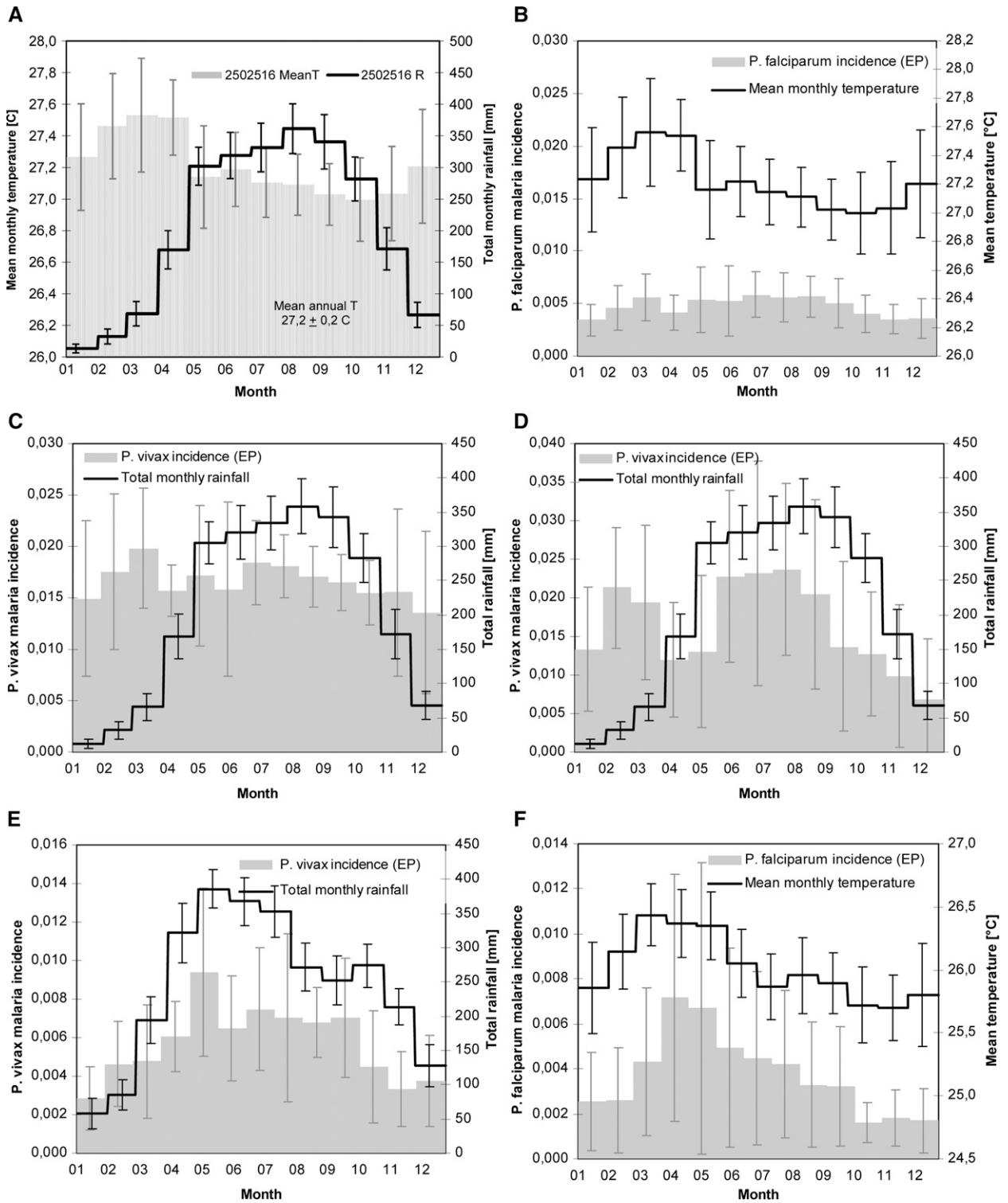


FIGURE 3. Annual cycles of temperature, rainfall, *Plasmodium falciparum* and *P. vivax* malaria observed in the selected pilot sites. Panels A–D display information of the municipalities of Montelíbano and Puerto Libertador; panels E and F show the annual cycles observed in the municipalities of San José del Guaviare and Buenaventura, respectively. The gray solid bars in panel A and the black solid line in panel B depict the historical mean monthly temperatures observed in the surroundings of the municipalities of Montelíbano and Puerto Libertador, according to available climatic records gathered at the local weather station during 1978–2009. The black solid lines in panels A, C, and D show the total monthly rainfall observed at the same weather station during 1973–2009. The black solid line in panel E denotes the total monthly rainfall observed in the municipality of San José del Guaviare, according to records gathered at the local weather station during 1982–2009. The black solid line in panel F shows the mean monthly temperatures observed at the local weather station of the municipality of Buenaventura during 1983–2009. See also the annual cycles of *Plasmodium falciparum* and *P. vivax* malaria incidence per epidemiological period (EP) observed in the municipalities of Montelíbano (panels B and C), Puerto Libertador (panel D), San José del Guaviare (panel E), and Buenaventura (panel F) according to malaria data provided by the passive Colombian Public Health Surveillance System. Error bars indicate confidence intervals for a $\alpha = 0.05$ significance level.

