

Universidad Tecnológica de Pereira (UTP)
Secretaría de Salud y Seguridad Social de Pereira
Secretaría de Salud de Risaralda
Asociación Colombiana de Infectología (ACIN)
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Grupo y Semillero de Investigación Salud Pública e Infección, UTP
Pereira, Risaralda, Colombia



Jueves 23 de abril de 2015 (2 a 6pm)
Pereira, Risaralda, Colombia.
Auditorio 1 del Bloque Y, UTP.

Simposio

“Día Mundial de la Lucha Contra la Malaria
2015”

25 Abril 2015
Invirtamos en el futuro, derrotemos la malaria



Diapositivas disponibles en:
<http://blog.utp.edu.co/arodriguezm>



Symposio
Día de la Lucha Mundial
contra la Malaria

25 Abril **2015**
Invirtamos en el futuro, derrotemos la malaria



Epidemiología de la Malaria en el Mundo, América Latina y Colombia y su Manejo a través de Guías de Atención

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Editor, Journal of Infection in Developing Countries (JIDC). Editorial Board, Travel Medicine & Infectious Diseases (TMAID).

Comité de Zoonosis y Fiebres Hemorrágicas, Asociación Colombiana de Infectología

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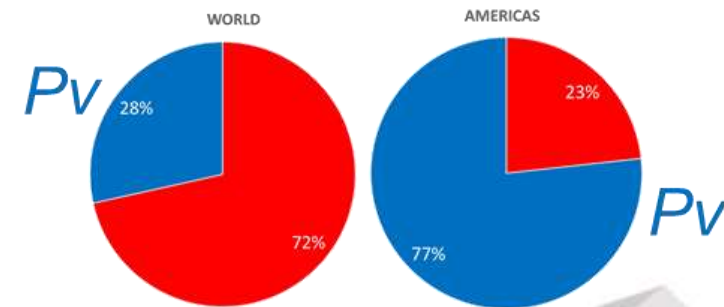
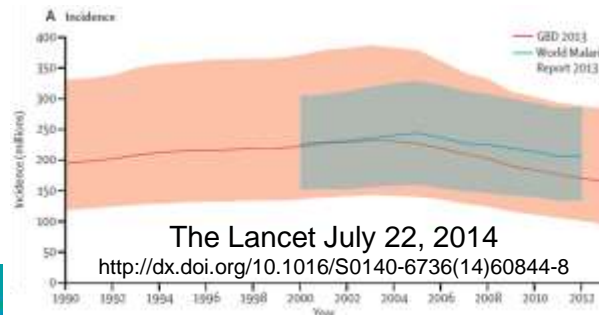
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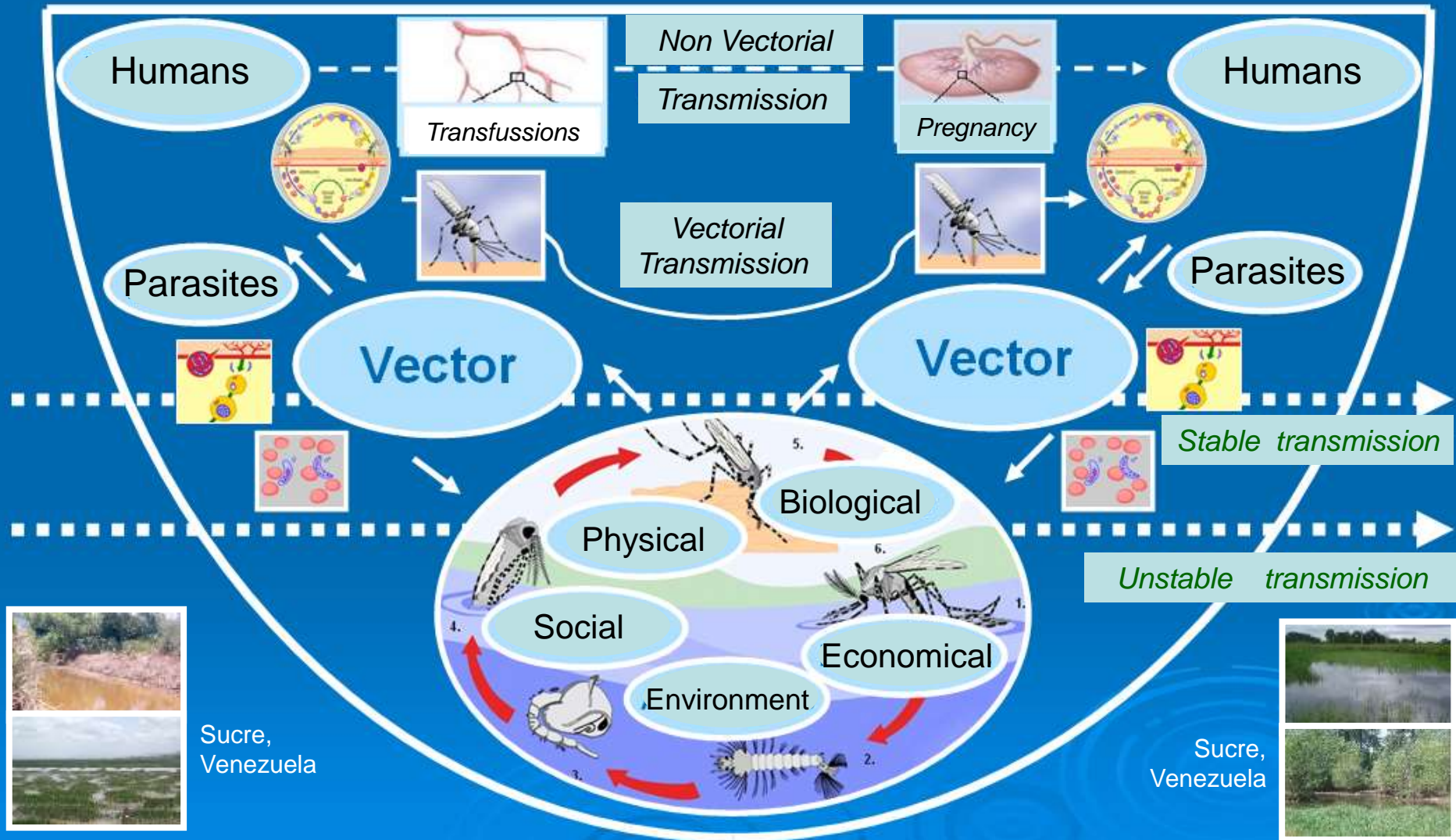
Still, a globally important parasitic disease...

- Allmost 90 million cases, just in 2012
- However, worldwide, between 2000 and 2012, estimated malaria mortality rates fell by 42% in all age groups and by 48% in children under 5 years of age.

Regional Summary	Population				Reported malaria cases			
	UN population	At risk (low + high)	At risk (high)	Number of people living in active foci	Suspected malaria cases	Presumed and confirmed malaria cases	% from total	API (cases/1000pop)
African	888 530 874	750 159 788	609 725 673	23 086 332	120 798 507	77 613 172	86.4%	87.34
Region of the Americas	567 176 164	103 978 618	24 284 204	4 898 451	7 629 247	469 369	0.5%	0.83
Eastern Mediterranean	429 415 046	273 565 047	118 950 012	3 063 762	13 119 024	7 033 879		(82.76
European	129 688 955	N/A	N/A	2 195 740	1 869 184	422		per
South-East Asia	1 833 020 203	1 356 418 365	344 905 112	19 714 597	130 013 789	3 760 367		10000)
Western Pacific	1 672 284 393	706 864 720	39 532 564	4 946 419	14 013 470	888 438		
Total	5 520 115 635	3 190 986 539	1 137 397 565	57 905 301	287 443 221	89 765 647	100%	16.25



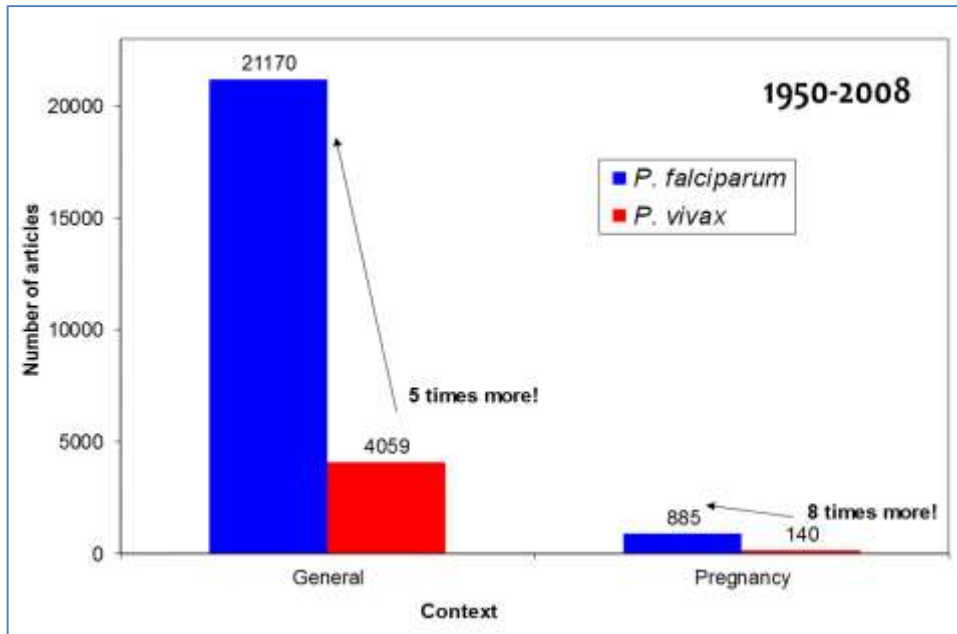
ECOEPIDEMIOLOGY OF MALARIA



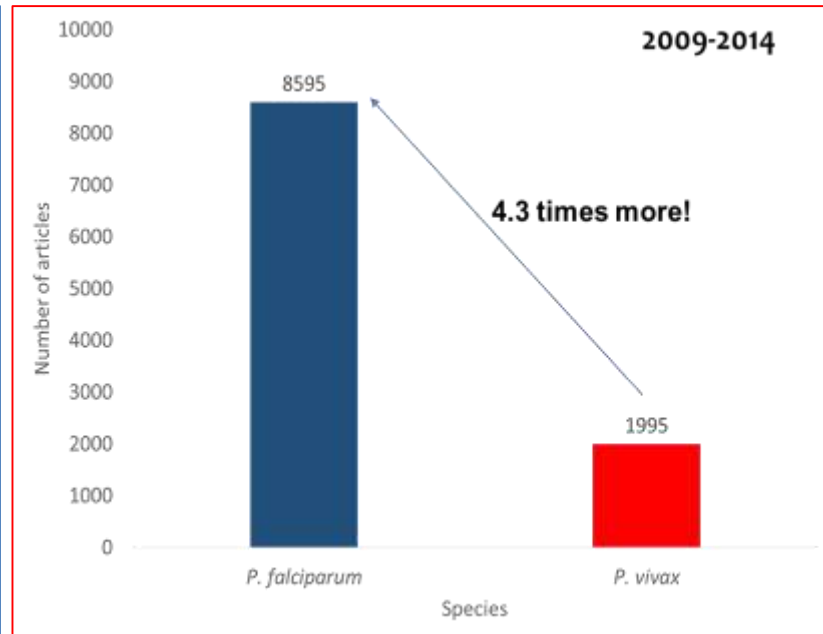
Rodriguez-Morales, 2005

P. falciparum vs *P. vivax*

Medline, July 20, 2008



Medline, August 6, 2014



TOPSY

Plasmodium falciparum

Plasmodium vivax

basketball

Search

Advanced search

Journal of Antimicrobial Chemotherapy Advance Access published May 26, 2014
Journal of Antimicrobial Chemotherapy

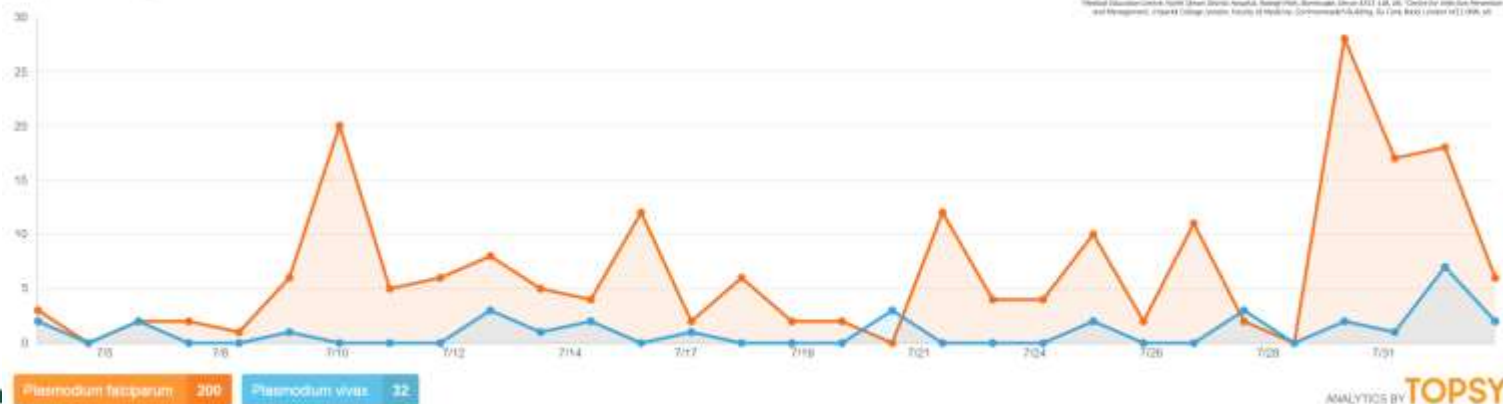
Tweets per day: Plasmodium falciparum and Plasmodium vivax
July 4th — August 3rd

What makes people talk about antibiotics on social media?
A retrospective analysis of Twitter use

Olivier J. Pfyffer, Enrique Castro-Sánchez* and Alison H. Kobayashi*

*Medical Education Centre, North Devon District Hospital, Barnstaple, Devon EX31 4LH, UK; Centre for Antibiotic Research and Management, Imperial College London, Faculty of Medicine, St Mary's Hospital, Du Cane Road, London W2 1PG, UK