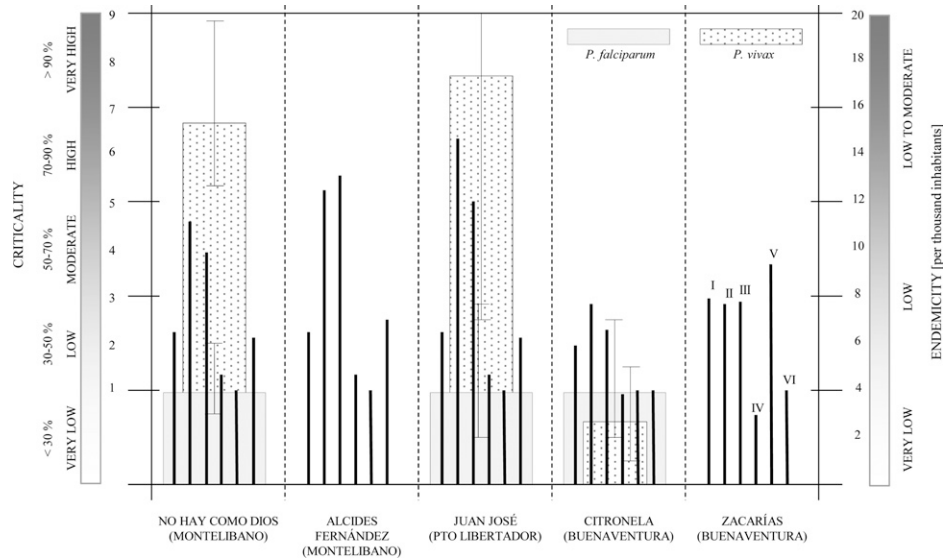


FIGURE 4. Criticality of local conditions at the county level in three of the four pilot sites, Colombia. Black solid bars depict the representative groups of non-climatic factors, such as (I) immunity of human populations; (II) risk of contact; (III) local installed capacity; (IV) disease knowledge, customs and beliefs; (V) access to health services; and (VI) malaria interventions (their levels of criticality are plotted on the left y-axis). Solid and shaded bars depict, respectively, the historical *Plasmodium falciparum* and *P. vivax* malaria incidence (plotted on the right y-axis); error bars indicate confidence intervals. Malaria incidence in Montelibano is plotted in the box for No Hay Como Dios County, and malaria incidence in Buenaventura is plotted in the box for Citronela County.

In Puerto Libertador, malaria infections seemed to respond to a combination (or synergistic effects) of rainfall and temperature: in February and March, when rainfall is limited (i.e., monthly values in the range of 100–300 mm), increases in mean temperature seem to drive the increases in malaria incidence. In June–August, when temperatures reach lower values, increases in monthly rainfall amounts could favor the increase in vector densities and malaria incidence.

In the municipality of San José del Guaviare, *P. falciparum* malaria (not the predominant type of infection) reached an average incidence of 3 positive cases per 1,000 inhabitants, and a peak of 5 cases in May. The predominant infection, *P. vivax*, showed an average incidence of approximately 5 positive cases and a unimodal distribution with a peak in May of approximately 9 positive cases (Figure 3). The mean temperature is favorable year round and monthly rainfall was

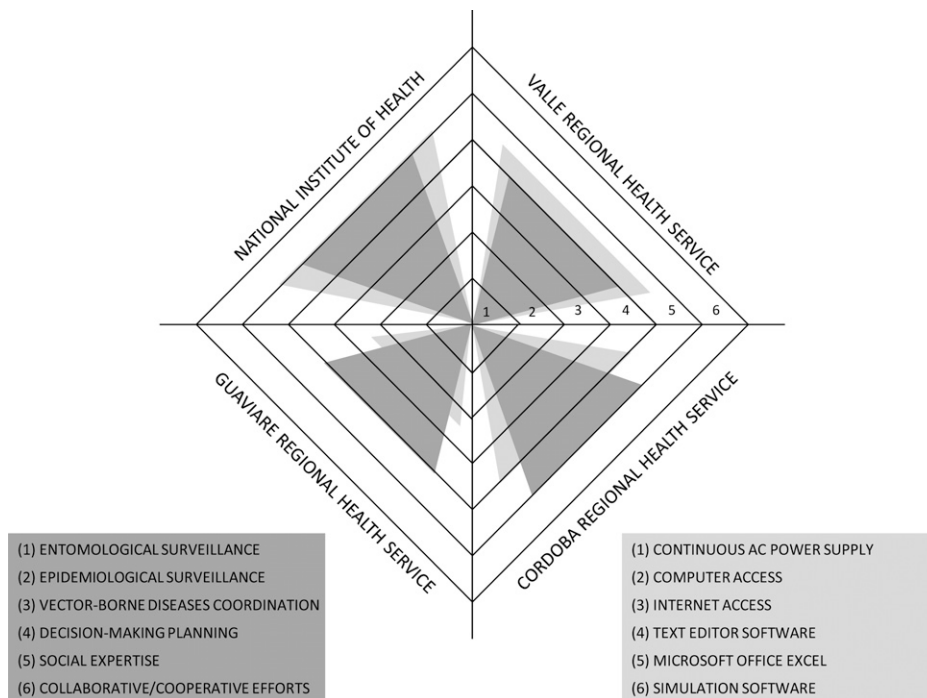


FIGURE 5. Capacity in state and municipal health authorities to implement malaria dynamic models, Colombia. Workforce-related aspects are represented by the gray solid triangles; installed/available tools-related aspects are represented by the light gray solid triangles.

TABLE 3
Plasmodium falciparum- and *P. vivax*-malaria positive cases observed, Colombia, 2000–2010*

Study site	<i>P. falciparum</i> infection				<i>P. vivax</i> infection			
	Approximate average annual value	Maximum annual value (year of occurrence)	Maximum value per EP (EP)	Maximum value per EW	Approximate average annual value	Maximum annual value (year of occurrence)	Maximum value per EP (EP)	Maximum value per EW
Montelíbano	1,800	2,600 (2001)	> 500 (sixth EP of 2001)	≈180	4,000	7,000 (2007)	> 860 (sixth EP of 2001)	≈280
Puerto Libertador	1,400	2,800 (2002)	> 420 (one-seventh EP of 2003)	≈170	4,000	6,600 (2007)	> 950 (one-third EP of 2007)	≈430
San José del Guaviare	700	850 (2000)	> 180 (one-fifth EP of 2000)	≈95	1,200	1,800 (2008)	> 340 (one-fifth EP of 2008)	≈200
Buenaventura	1,800†	4,900 (2002)	> 730 (one-fifth EP of 2004)	≈260	1,500	3,400 (2004)	> 560 (one-fourth EP of 2004)	≈320

*EP = epidemiologic period; EW = epidemiologic weeks. One EP is equivalent to four EWs.

†Significant difference between 2001–2005 and 2006–present.

suitable only during March–December. Historical *P. vivax* and *P. falciparum* malaria incidence followed the annual cycle of rainfall: for total monthly rainfall of 0–200 mm, *P. falciparum* and *P. vivax* malaria infections showed average incidence of 2 and 3–4 positive cases per 1,000 inhabitants, respectively. For rainfall > 200 mm per month, *P. falciparum* malaria increased at a rate of 0.7–1 positive cases per 1,000 inhabitants per 100 mm increase in rainfall. *Plasmodium vivax* malaria increased at a rate of 1 primary case per 1,000 inhabitants per 100-mm increase in rainfall.