Relative importance on social media: e.g. Twitter



ANALYTICS BY TOPSY

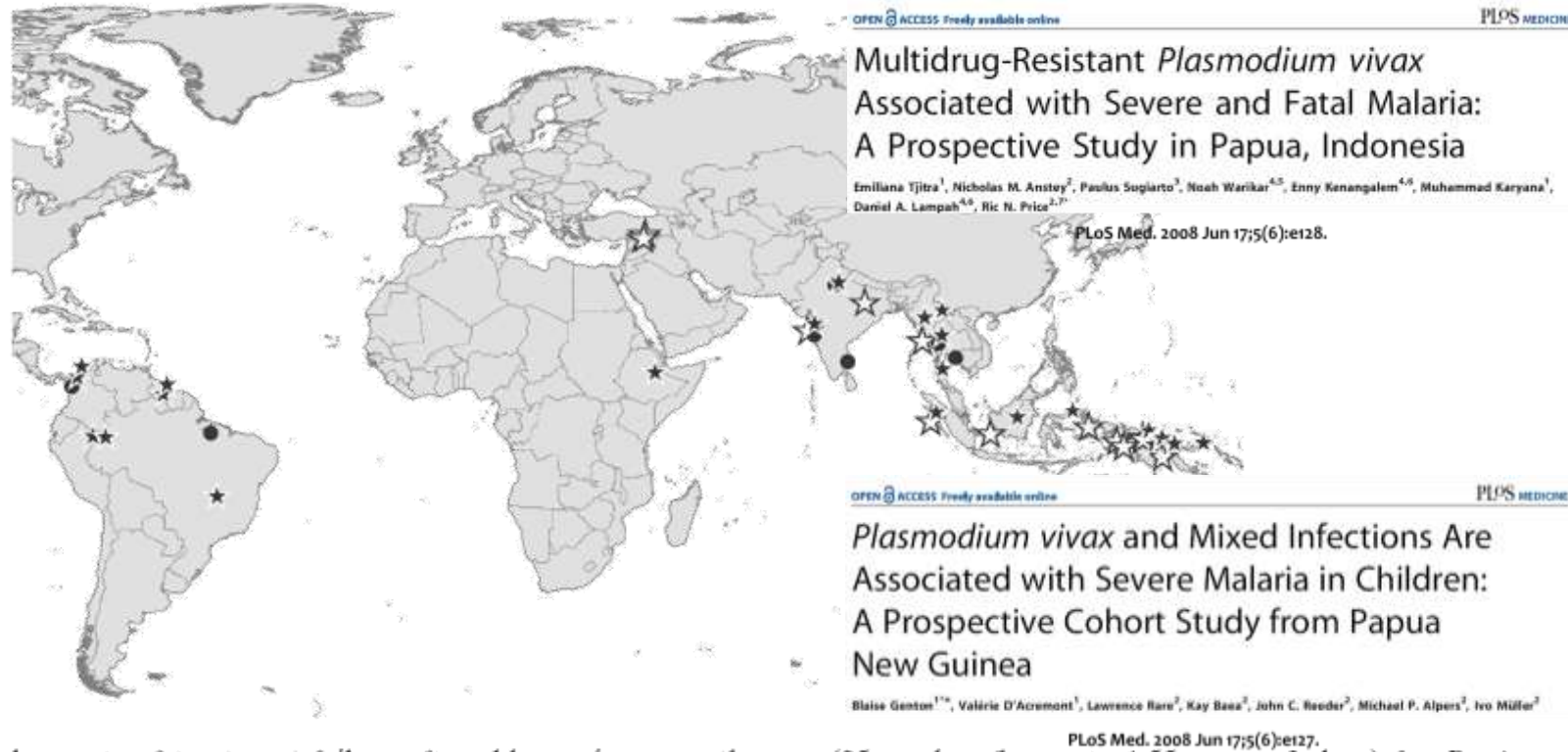


FIGURE 1. Published reports of treatment failure after chloroquine monotherapy (25 mg base/kg up to 1.55 g over 3 days) for *P. vivax* infections. Large white stars = clinical trials of chloroquine monotherapy with > 10% recurrence rate by day 28; small black stars = case series with < 5 recurrences before day 28 (with or without chloroquine plasma drug levels); black circles = clinical trials after 2000, with no recurrences by day 28.

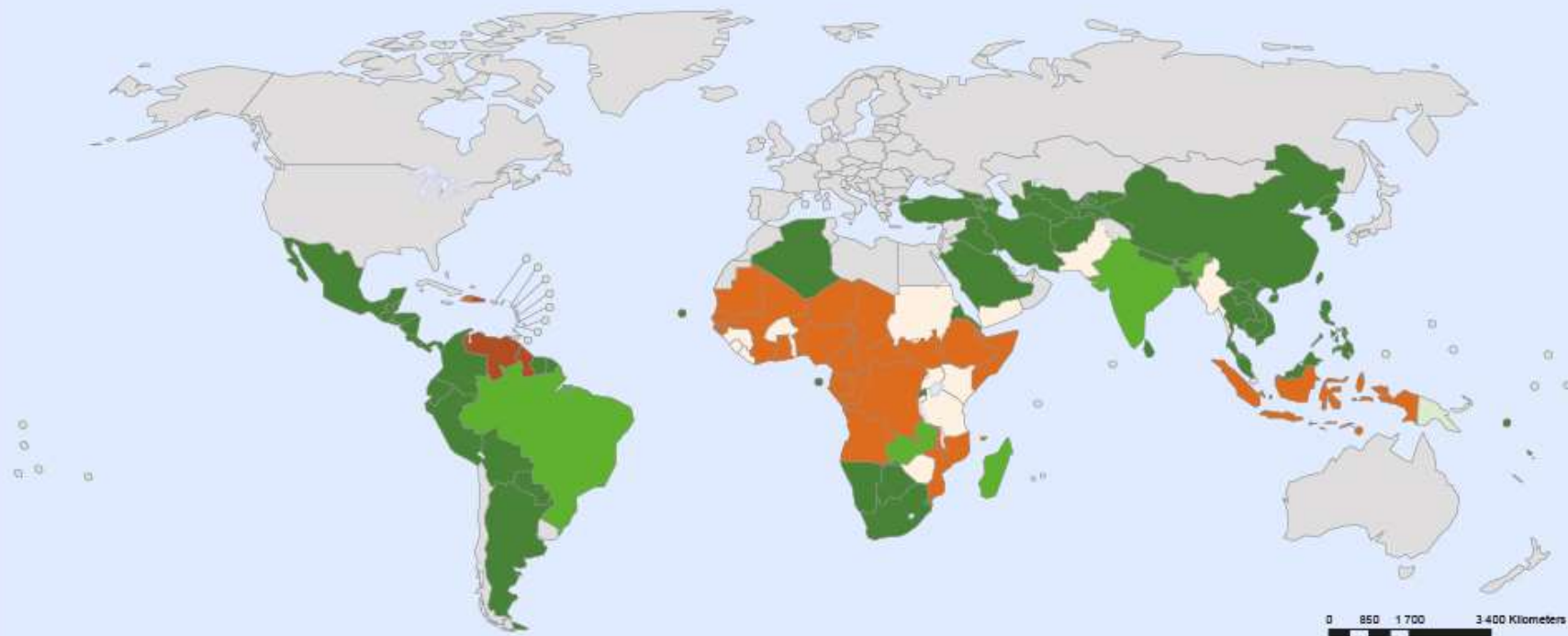
Price RN, Tjitra E, Guerra CA, Yeung S, White NJ, Anstey NM.

Vivax Malaria: Neglected and Not Benign.

Am J Trop Med Hyg 2007 Dec;77(6 Suppl):79-87.



Trends in reported malaria incidence, 2000–2012



0 850 1 700 3 400 Kilometers

Trends in malaria incidence

- Not applicable or malaria-free
- On track for $\geq 75\%$ decrease in incidence 2000–2015
- 50%–75% decrease in incidence projected 2000–2015
- <50% decrease in incidence projected 2000–2015
- Progress in reducing cases sub-nationally where interventions have been intensified OR Country has recently expanded diagnostic testing
- Insufficiently consistent data to assess trends
- Increase in incidence 2000–2012

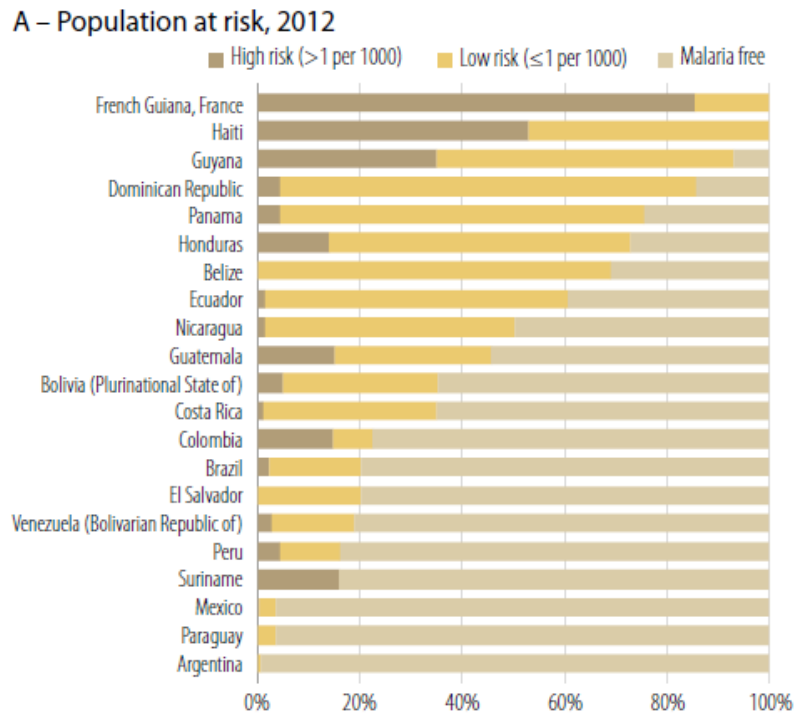
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
World Malaria Report 2013
Map Production: Global Malaria Programme
World Health Organization

 World Health Organization
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Current situation

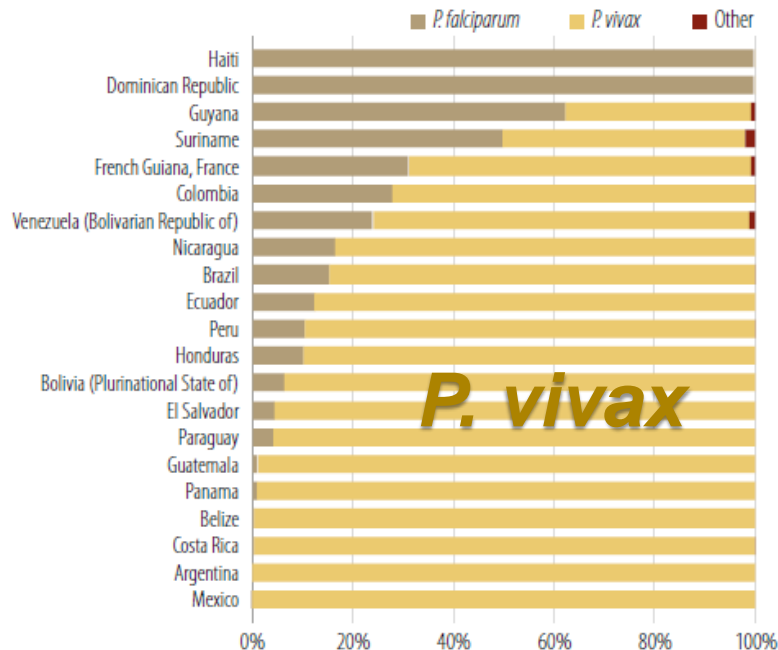
- In the WHO Region of the Americas, about 120 million people in 21 countries are estimated to be at some risk for malaria, of which 25 million people are considered at high risk



Current situation

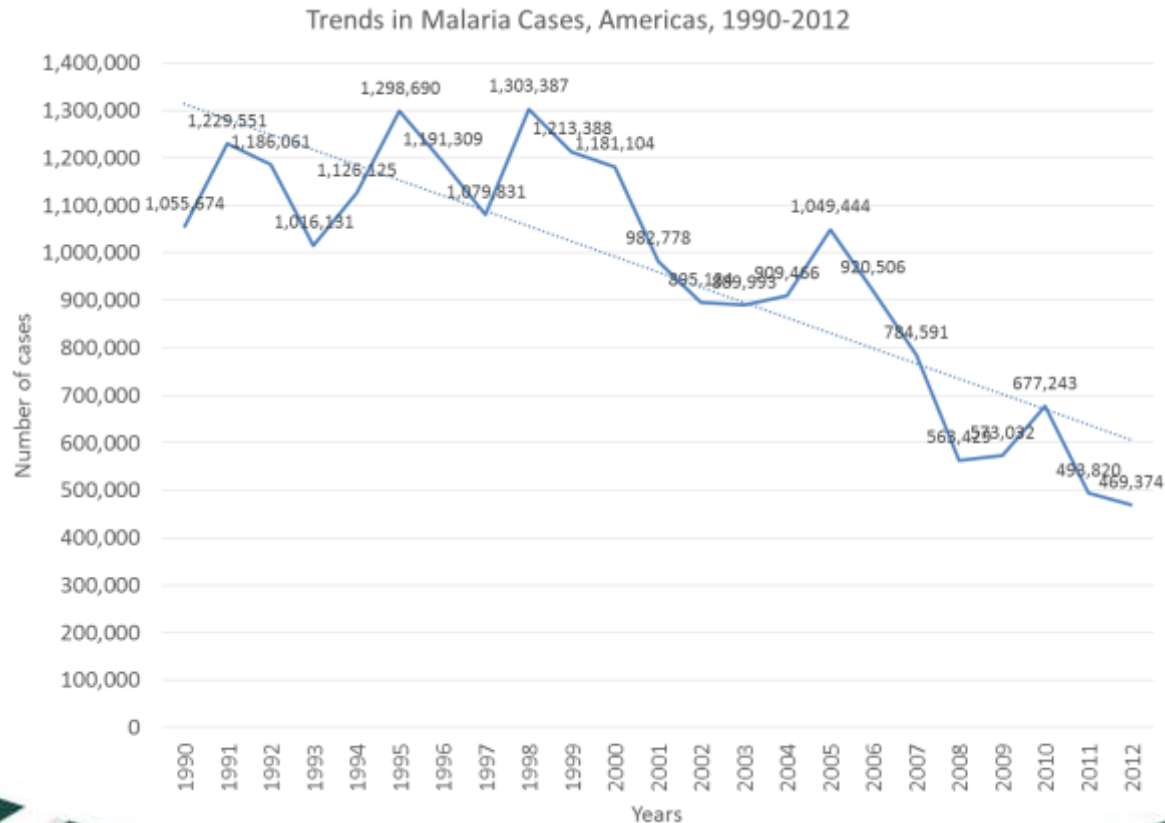
- *Plasmodium vivax* is responsible for >70% of malaria cases overall in the region, although the proportion is less than 50% in Guyana and Suriname and almost 0% in the Dominican Republic and Haiti