In the municipality of Buenaventura *P. falciparum* malaria has been the critical burden (Figure 3). It showed a unimodal distribution and, an average incidence of 4 positive cases and a peak of 7 positive cases in April. *Plasmodium vivax* malaria incidence is also unimodal and has an average of 3 positive cases and a peak of 5 positive cases usually reached in April. Although mean temperature and monthly rainfall in this locality are favorable year round, *P. vivax* and *P. falciparum* malaria incidence followed mainly the annual cycle of temperature: their incidence increase at rates of approximately +5.6 and +3.8 positive cases per 1,000 inhabitants per 1°C increase in mean monthly temperature, respectively. A one-month lag with respect to the monthly peak in temperature was observed in the annual cycle of *P. falciparum* malaria incidence.

Vector species, mosquito densities, prevalence of infection, and feeding frequencies. Fifteen species were identified in the study sites, including *An. darlingi*, *An. nuneztovari*, *An. punctimacula*, *An. pseudopunctipennis*, *An. oswaldoi* s.l., *An. rangeli*, *An. albicans* s.l., and *An. neomaculipalpus*. Species collected in Montelíbano included *An. nuneztovari* (96.1% of the total number of collected mosquitoes) and *An. darlingi* (3.3%); in Puerto Libertador, mosquito species included *An. nuneztovari* (83.4%) and *An. darlingi* (15.7%); in San José del Guaviare, *An. albicans* s.l. (45.6%), *An. braziliensis* (19.2%), *An. oswaldoi* s.l. (18.1%), and *An. darlingi* (15.0%); in Buenaventura, 99.5% of the total number of collected mosquitoes were *An. nuneztovari* species. These proportions are consistent with previous mosquito collection campaigns conducted by municipal and state health services,³³ except for the case of Buenaventura, where *An. albicans* has been frequently incriminated in malaria transmission.^{36,37}

In the municipalities of Montelíbano and Puerto Libertador, *An. darlingi* showed almost constant (throughout the sampling period) HBRs ranging from 0.3 to 8.6 mosquitoes per human host per night. In San José del Guaviare, this *Anopheles* species reached HBRs of approximately 1.6 and 41.0 mosquitoes per human host per night during the dry and wet seasons of the sampling period, respectively. *Anopheles nuneztovari* showed high HBRs ranging from 28 to approximately 72 mosquitoes per human host per night in Montelíbano and Puerto Libertador, and 21 and 66 mosquitoes per host per night in the municipality of Buenaventura during the wet and dry seasons, respectively. Roughly speaking, a significant difference between indoor and outdoor mosquito densities was not observed in the selected pilot sites.

In Montelíbano, the *P. vivax* VK210 and *P. vivax* VK 247 natural prevalence of infection of *An. nuneztovari* mosquitoes (n = 1,470) reached 0.3%. In Puerto Libertador, *P. falciparum* and *P. vivax* VK210 natural prevalence of infection of *An. nuneztovari* mosquitoes (n = 707) reached 0.4%. These findings confirm that *An. nuneztovari* s.l. is the primary vector incriminated in malaria transmission in these two

municipalities of the Department of Córdoba. In the county of Citronela for the municipality of Buenaventura, *P. vivax* VK 247 was detected in two *An. nuneztovari* mosquitoes ($n = 387$), suggesting a natural prevalence of infection of approximately 0.5%.

Experiments conducted under controlled laboratory conditions suggest that the anthropophilic *An. darlingi* feeds on humans every 5.0 and 3.7 days at ambient temperatures of 24 and 30°C, respectively (Figure 2). Previous studies also conducted in Colombia suggest that *An. albimanus* mosquitoes have less anthropophilic habits but more frequent blood meals every 3.6 and 2.8 days at temperatures of 24 and 30°C, respectively.³⁸ To reflect these inferred feeding intervals, the total number of degree days required for digestion of a portion of ingested blood and the minimum temperature required for the digestion of a blood meal were then set to 67°C-day and 11°C for *An. darlingi*, and 53°C-day and 10°C for *An. albimanus*.

Annual values of climate variables, climatology and long-term trends. In surroundings of the municipalities of Montelíbano and Puerto Libertador, rainfall records reached a historical mean \pm SD average annual value of $2,383 \pm 160.5$ mm ($\beta = 95\%$) and showed a unimodal intraannual distribution and a peak of 350 mm in August and a minimum value of approximately 20 mm in January. Historical rainfall does not exceed 70 mm per month over the dry period of December–February (Figure 3). Mean temperatures reached a mean \pm SD annual value of $27.2 \pm 0.2^\circ\text{C}$ ($\beta = 95\%$), maxima of 27.5°C in March and April, and minima of approximately 27.0°C during September–November. In the municipality of San José del Guaviare, rainfall records reached an historical mean \pm SD annual value of $2,796 \pm 151$ mm ($\beta = 95\%$) and also reached a unimodal intraannual distribution but with a peak of 380 mm in May and a minimum value of about 70 mm in January. Over the period December–February, rainfall records did not exceed 125 mm per month. Mean temperature reached a mean \pm SD annual value of $25.3 \pm 0.2^\circ\text{C}$ ($\beta = 95\%$) and maximum and minimum values of approximately 26.5 and 24.1°C in February and July, respectively. In the municipality of Buenaventura, the historical mean \pm SD annual rainfall reached $6,532 \pm 248$ mm ($\beta = 95\%$) and its annual cycle was bimodal with two peaks commonly in May (630 mm) and October (820 mm). The long dry season is usually observed during January–March, when monthly rainfall amounts do not exceed 400 mm per month. Mean temperatures in this locality reached mean \pm SD annual values of approximately $26.0 \pm 0.2^\circ\text{C}$ ($\beta = 95\%$) and maximum and minimum values of approximately 26.4 and 25.7°C in April and November, respectively.

Annual rainfall amounts and annual minimum temperatures observed in the surroundings of the pilot sites of Montelíbano and Puerto Libertador increased at rates of approximately +7.0% and $+0.2^\circ\text{C}$ per decade over the periods 1973–2008 and 1978–2008, respectively. In the municipality of San José del Guaviare, annual minimum temperatures increased at a rate of $+0.4^\circ\text{C}$ per decade over the period 1982–2007. In the area of the municipality of Buenaventura, rainfall also increased over the past 40 years but at a lower rate of +3.4% per decade. The rest of the historical time series did not exhibit increasing/decreasing statistically significant long-term trends.

Non-climatic factors. The total number of inhabitants living in the selected malaria pilot sites as of 2008 reached values in

the range from 38,700 persons in Puerto Libertador to approximately 349,000 persons in Buenaventura. Their estimated total populations at risk (i.e., persons living in rural areas) were approximately 23,800 and 35,300 inhabitants, respectively (Figure 1). Population growth rates during 2000–2010 ranged from 23 newborns per 1,000 inhabitants per year in Montelíbano and San José del Guaviare, to approximately 39 new susceptible persons per year in Puerto Libertador. Information on differential (disease-induced) mortality rates or case-fatality rates and individual (economic-driven) migration patterns are not available. Massive forced (displaced) human migrations recently increased the total number of inhabitants in Montelíbano and San José del Guaviare by approximately 16% and 4%, respectively. However this information is limited to 2007–2008, despite multiple coerced displacements (particularly in those two pilot areas) that have characterized the conflict in Colombia over recent decades.

Information on vector control activities, such as annual indoor residual spraying (IRS) campaigns, blocking and screening programs, and breeding site control, were available for only a few interventions. According to municipal health authorities, in the municipalities of Montelíbano and Puerto Libertador, the highest percentage coverage achieved by IRS with deltamethrin campaigns reached 2.7% during 2005–2008. The distribution of long-lasting insecticide-treated bed nets has achieved 47% of the total populations at risk in these pilot sites. A maximum percentage of 78.6% of productive breeding sites was intervened (e.g., with *Bacillus sphaericus* and *Bacillus thuringiensis* bacteria) during 2007–2008. In the municipality of San José del Guaviare, the highest percentage coverage achieved by IRS campaigns reached 3.2% of the total population at risk in 2007, and the distribution of long-lasting insecticide-treated bed nets reached a maximum coverage of 11% in 2008. As for intervened breeding sites in this municipality, information is only limited to the product used in control campaigns (i.e., there is no information on achieved coverage). In the municipality of Buenaventura, the highest percentage coverage achieved by IRS campaigns reached 1.8% and 1.9% of the total population at risk in 2008 and 2009, respectively, and the distribution of long-lasting insecticide-treated bed nets reached 0.1% and 1.2% in 2006 and 2009, respectively. Similar to the case of San José del Guaviare, there is no information on intervened productive breeding sites in Buenaventura.