B – Percentage of cases due to *P. falciparum* and *P. vivax*, 2008–2012



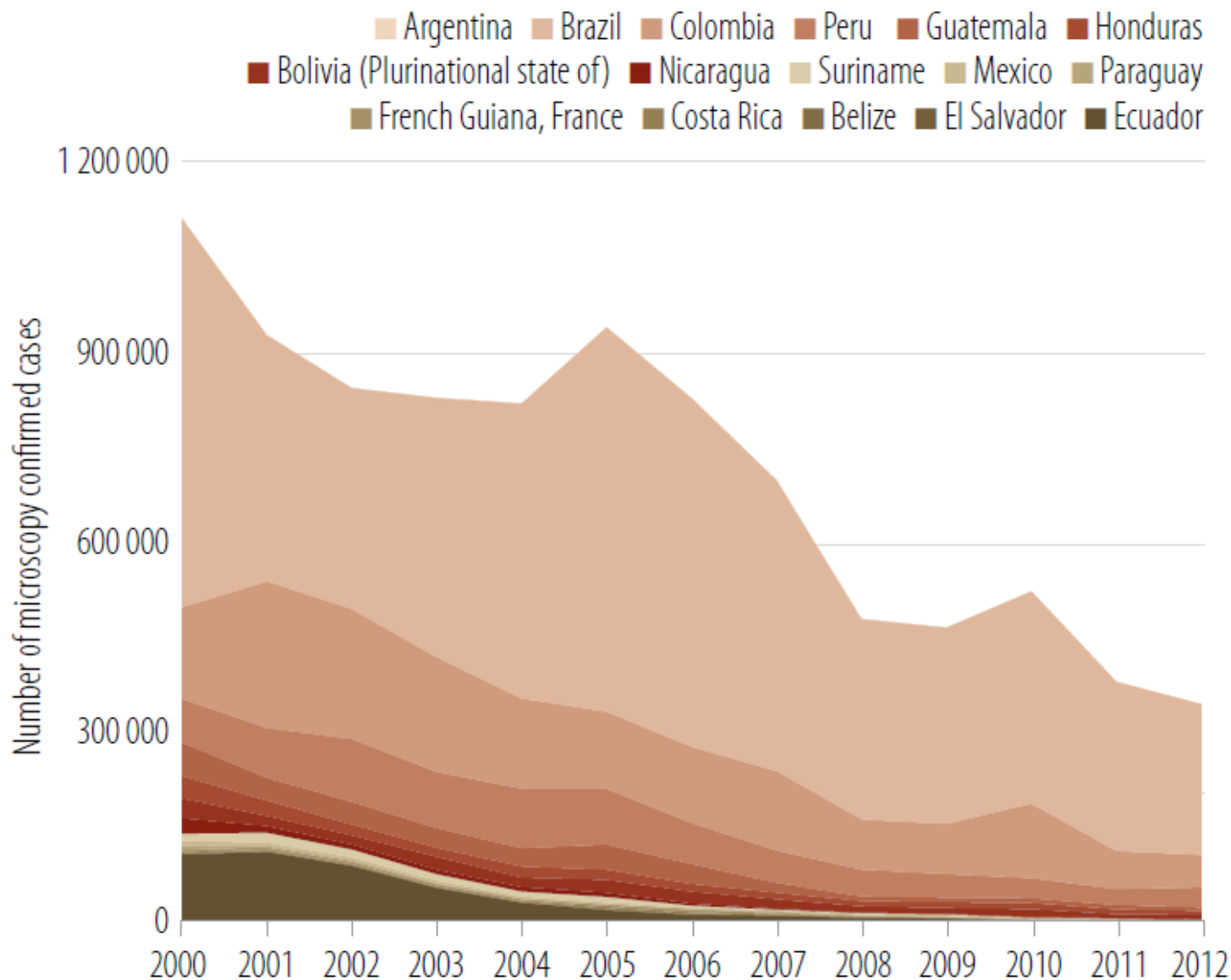
Trends 1990-2012

- The number of confirmed malaria cases reported in the region decreased by almost 58%, from 1.1 million in 2000 to 469,000 in 2012.



Modified from WHO 2014.

E – Countries projected to achieve >75% decrease in incidence of microscopically confirmed cases by 2015



Gallego V, Berberian G, Lloveras S, Verbanaz S, Chaves TSS, Orduna T, Rodriguez-Morales AJ. **The 2014 FIFA World Cup: Communicable Disease Risks and Advice for Visitors to Brazil – a review from the Latin American Society for Travel Medicine (SLAMVI).** *Travel Medicine & Infectious Disease* 2014 May-Jun; 12(3):208-218



Fig. 1. Map of Brazil, showing regions of the country, states (ST) and the host cities for the FIFA World Cup 2014 (in yellow stars), as well the areas of yellow fever, malaria and dengue transmission.

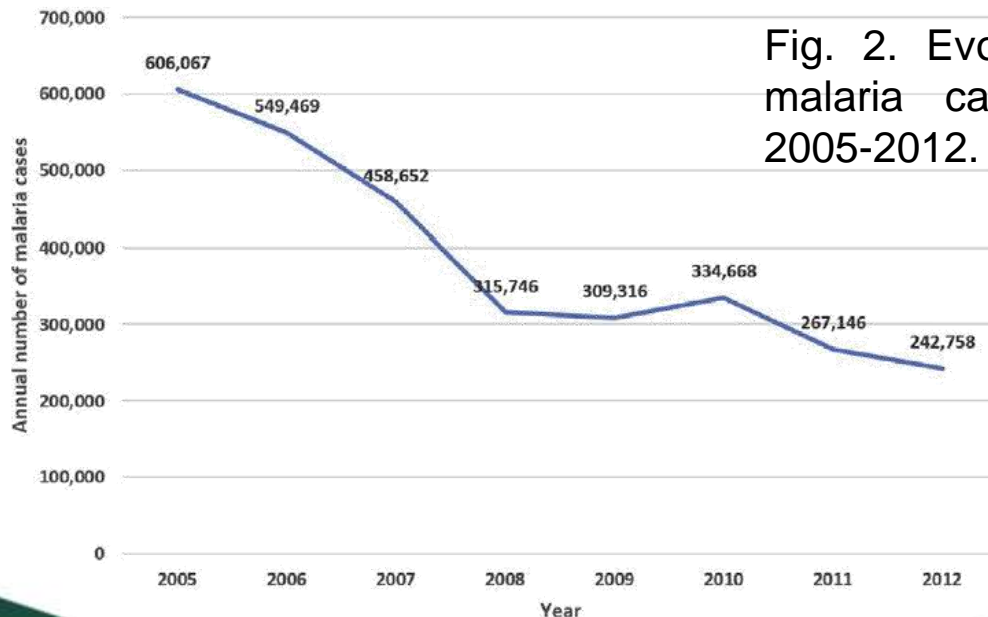


Fig. 2. Evolution of the number of malaria cases reported in Brazil, 2005-2012.



II. Intervention policies and strategies

Intervention	Policies/strategies	Yes/No	Year adopted
ITN	ITNs/LLINs distributed free of charge	Yes	2007
	ITNs/LLINs distributed to all age groups	Yes	2007
IRS	IRS is recommended	Yes	1945
	DDT is used for IRS	No	–
Larval control	Use of larval control	No	–
IPT	IPT used to prevent malaria during pregnancy	N/A	–
Diagnosis	Patients of all ages should receive diagnostic test	Yes	1972
	Malaria diagnosis is free of charge in the public sector	Yes	1972
Treatment	ACT is free for all ages in public sector	Yes	2006
	Artemisinin-based monotherapies withdrawn	Yes	2010
	Single dose of primaquine (0.25 mg base/kg) is used as gametocidal medicine for <i>P. falciparum</i>	Yes	2011
	Primaquine is used for radical treatment of <i>P. vivax</i>	Yes	1972
	G6PD test is a requirement before treatment with primaquine	No	–
	Directly observed treatment with primaquine is undertaken	No	–
	System for monitoring of adverse reaction to antimalarials exists	No	–

Intervention	Policies/strategies	Yes/No	Year adopted
Surveillance	ACD for case investigation (reactive)	Yes	–
	ACD at community level of febrile cases (pro-active)	Yes	–
	Mass screening is undertaken	Yes	–
	Uncomplicated <i>P. falciparum</i> cases routinely admitted	Yes	–
	Uncomplicated <i>P. vivax</i> cases routinely admitted	Yes	–

Antimalaria treatment policy	Medicine	Year adopted
First-line treatment of unconfirmed malaria	–	–
First-line treatment of <i>P. falciparum</i>	AL+PQ(1d); AS+MQ+PQ(1d)	2012
For treatment failure of <i>P. falciparum</i>	–	–
Treatment of severe malaria	AM+CL; AS+CL	2012
Treatment of <i>P. vivax</i>	CQ+PQ(7d); CQ+PQ(14d)	2006
Dosage of primaquine for radical treatment of <i>P. vivax</i>	0.5 mg/kg (7 days)	

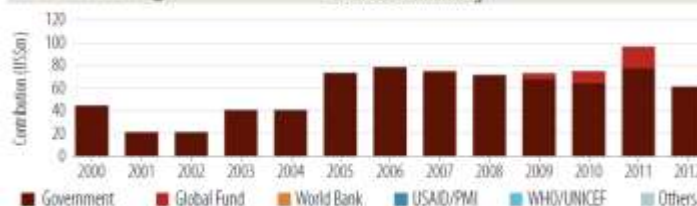
Type of RDT used

Therapeutic efficacy tests (clinical and parasitological failure, %)

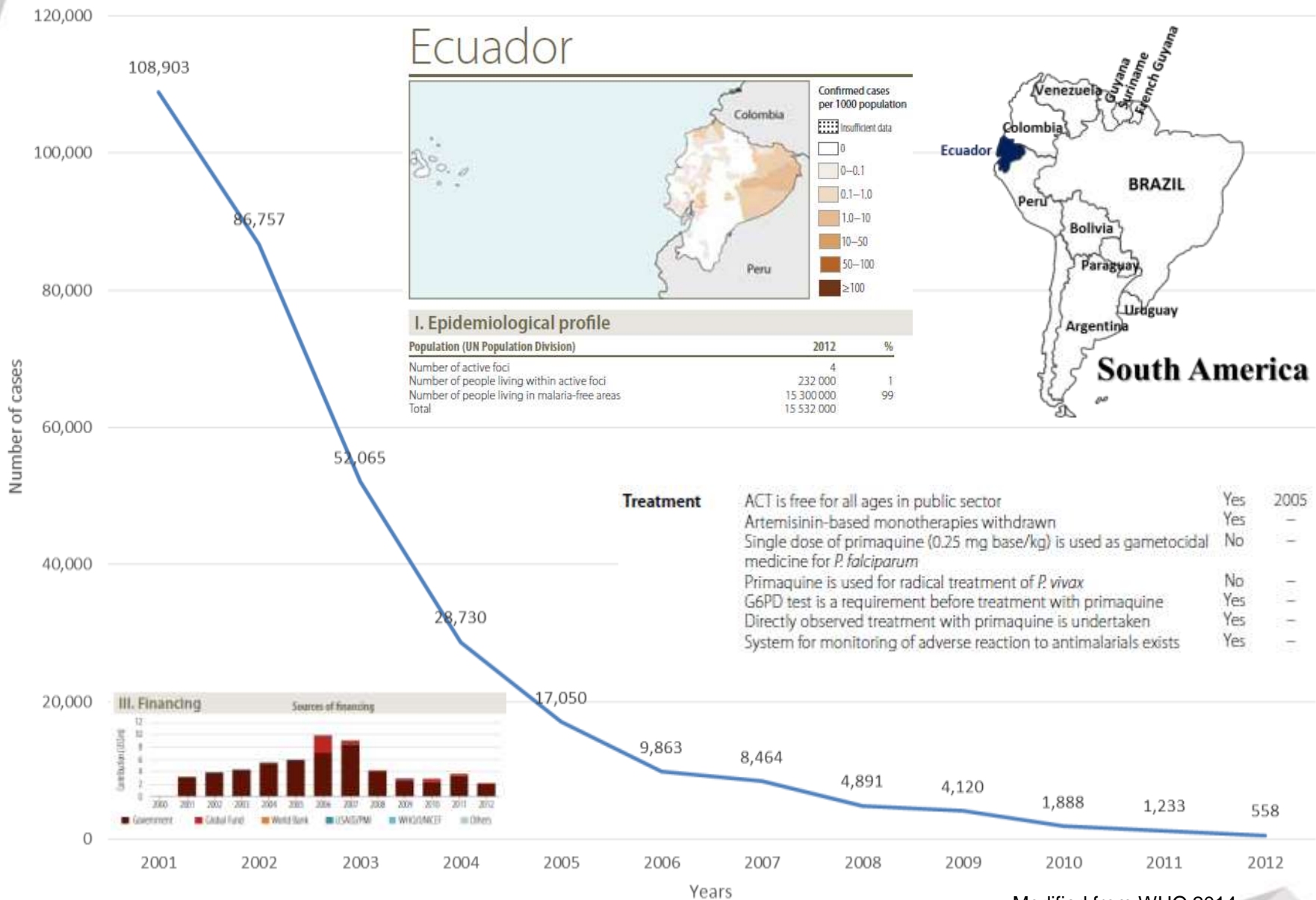
Medicine	Year	Min	Median	Max	Follow-up	No. of studies	Species
AS+MQ	2005–2007	0	0	0	42 days	3	<i>P. f.</i>
AL	2005–2007	0	0	0	28 days	2	<i>P. f.</i>

III. Financing

Sources of financing

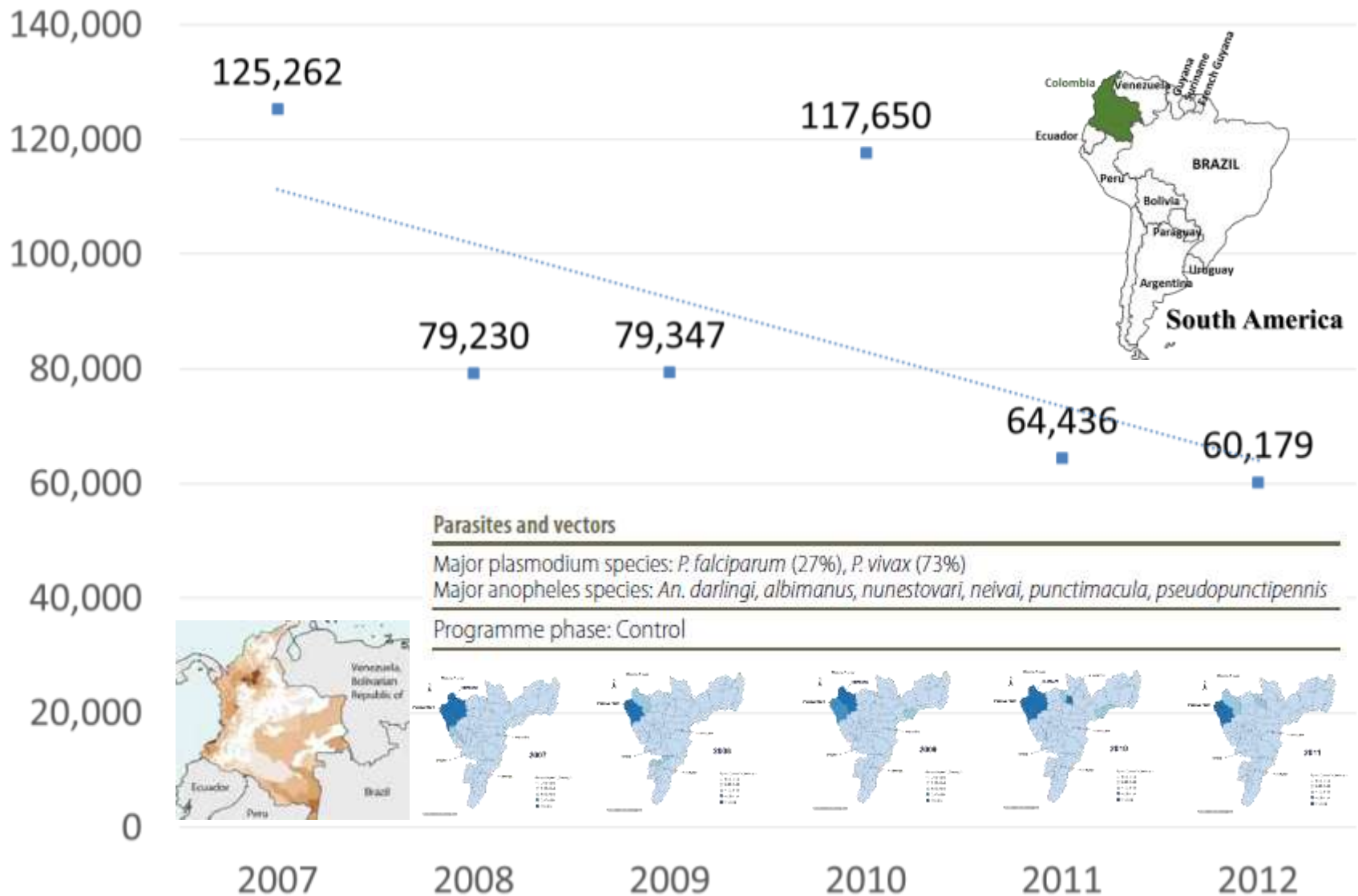


Malaria Cases, Ecuador, 2001-2012



Modified from WHO 2014.