Information on economic variables, such as access to municipal and state health services, coverage of malaria treatment, living conditions, and employment, is limited. However, it can be argued that despite the fact that numerous economic activities, such as agriculture, fisheries, gold and coal mining, cattle grazing, handcrafting, and ecotourism, are conducted in these municipalities, human populations in rural areas have unsatisfied basic needs that reach 72.0% in Montelíbano and Puerto Libertador, 77.4% in San José del Guaviare, and 47.5% in Buenaventura. Public services, such as water and energy distribution networks, sewage systems, landfills, primary and secondary schools, and hospitals have also low coverage levels or are even absent in their rural areas, as observed in many places throughout rural Colombia. Although information on institutional arrangements, political and public interests, and social organizations or non-institutional arrangements is deemed important to the study, it was not available.

Information on cultural quantitative and qualitative factors was scarce and difficult to access. When available at one pilot site, they were frequently unavailable at others. Based on the analysis of the household samples in the municipalities of Montelíbano, Puerto Libertador, and Buenaventura, it can be argued that non-climatic factors related to the level of immunity of human populations, disease knowledge, access to health services, and malaria interventions lie in the very low to low intervals of the proposed levels of criticality (Figure 4). Non-climatic factors describing the risk of contact between mosquito populations and human hosts, and the local capacity in, particularly, the municipalities of Montelíbano and Puerto Libertador, lie in the moderate to high intervals of the proposed levels of criticality, and could be the socioeconomic drivers behind the low to moderate prevalence of *P. vivax* malaria in their populations at risk (Figure 4).

Currently, state and municipal health authorities have moderate to high workforce levels (from 4 to 5 points in a desired 6-level scale) for implementation of malaria dynamic models (Figure 4). Their installed technological capacities range from 2.5 points in San José del Guaviare to 5 points at the CNIH. In general, their major constraints include lack of expertise in social aspects, restricted knowledge in decision-making approaches and tools, limited collaborative and cooperative efforts, and lack of appropriate software and modeling skills.

DISCUSSION

This report describes the local climatic, demographic, entomologic, and socioeconomic settings of four *hypoendemic* malaria-prone municipalities where malaria process-based mathematical models are currently being implemented as part of the activities of the Colombian ISCS. The selected malaria pilot sites have different ecoepidemiologic settings, particularly cultural diversity and socioeconomic conditions, that challenge the implementation of not only the ISCS but many other initiatives. Two of the sites also have displaced populations because of the armed conflict, which make characterization of their ecoepidemiologic profiles particularly difficult. However, health services in all malaria pilot sites have a favorable workforce and technologic conditions that could enable a successful implementation of malaria dynamic models in their routine activities at the municipality level.

A qualitative index was explored by the research group to assess the level of understanding (low, moderate, or good) of local epidemiologic settings, taking into account the different determinants of malaria transmission. Research activities provided moderate to high levels of understanding of the malaria situation of malaria pilot sites, as well as their entomologic and climatic conditions. In particular, our first set of experiments conducted under controlled laboratory conditions resulted in assessment of the gonotrophic cycle length of *An. darlingi* mosquitoes that filled gaps in the entomologic records for Colombia. Along with previous assessments for *An. albimanus*,^{38,39} state health services now have good estimates of the feeding frequencies of the two primary vectors in Colombia. Research activities also provided a better understanding (although still limited) of the non-climatic factors of malaria pilot sites. In particular, non-climatic variables describing spray programs, activities blocking adult female-human host interactions, and activities controlling immature

mosquitoes lack continuous and homogenous records over the available observational period of malaria cases or are limited to only a few set of interventions. We suggest that these gaps, along with the detected missing data, inconsistent records, and strong changes in the historical time series of malaria primary cases, need to be reviewed before assessing skill levels of process-based malaria mathematical models. Also, we suggest that current state and municipal epidemiologic surveillance systems should be improved for collecting information on malaria interventions, socioeconomic factors, and primary cases systemically, routinely, and confidently.

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