Malaria in Colombia, 2007-2012



Parasites and vectors

Major plasmodium species: *P. falciparum* (27%), *P. vivax* (73%)

Major anopheles species: *An. darlingi*, *albimanus*, *nunezovari*, *neivai*, *punctimacula*, *pseudopunctipennis*

Programme phase: Control



Modified from WHO 2014.

RESEARCH

Open Access

Characterization of a malaria outbreak in Colombia in 2010

Pablo Chaparro^{1,2*}, Julio Padilla³, Andrés F Vallejo^{4,5} and Sócrates Herrera^{4,5}

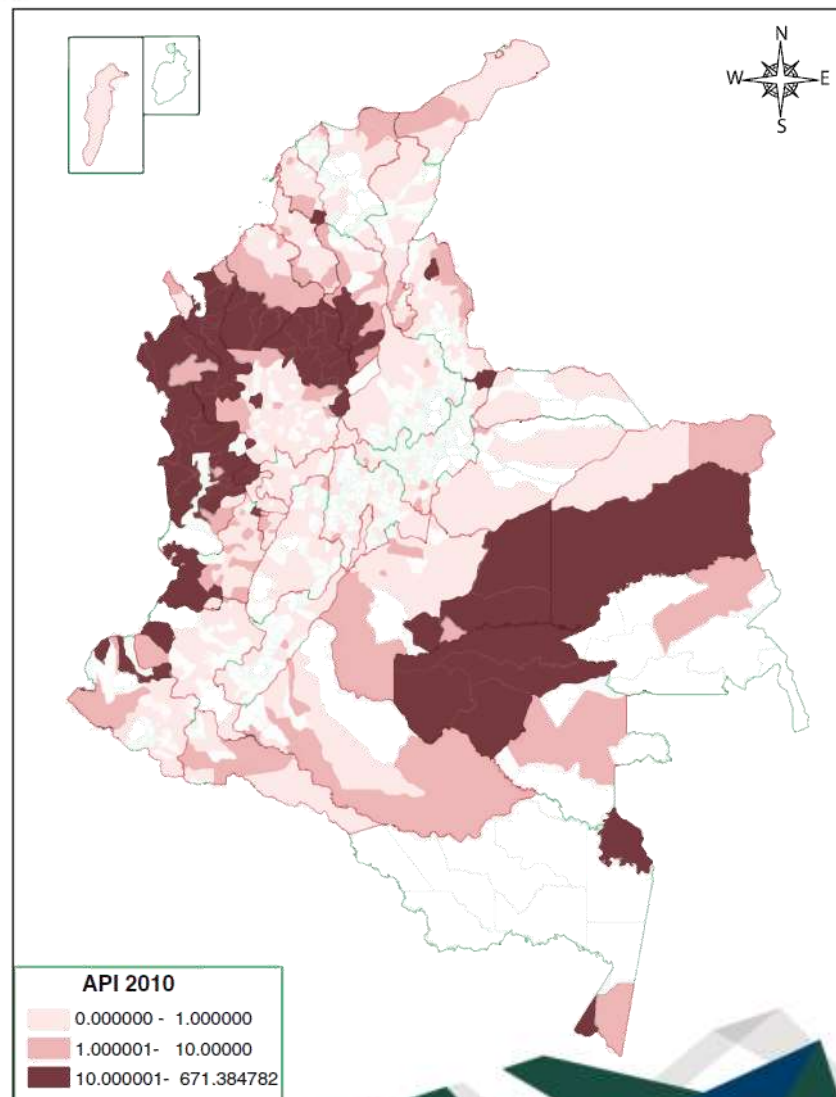
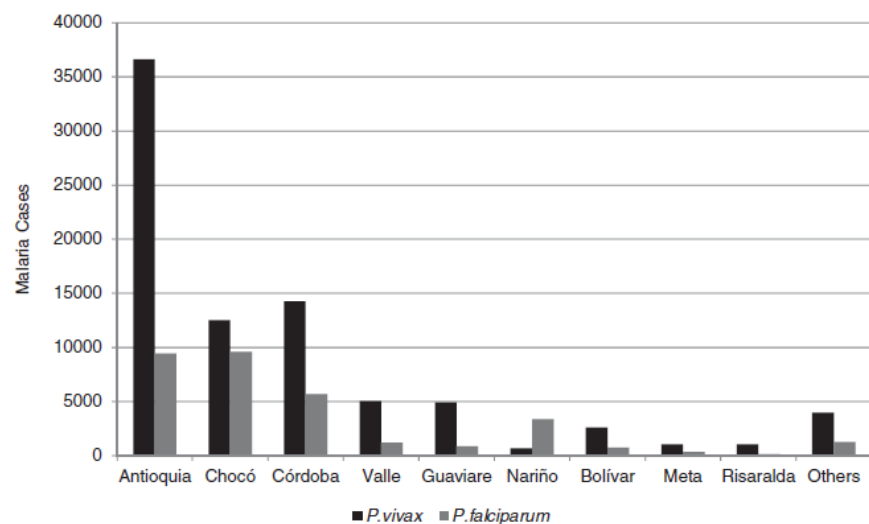


Figure 3 Distribution of malaria by department, Colombia, 2010.

III. Financing

Sources of financing

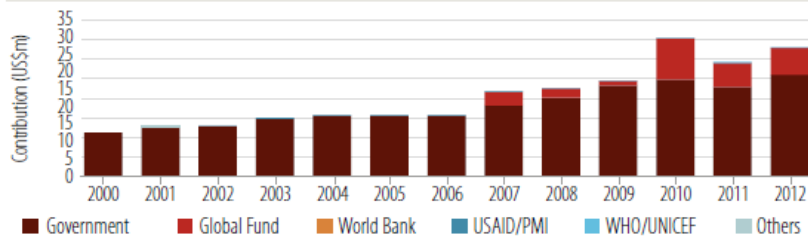


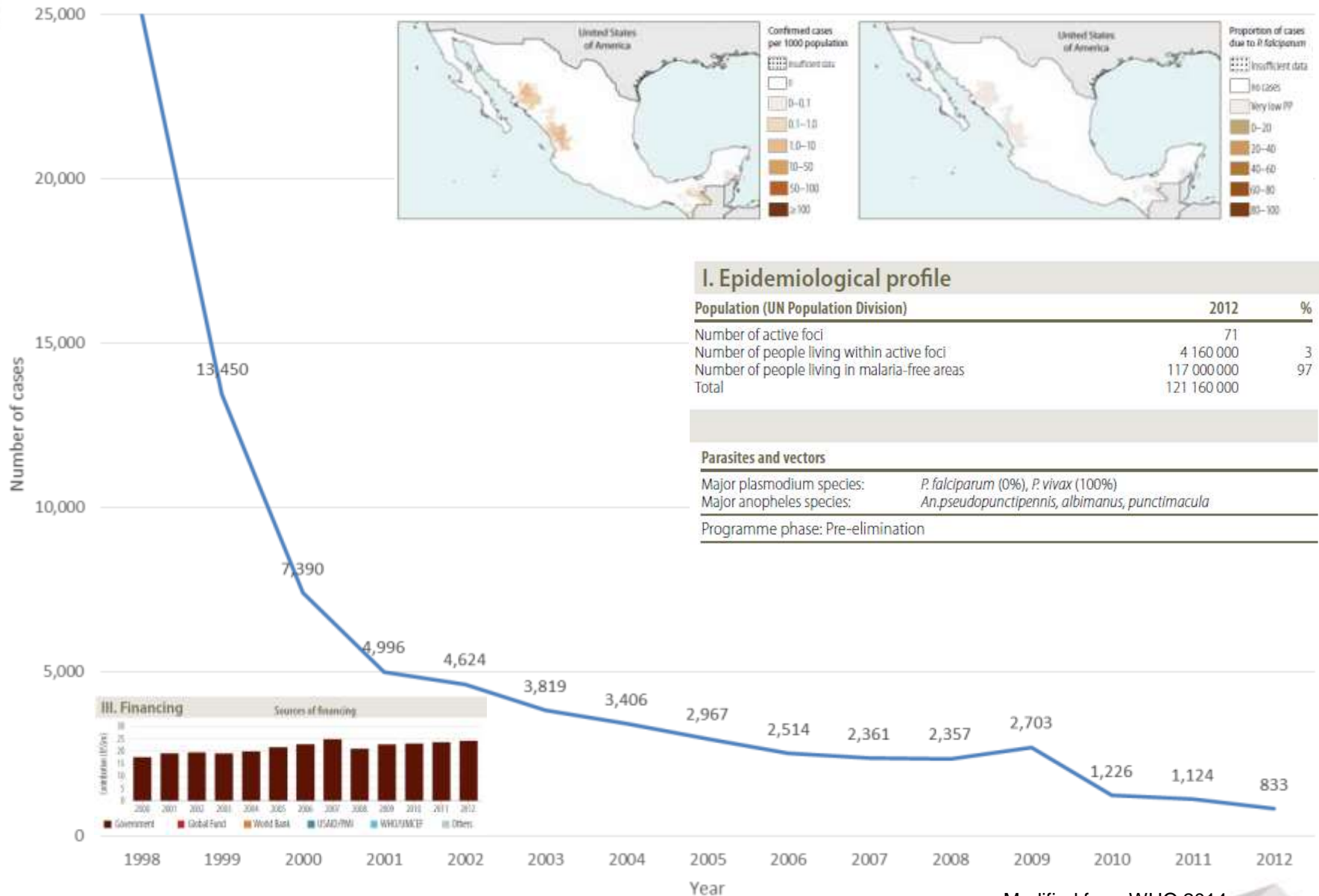
Figure 2 Annual parasite index by territorial entity.

Table 2 Distribution of malaria cases by parasite species and department (=state)

Territorial entity	2009				2009				Rate of change
	<i>P. vivax</i>		<i>P. falciparum</i>		<i>P. vivax</i>		<i>P. falciparum</i>		
	n	%	n	%	n	%	n	%	
Antioquia	26.341	33,42	6.059	7,69	36.620	31,27	9.463	8,08	29,7
Córdoba	10.248	13	3.008	3,82	14.281	12,19	5.696	4,86	33,6
Chocó	5.180	6,57	2.931	3,72	12.543	10,71	9.608	8,2	63,4
Guaviare	1.065	4,3	1.184	1,5	4.940	4,22	877	0,75	21,4
Nariño	3.388	1,35	4.505	5,72	693	0,59	3.381	2,89	-36,7
Valle del Cauca	991	1,26	913	1,16	5.061	4,32	1.213	1,04	69,7
Meta	1.427	1,81	265	0,34	1.069	0,91	372	0,32	-17,4
Cauca	149	0,19	1.730	2,19	151	0,13	708	0,6	-118,7
Amazonas	1.729	2,19	82	0,1	747	0,64	33	0,03	-132,2
Vichada	1.226	1,56	246	0,31	535	0,46	269	0,23	-83,1
Risaralda	1.010	1,28	29	0,04	1.053	0,9	139	0,12	12,8
Bolívar	849	1,08	65	0,08	2,6	2,22	755	0,64	-20,6
La Guajira	955	1,21	24	0,03	315	0,27	42	0,04	-174,2
Putumayo	721	0,91	6	0,01	236	0,2	11	0,01	-194,3
Norte Santander	237	0,3	1	0	346	0,3	2	0	31,6
Caquetá	169	0,21	44	0,06	220	0,19	33	0,03	15,8
Sucre	182	0,23	27	0,03	177	0,15	23	0,02	-4,5
Vaupés	100	0,13	24	0,03	205	0,18	4	0	40,7
Caldas	26	0,03	28	0,04	201	0,17	21	0,02	75,7
Magdalena	104	0,13	61	0,08	35	0,03	7	0,01	-292,9
Guainía	105	0,13	14	0,02	72	0,06	4	0	-56,6
Quindío	76	0,1	11	0,01	83	0,07	22	0,02	17,1
Boyacá	62	0,08	4	0,01	118	0,1	5	0	46,3
Outside	102	0,13	7	0,01	55	0,05	10	0,01	-67,7
Cundinamarca	40	0,05	4	0,01	97	0,08	8	0,01	58,1
Tolima	55	0,07	9	0,01	67	0,06	11	0,01	17,9
Santander	53	0,07	16	0,02	61	0,05	8	0,01	0,0
Without information	42	0,05	16	0,02	50	0,04	13	0,01	7,9
Cesar	24	0,03	3	0	65	0,06	2	0	59,7
Casanare	33	0,04	10	0,01	36	0,03	7	0,01	0,0
Huila	22	0,03	4	0,01	22	0,02	3	0	-4,0
Arauca	30	0,04	3	0	13	0,01	0	0	-153,8
Atlántico	23	0,03	6	0,01	10	0,01	1	0	-163,6
Santa Marta		0		0	38	0,03	2	0	100,0
Cartagena		0		0	16	0,01	12	0,01	100,0
Bogotá	16	0,02		0	5	0	5	0	-60,0
Barranquilla		0		0	15	0,01	4	0	100,0
San Andrés		0	1	0	5	0	3	0	87,5
Total	56.780	72,04	21.340	21,340	82.856	70,75	32.777	27,99	

>50%

Malaria Cases, Mexico, 1998-2012



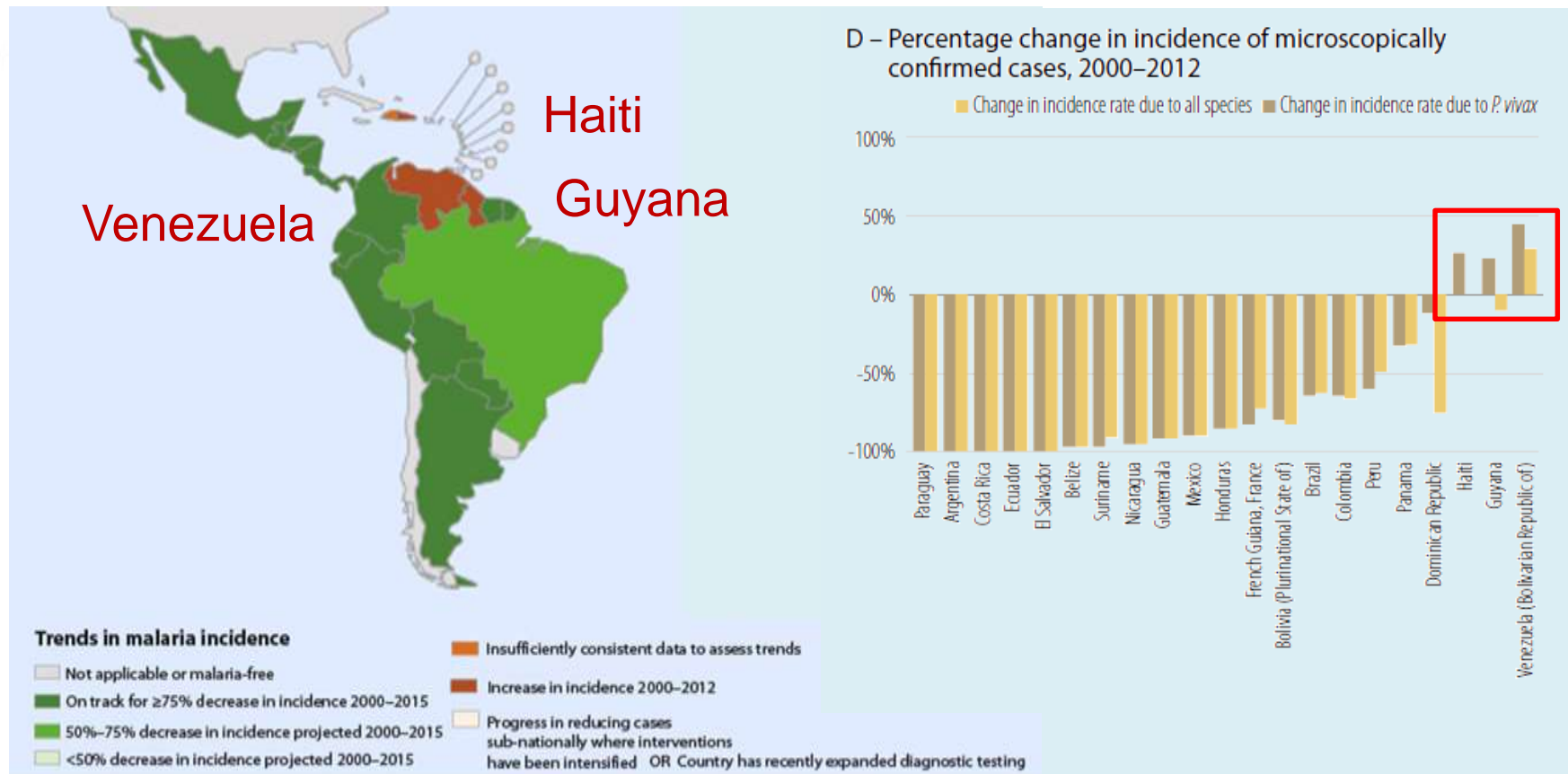
I. Epidemiological profile

Population (UN Population Division)	2012	%
Number of active foci	71	
Number of people living within active foci	4 160 000	3
Number of people living in malaria-free areas	117 000 000	97
Total	121 160 000	

Parasites and vectors

Major plasmodium species: *P. falciparum* (0%), *P. vivax* (100%)
 Major anopheles species: *An. pseudopunctipennis*, *albimanus*, *punctimacula*
 Programme phase: Pre-elimination

Modified from WHO 2014.



In Venezuela—a country with a Human Development Index (HDI) of 0.748 [#71, 2012] and Gross national income [GNI] per capita of US\$11,475), malaria incidence increased between 2000-12.

A similar increased in incidence was seen in Guyana and Haiti, but both of these countries have a much lower HDI than Venezuela [0.636, ranked 118 and 0.456, ranked 161, for 2012, respectively; GNI per capita of US\$3,387 and US\$1,070, respectively], and a devastating earthquake hit Haiti during that period.

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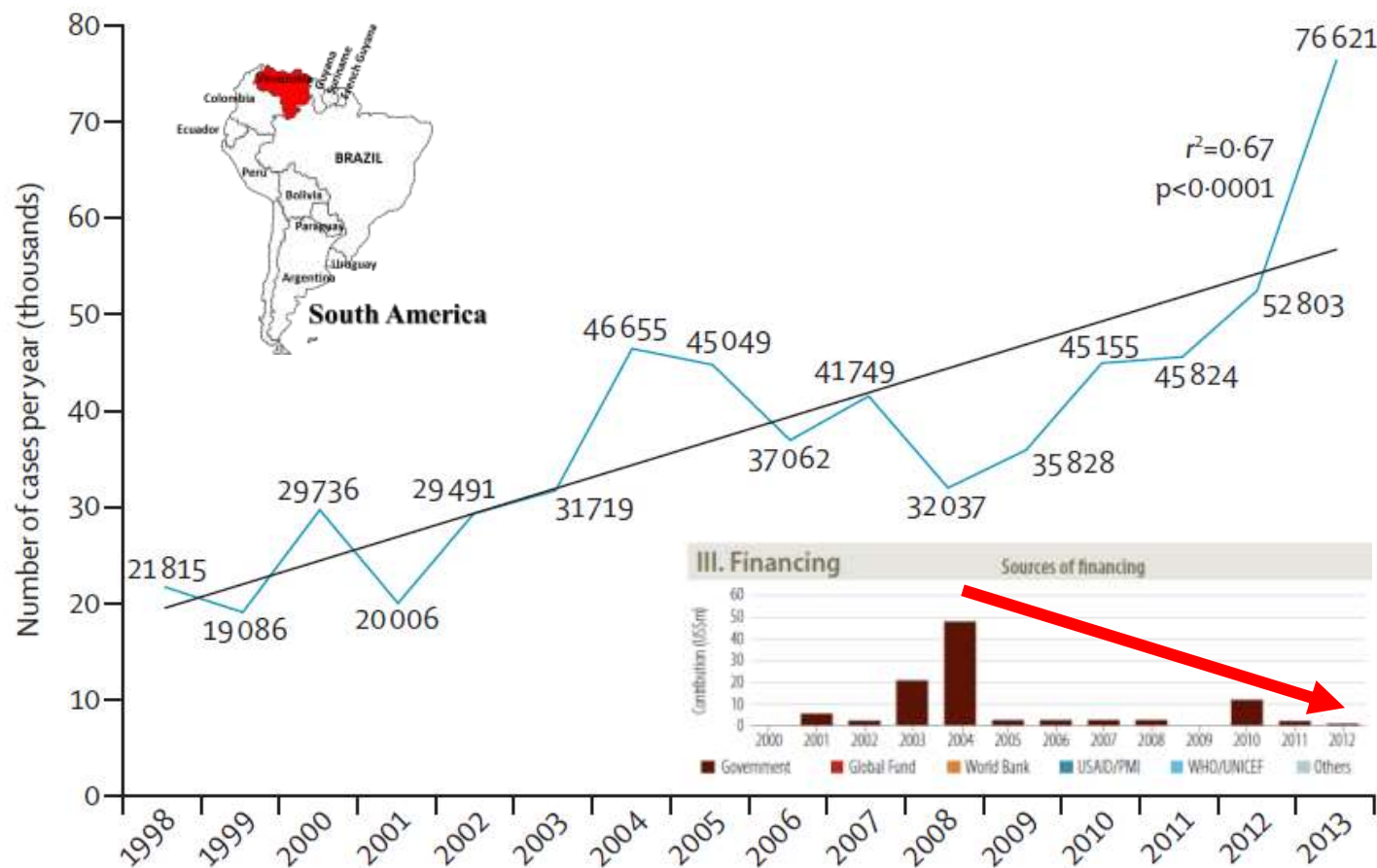


Figure: Malaria in Venezuela, 1998–2013

Rodríguez-Morales AJ, Paniz-Mondolfi AE. **Venezuela’s failure in malaria control.** *The Lancet* 2014; 384(9944):663-4.

ORDINARY MEETING

of the Society held at

Manson House, 26, Portland Place, London, W.1,

on

Thursday, 21st July, 1949, at 7.30 p.m.

THE PRESIDENT,

Professor H. E. SHORTT, C.I.E., M.D., D.Sc., D.T.M. & H., Col. I.M.S. (ret.)
in the Chair.

PAPER

THE NATION-WIDE CAMPAIGN AGAINST MALARIA IN VENEZUELA

BY

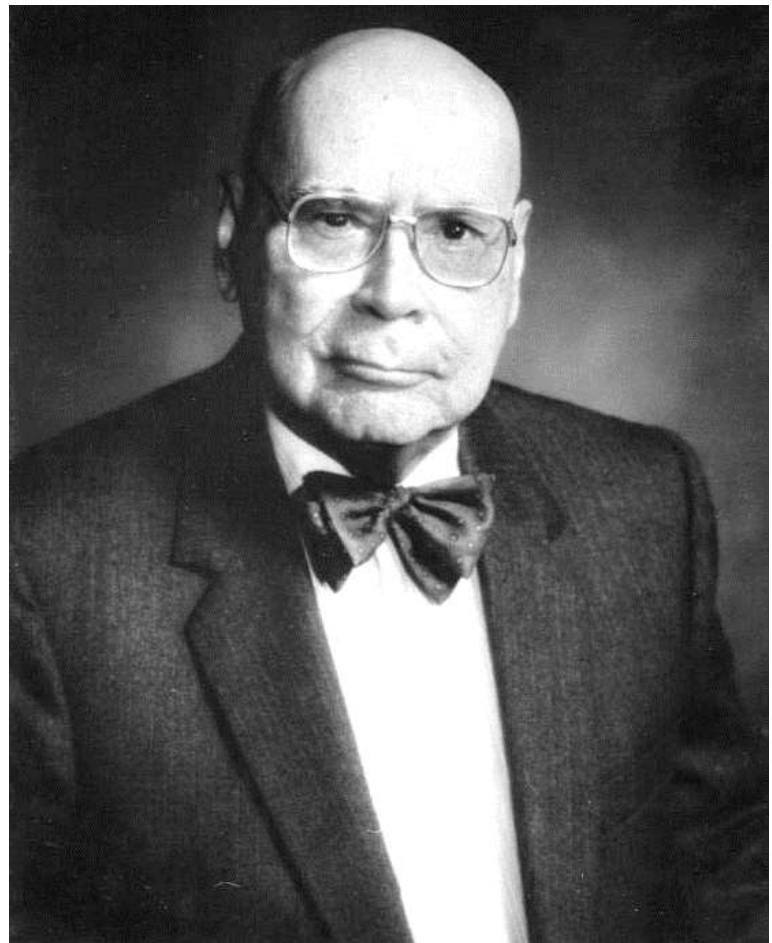
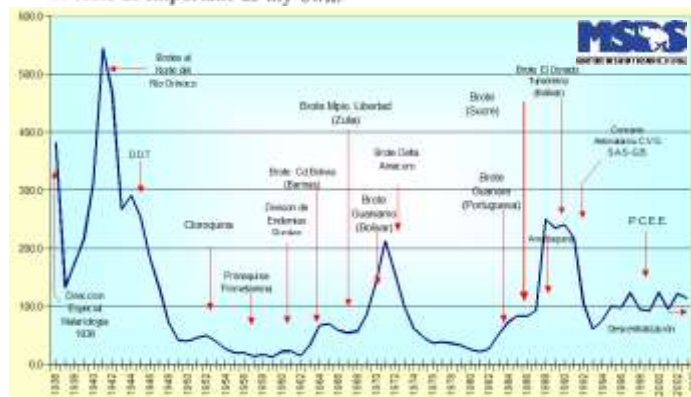
ARNOLDO GABALDON, PH.B., M.D., S.C.D.,
*División de Malariología Dirección de Salubridad Pública Ministerio de Sanidad y
Asistencia Social Maracay, Aragua, Venezuela.*

PART I

INTRODUCTION.
VECTORS.
DISTRIBUTION.

"CONDITION" OF MALARIA.
TREND LINE.
MALARIA PERIODICITIES.

This is the story of an effort against malaria carried out in Venezuela, where it was the most important disease which handicapped the social and economic life of the country. I had the opportunity of directing these anti-malaria activities from their establishment in 1936, and it is a great honour to be able to present an account of their development here tonight. This action against malaria has not been by any means the result of my work alone, but the joint enterprise of a group of men who have devoted their entire time to this work for the last 13 years. Their contribution to this campaign has been at least as important as my own.



Achievements

- The region has made substantial progress in reducing malaria case incidence in the past decade.
- Reductions in incidence of >75% in confirmed malaria cases were reported in 13 countries between 2000 and 2012, and a further 3 countries are projected to achieve reductions of >75% by 2015 (16 in total).
- Seven countries are now classified as being in the pre-elimination phase:



Countries in the pre-elimination phase

Argentina (0 foci)

Belize

Costa Rica (1 foci)

Ecuador (4 foci)

El Salvador (10 foci)

Mexico (71 foci)

Paraguay (15 foci)



Research in Translation

Severe Vivax Malaria: Newly Recognised or Rediscovered?

Stephen J. Rogerson*, Richard Carter

PLoS Med. 2008 Jun 17;5(6):e136.

Box 1. Crucial Tools for *P. vivax* Control

- **Effective first-line treatment.** Artemisinin-based combination therapies are generally effective, but longer-acting combinations may additionally prevent early relapses.
- **Highly sensitive rapid diagnostic tests.** Present tests are inadequately sensitive at low parasitaemia, which is common in *P. vivax*.
- **Preventive therapy.** The role of intermittent preventive treatment in pregnancy or childhood against vivax is unknown. Small studies suggest that insecticide-treated bed nets decrease disease.
- **Safe drugs for elimination of liver stages.** G6PD deficiency, selected for by malaria, can result in fatal haemolysis from current agents.
- **Vaccination.** New vaccines are entering human trials. If efficacious, their deployment will require major planning efforts.

Five Key Papers in the Field

Grimberg et al., 2007 [19]

The investigators show that antibodies directed against "region two" of PvDBP inhibit merozoite invasion, suggesting that vaccines targeted towards this region could reduce blood stage infection.

Barcus et al., 2007 [7]

Along with the two new papers in this issue of *PLoS Medicine* [1,2], Barcus and colleagues' study contributes to our understanding of the importance of *P. vivax* as a cause of severe clinical disease.

Walzer et al., 1974 (Am J Trop Med Hyg)

Two fatal cases of *P. vivax*

- 1) A Vietnam veteran with *P. vivax* infection who died with a ruptured spleen; and
- 2) A man with a previous splenectomy who died of a severe *P. vivax* infection acquired through blood transfusion.

Panichakul et al., 2007 [21]

This paper represents a significant advance in the difficult process of developing robust in vitro culture systems for *P. vivax*.

Ratcliff et al., 2007 [5]

Both treatments cured falciparum and vivax malaria with high efficacy, but dihydroartemisinin-piperaquine was much better than artemether-lumefantrine at preventing re-infections with *P. falciparum* and relapses of *P. vivax* during a six-week follow-up.

Singh et al., 2006 [18]

This paper shows how the Duffy binding protein interacts with its ligand, which is also relevant to understanding structure and interactions of other important adhesive proteins of malaria parasites.

CFR of Malaria, Venezuela, 1995-2004

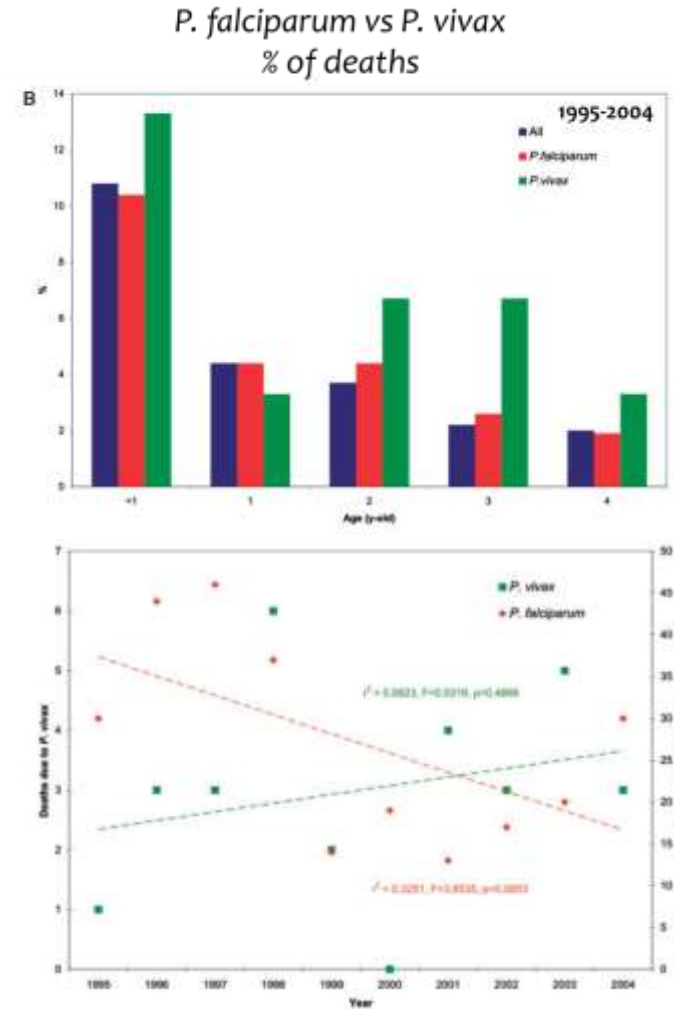
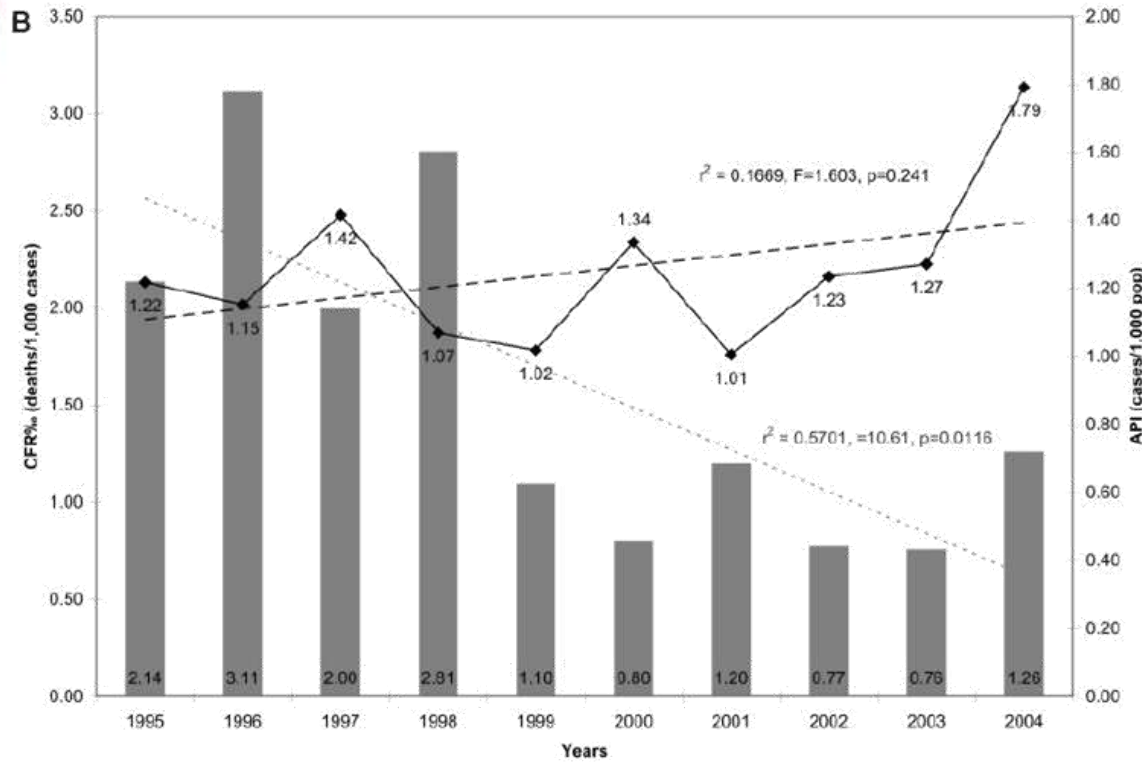


FIG. 2. Malaria mortality trend in Venezuela, 1995–2004. (A) Number of deaths due to malaria and mortality rates; (B) CFR in malaria (%) and API trends.

Epidemiology of Severe *P. vivax* malaria

Hematological

Tan, Lancet Infect Dis 2008; 8: 449–54

	Year	Country of disease origin	Cases	Clinical features	Comments
Blood					
Mohapatra et al ³⁰	2002	India	8	Severe anaemia*	Study of 110 cases of <i>P vivax</i> malaria
Rodriguez-Morales et al ³²	2006	Venezuela	8	Severe anaemia*	Study of 78 children admitted to hospital with <i>P vivax</i> malaria
Makkar et al ³²	2002	India	1	Severe thrombocytopenia†	Adult case
Kakar et al ³³	1999	India	1	Severe thrombocytopenia†	Case of 43-year-old woman
Aggarwal et al ³⁴	2005	India	1	Severe thrombocytopenia†	Case of 7-year-old boy
Aouba et al ³⁵	2000	Costa Rica	1	Haemophagocytic syndrome	Case of 41-year-old woman
Park et al ³⁶	2003	South Korea	1	Haemophagocytic syndrome	Case of 23-year-old man

Anemia and Thrombocytopenia in Children with *Plasmodium vivax* Malaria

by Alfonso J. Rodriguez-Morales,^{1,2} Elia Sánchez,³ Miguel Vargas,⁴ Carmelina Piccolo,⁵ Rosa Colina,⁵ and Melissa Arria⁶
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J Trop Pediatr. 2006 Feb;52(1):49-51.

Is Anemia in Plasmodium vivax Malaria More Frequent and Severe than in Plasmodium falciparum?

The American Journal of Medicine (2006) 119, e9-e10

White Blood Cell Counts in *Plasmodium vivax* Malaria

Alfonso J. Rodriguez-Morales,¹ Elia Sánchez,² Melissa Arria,³ Miguel Vargas,² Carmelina Piccolo,³ Rosa Colina,² and Carlos Franco-Paredes^{4,5}

The Journal of Infectious Diseases 2005;192:1675–6

Occurrence of Thrombocytopenia in *Plasmodium vivax* Malaria

Clinical Infectious Diseases 2005; 41:130–1

REVIEW

Open Access

Understanding the clinical spectrum of complicated *Plasmodium vivax* malaria: a systematic review on the contributions of the Brazilian literature

Marcus VG Lacerda^{1,2,3*}, Maria PG Mourão^{1,2,3}, Márcia AA Alexandre^{1,2,3}, André M Siqueira^{1,2}, Belisa ML Magalhães^{1,2}, Flor E Martinez-Espinosa^{1,2,4}, Franklin S Santana Filho^{1,2}, Patrícia Brasil⁵, Ana MRS Ventura⁶, Mauro S Tada⁷, Vanja SCD Couto⁸, Antônio R Silva⁹, Rita SU Silva¹⁰ and Maria GC Alecrim^{1,2,3}

“A key description of anaemia in vivax malaria children in Latin America was published in Venezuela in 2006 [98].”

98. Rodriguez-Morales AJ, Sanchez E, Vargas M, Piccolo C, Colina R, Arria M: Anemia and thrombocytopenia in children with *Plasmodium vivax* malaria. *J Trop Pediatr* 2006, **52**:49-51.

Pulmonary

	Year	Country of disease origin	Cases reported	Details	Outcome
Carlini et al ⁸	1999	Colombia	1	Hypotension, 5% parasitaemia, 10 days mechanical ventilation	Survived
Curlin et al ⁹	1999	North India	1	1% parasitaemia	Survived
Curlin et al ⁹	1999	Honduras	1	0.8% parasitaemia, 5 days mechanical ventilation	Survived
Habib and Singh ¹⁰	2004	Indonesia	1	1.2% parasitaemia, diuretics, and 20% albumin	Survived
Islam and Qamruddin ¹¹	1995	Pakistan	1	Cerebral malaria, disseminated intravascular coagulation, and ARDS	Survived
Lawn et al ¹²	2003	French Guiana	1	Hypotension, <1% parasitaemia, mechanical ventilation for 3 days, haemoglobinuria	Survived
Lomar et al ¹³	2005	Brazil	1	Hypotension, ARDS, mechanical ventilation 9 days, vasopressors	Survived
Munteis et al ¹⁴	1997	Pakistan	1	Oxygen therapy	Survived
Pukrittayakamee et al ¹⁵	1998	Thailand	1	Oxygen therapy and diuretics, helminth co-infection	Survived
Saleri et al ¹⁶	2006	Venezuela	1	Non-invasive positive pressure ventilation	Survived
Tanios et al ¹⁷	2001	Papua New Guinea	1	0.5% parasitaemia, ARDS, mechanical ventilation for 9 days	Survived
Torres et al ¹⁸	1997	Venezuela	1	2.8% parasitaemia, ALI, oxygen therapy, and diuretics	Survived
Kumar et al ¹⁹	2007	Pakistan	1	Intensive care unit admission, haemofiltration, and inotropic support	Survived
Price et al ²⁰	2007	India	1	Non-invasive continuous positive pressure ventilation	Survived
Kotwal et al ²¹	2005	Afghanistan	1	Case series of 38 US Army Rangers, ARDS in one case, high frequency mechanical ventilation, bilateral tube thoracostomies	Survived
Kochar et al ²²	2005	India	4	Case series of 11 severe cases of <i>P vivax</i> malaria. Four cases complicated by ARDS	2 patients died, 2 survived
Maguire et al ²³	2007	Afghanistan	1	Parasitaemia 0.1%, mechanical ventilation 21 days (including high frequency oscillatory ventilation and prone positioning), spontaneous splenic rupture	Survived
Agarwal et al ²⁴	2007	India	1	Bi-level non-invasive positive pressure ventilation	Survived

Epidemiology of Severe *P. vivax* malaria

Renal

Year Country of disease origin Cases Clinical features Comments **Tan, Lancet Infect Dis 2008; 8: 449–54**

Kidney

Prakash et al ⁴²	2003	India	13	Acute renal failure	Study of 93 cases of acute renal failure associated with malaria; six further cases had mixed <i>P vivax</i> and <i>P falciparum</i> infection
Mehta et al ⁴³	2001	India	3	Acute renal failure	Study of 402 cases of malaria, of which 24 developed acute renal failure; five further cases had mixed <i>P vivax</i> and <i>P falciparum</i> infection
Naqvi et al ⁴⁴	2003	Pakistan	3	Acute renal failure	Study of 124 cases of acute renal failure associated with malaria

Atypical *Plasmodium vivax* Malaria in a Traveler: Bilateral Hydronephrosis, Severe Thrombocytopenia, and Hypotension

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Journal of Travel Medicine, Volume 15, Issue 2, 2008, 119–121

Vivax malaria No more benign ?



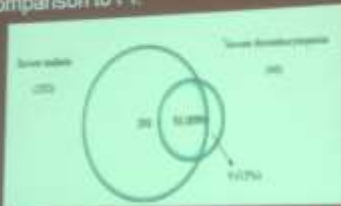
Dr. D.K. Kochar

Chief Research Co-ordinator &
Sr. Consultant, Dept. Of Medicine
Kothari Medical & Research Institute, Bikaner

Former Professor & Head,
Department of Medicine, S.P. Medical College, Bikaner

Thrombocytopenia in childhood malaria with special reference to *P. vivax* mono-infection: A study from Bikaner (Northwestern India)
Tamsar GS, Khatri PG, Kochhar DK et al, Platelets 2011; 1 - 6

- Study related to prognostic value of thrombocytopenia – 676 patients
- Association of thrombocytopenia was statistically significant with Pv malaria versus Pf malaria ($p < 0.0001$) or mixed infection ($p < 0.032$).
- The risk of severe thrombocytopenia ($< 20,000$) was more in Pv mono-infection in comparison to Pf.



- There was significant association between severe thrombocytopenia and other manifestations of severe malaria ($p < 0.014$)
- We advocate inclusion of severe thrombocytopenia ($< 20,000$) as criteria of severe malaria of WHO



SHORT REPORT: PREGNANCY OUTCOMES ASSOCIATED WITH *PLASMODIUM VIVAX* MALARIA IN NORTHEASTERN VENEZUELA
ALFONSO I RODRIGUEZ MORALES, ELIA SANCHEZ, MIGUEL VARGAS, CARMELINA PICCOLO, ROSA COLINA, MELISSA ARRA, and CARLOS FRANCO PAREDES*

- This Venezuelan study on pregnant women infected with *P. vivax* reported significant degree of severe anemia and thrombocytopenia along with miscarriage and preterm delivery.

Table 1. Clinical characteristics of severe vivax malaria patients

Patient No.	Age (y)/sex	Clinical presentation*	Parasitemia (density) (<i>P. vivax</i> /mm ³)	Diagnostic tests for malaria			
				PBF	RMDT OptiMAL test†	PCR	
1	30, F	ARDS	6,000	+	Positive	+	
2	17, M	Renal failure, bleeding diathesis	20,000	+	Positive	+	
3	53, M	Jaundice‡	35,000	+	Positive	+	
4	20, F	Cerebral (GCS- 3) anemia, ARDS, PCF	15,000	+	Positive	+	
5	45, M	Renal failure, jaundice‡	36,000	+	Positive	+	Recovered
6	22, F	Cerebral (GCS - 6) anemia	8,000	+	Positive	+	Puerpural period 3 rd gravida CSF - N CT scan head - N Recovered Baby died on 14th day at residence
7	18, F	Cerebral (GCS - 5) anemia	10,000	+	Positive	+	Primigravida CSF - Normal CT scan head - N Recovered PMNS - Psychosis Premature delivery Baby survived
8	28, F	Renal failure, ARDS, PCF	44,000	+	Positive	+	Gross hematuria BP <70 mm Hg systolic Recovered
9	25, F	Jaundice‡, haemoglobinurea	90,400	+	Positive	+	Secondgravida Recovered Pregnancy continued
10	50, M	Jaundice‡	18,000	+	Positive	+	Recovered
11	18, F	Renal failure, anemia, pulmonary edema	34,000	+	Positive	+	Skiagram chest - pulmonary edema Recovered Underwent hemodialysis

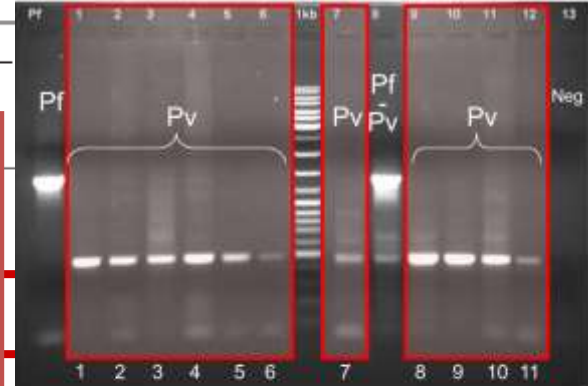


Figure. Polymerase chain reaction analysis of patient samples: lane Pf = positive control showing *Plasmodium falciparum* band at position 1,400 bp; lanes 1-7 and 9-12 = *P. vivax*-positive samples showing band at ~500 bp; (lanes 1-7 correspond to cases 1-7, and lanes 9-12 correspond to patients 8-11 numbered in Tables 1 and 2.); lane 8 = sample showing bands at ~1,400 bp and 500 bp, indicating mixed infection; lane 13 = negative control, normal human DNA; lane 1kb = 1kb DNA ladder mix (MBI Fermentas, SM#0331)

Splenic

Am. J. Trop. Med. Hyg., 39(1), 1988, pp. 11-14 (87-238)
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HYPERREACTIVE MALARIAL SPLENOMEGALY IN VENEZUELA

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CARMELINA PECEÑO,* AND CARLOS BOTTO A

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Epidemiology of Severe *P. vivax* malaria

Obstetrics

	Year	Country of disease origin	Cases	Clinical features	Comments
Pregnancy associated					
Nosten et al ³⁷	1999	Thailand	..	Anaemia and low birthweight	Study of 634 cases of <i>P vivax</i> . 249/322 (77.3%) anaemia; 98/525 (18.7%) low birthweight
Singh et al ³⁸	1999	India	..	Anaemia and low birthweight	Mean haemoglobin 90.5 g/L; 83 of 121 cases of <i>P vivax</i> (less than non-infected pregnant controls, p <0.0001) Mean birthweight 2.22 kg; 50 of 121 cases of <i>P vivax</i> (2.53 kg in non-infected pregnant controls)
Rodriguez-Morales et al ³⁹	2006	Venezuela	5	Miscarriage and preterm delivery	Two miscarriages and three preterm deliveries in observational study of 12 hospitalised pregnant women with <i>P vivax</i> malaria

SHORT REPORT: PREGNANCY OUTCOMES ASSOCIATED WITH *PLASMODIUM VIVAX* MALARIA IN NORTHEASTERN VENEZUELA

ALFONSO J. RODRIGUEZ-MORALES, ELIA SANCHEZ, MIGUEL VARGAS, CARMELINA PICCOLO, ROSA COLINA, MELISSA ARRIA, AND CARLOS FRANCO-PAREDES*

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TABLE I

Demographic and clinical characteristics of 12 pregnant women with *Plasmodium vivax* infection hospitalized in the Hospital Santos Anibal Dominicci, Sucre, Venezuela, 2000-2002*

Patient no.	Age, years	Gestational age, weeks	Gravidity	Underlying condition	Presenting symptoms	Hospitalization days	Hemoglobin levels, g/dL	Platelet count, cells × 10 ³ /mL	Platelet transfusion required	Antimalarial treatment	Outcome
1	25	23	PG	-	Fever, chills	15	7.0	53.0	Yes	CQ	Miscarriage
2	28	38	MG	Severe oligohydramnios	Fever, abdominal pain, jaundice	19	8.0	356.0	No	CQ	Recovered
3	24	36	PG	-	Fever, chills	9	8.2	21.0	Yes	CQ	Preterm delivery
4	17	27	PG	-	Fever, arthralgia	9	9.5	165.0	No	CQ	Recovered
5	35	36	MG	-	Fever, chills	10	11.2	133.0	No	CQ	Preterm delivery
6	20	26	PG	-	Fever, chills, headache, epistaxis	11	5.2	221.0	Yes	CQ	Recovered
7	37	19	MG	-	Fever, chills, genital bleeding	25	10.0	56.0	No	CQ	Miscarriage
8	21	29	PG	Hyperemesis gravidarum	Fever, headache, malaise, vomiting	3	9.3	131.0	No	CQ	Recovered
9	16	19	PG	Hyperemesis gravidarum	Fever, chills, headache	6	9.6	110.0	No	CQ	Recovered
10	40	37	MG	-	Fever, dysuria	7	10.3	86.0	No	CQ	Recovered
11	39	36	MG	-	Fever, chills, headache	7	8.5	117.0	No	CQ	Preterm delivery
12	30	21	MG	-	Genital bleeding	10	9.3	127.0	No	Q	Recovered

* PG - primigravidae; CQ - chloroquine; MG - multigravidae; Q - quinine.

100% Anemia


50% Thrombocytopenia

5/12 (42%): Severe complications (Abortion and preterm delivery)

3/12 (25%): preterm delivery

2/12 (17%): abortion





Tropical Biomedicine 28(2): 339–342 (2011)

Neonatal *Plasmodium vivax* malaria

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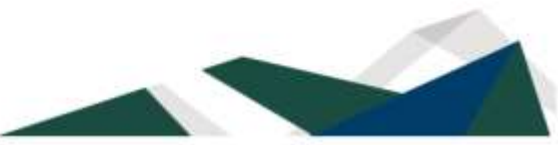

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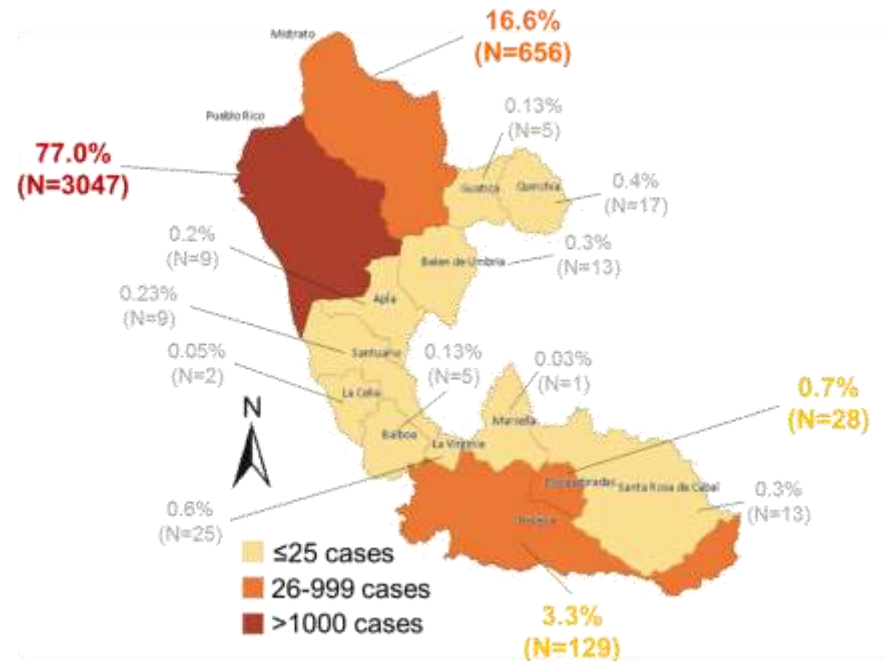
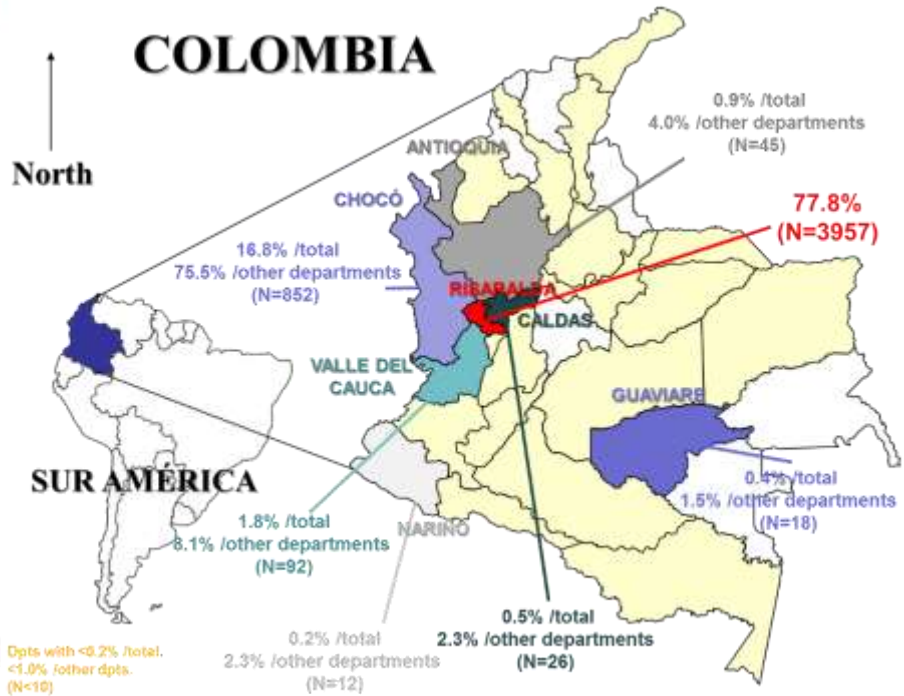
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Malaria in Risaralda, Colombia, 2008-2012



Rodríguez-Morales AJ, Herrera AC, Botero S, Cabrera-Libreros J, Herrera-García PA, Puentes-Mahecha S, Willamil-Gómez W. **Severe or complicated malaria due to *Plasmodium vivax* in Risaralda, Colombia, 2008-2012.** FLAP 2013.

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Mapping malaria in municipalities of the Coffee-Triangle Region of Colombia using Geographic Information Systems (GIS)

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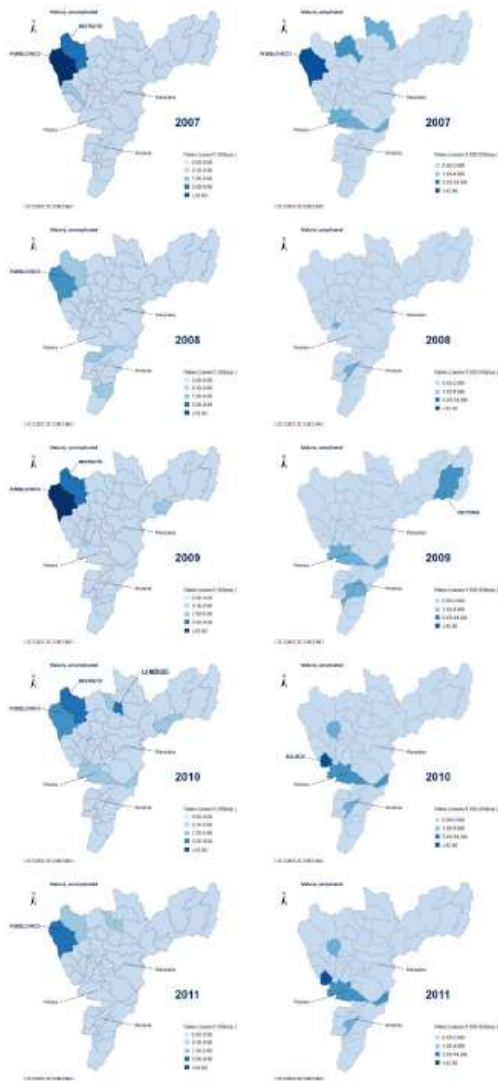
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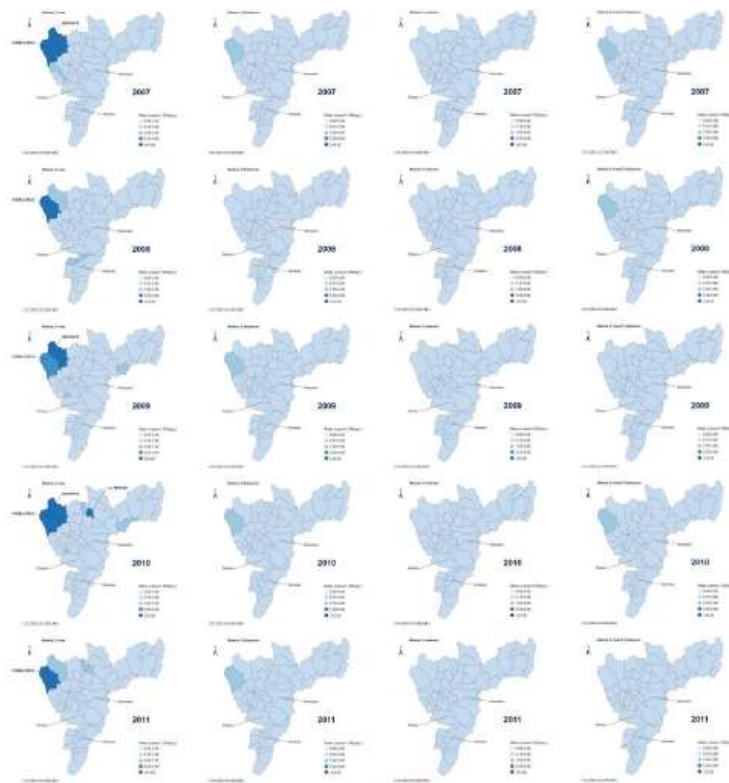
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Figure 2. Uncomplicated malaria (left) and complicated malaria (right), API, Coffee-Triangle Region, Colombia, 2007-2011.

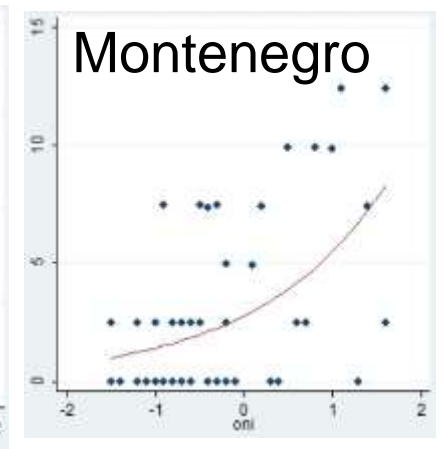
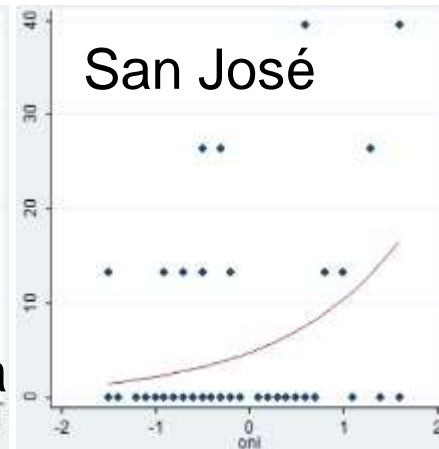
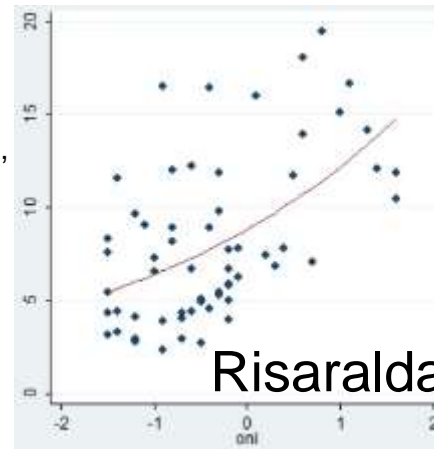
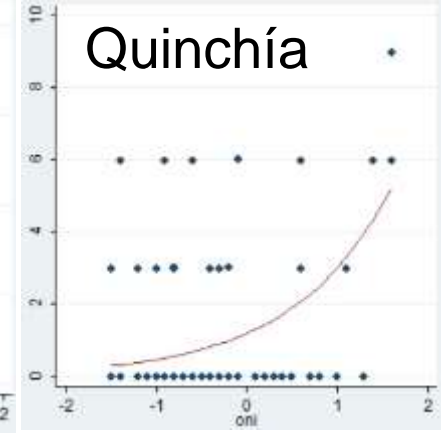
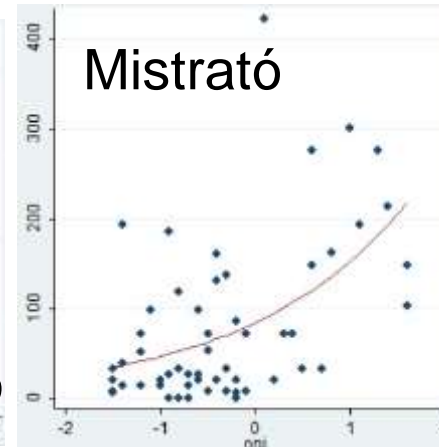
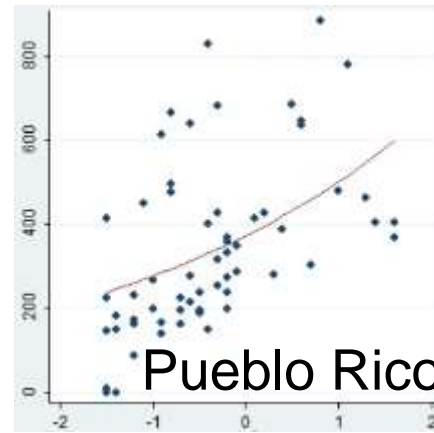


428 Figure 3. Malaria due to *P. vivax* (left), *P. falciparum* (center left), *P. malariae* (center right)
 429 and *P. falciparum/P. vivax* (right), API, Coffee-Triangle Region, Colombia, 2007-2011.



Impacto potencial de la variabilidad climática en la malaria por *Plasmodium vivax* en áreas endémicas del eje cafetero, Colombia, 2007-2011

Jaime A. Cardona-Ospina,¹ Cesar Orrego,¹ Yuliana Perilla,¹ David Murillo,¹ Erika Bolaños,¹ Guillermo J. Lagos-Grisales,¹ Alfonso J. Rodriguez-Morales.¹



Risaralda ($r^2=0,8437$; $p<0,0001$),
Quindío ($r^2=0,4781$; $p<0,0001$) y
Caldas ($r^2=0,4204$; $p<0,0001$),

Risaralda:

Pueblo Rico ($r^2=0,8024$; $p<0,0001$),
Mistrató ($r^2=0,5805$; $p<0,0001$),
La Virginia ($r^2=0,5371$; $p<0,0001$),
Quinchía ($r^2=0,3842$; $p<0,0001$),
Apia ($r^2=0,2288$; $p=0,0005$),
Belén de Umbría ($r^2=0,1754$, $p=0,0037$),
Santuario ($r^2=0,1212$; $p=0,0236$);

Quindío:

Armenia ($r^2=0,5624$; $p<0,0001$),
Montenegro ($r^2=0,5382$; $p<0,0001$),
Quimbaya ($r^2=0,2259$; $p=0,0006$),
Córdoba ($r^2=0,1417$, $p=0,0119$);

Caldas:

La Merced ($r^2=0,4326$; $p<0,0001$),
San José ($r^2=0,2943$; $p<0,0001$),
Risaralda ($r^2=0,1282$; $p=0,0187$),
Supía ($r^2=0,1271$; $p=0,0194$)



Potential impact of climatic variability on the epidemiology of dengue in Risaralda, Colombia, 2010–2011

Liseth Lorena Quintero-Herrera^a, Valeria Ramírez-Jaramillo^a, Sergio Bernal-Gutiérrez^a, Erika Vanessa Cárdenas-Giraldo^a, Edwin Andrés Guerrero-Matituy^a, Anderson Homero Molina-Delgado^a, Cindy Paola Montoya-Arias^a, Jhon Alejandro Rico-Gallego^a, Albert Cristian Herrera-Giraldo^{b, c}, Shirley Botero-Franco^d, Alfonso J. Rodríguez-Morales^{b, e, f, g}  

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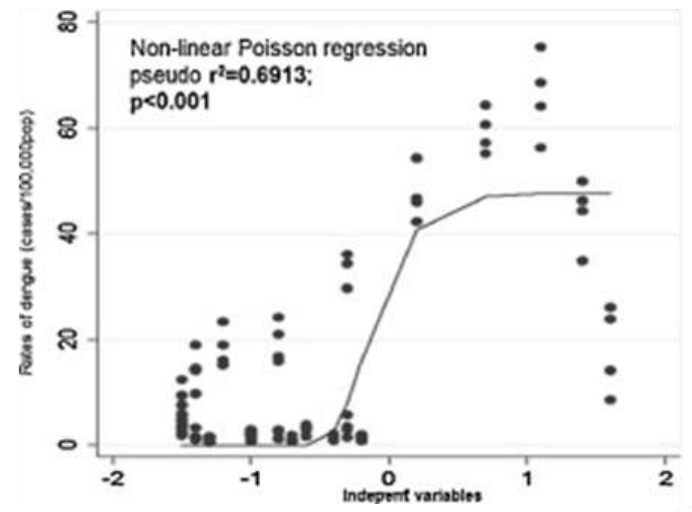
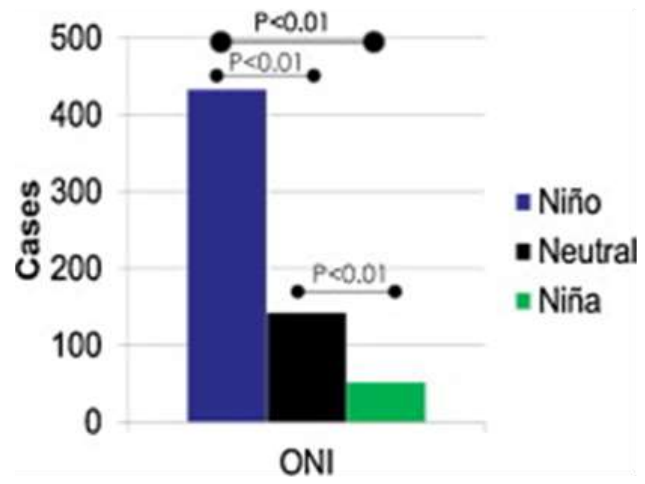
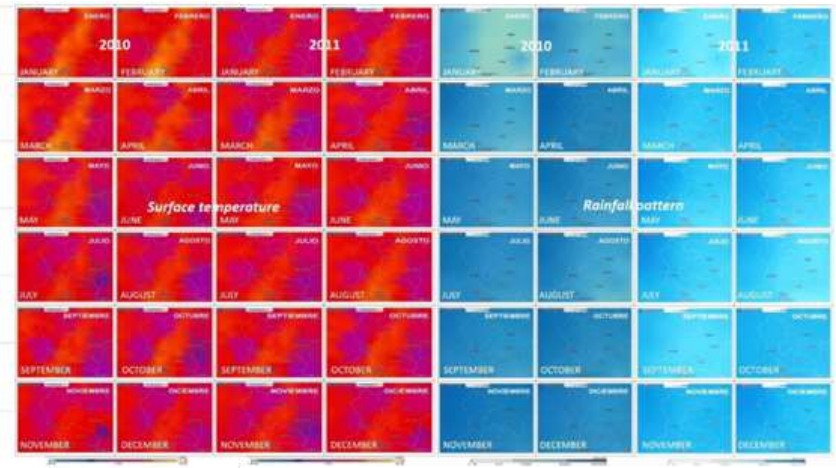
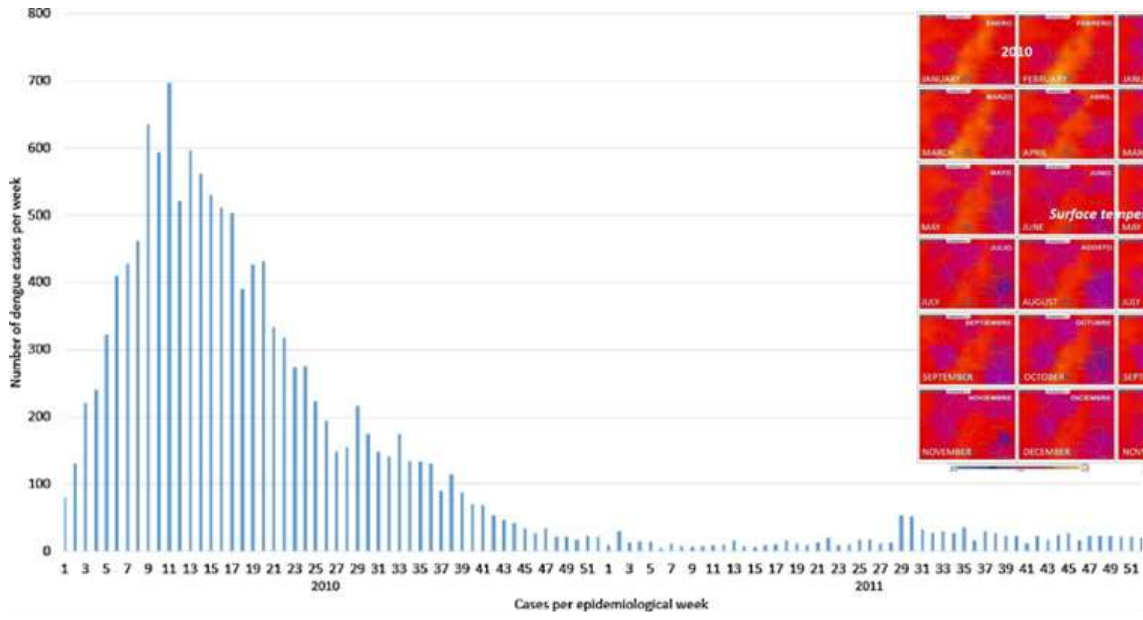
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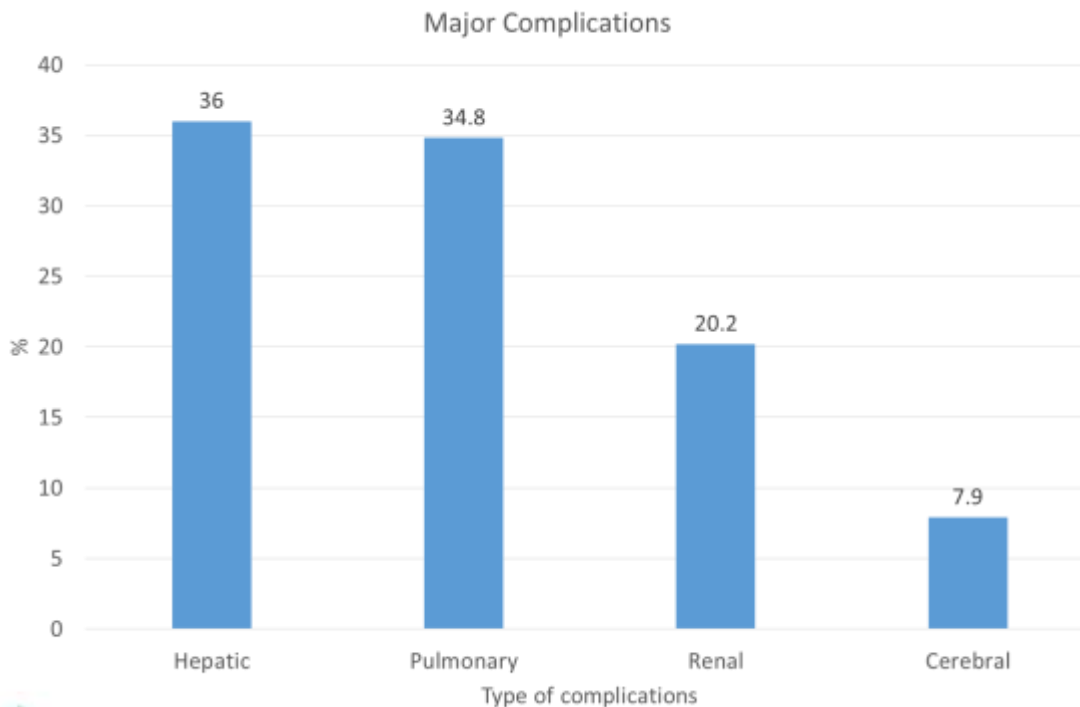
^f Committee on Zoonoses and Hemorrhagic Fevers of the Colombian Association of Infectious Diseases (Asociación Colombiana de Infectología, ACIN), Bogotá, Colombia

^g Fundacion Cenit Colombia, Pereira, Risaralda, Colombia



Epidemiology of *P. vivax* in Risaralda, Colombia

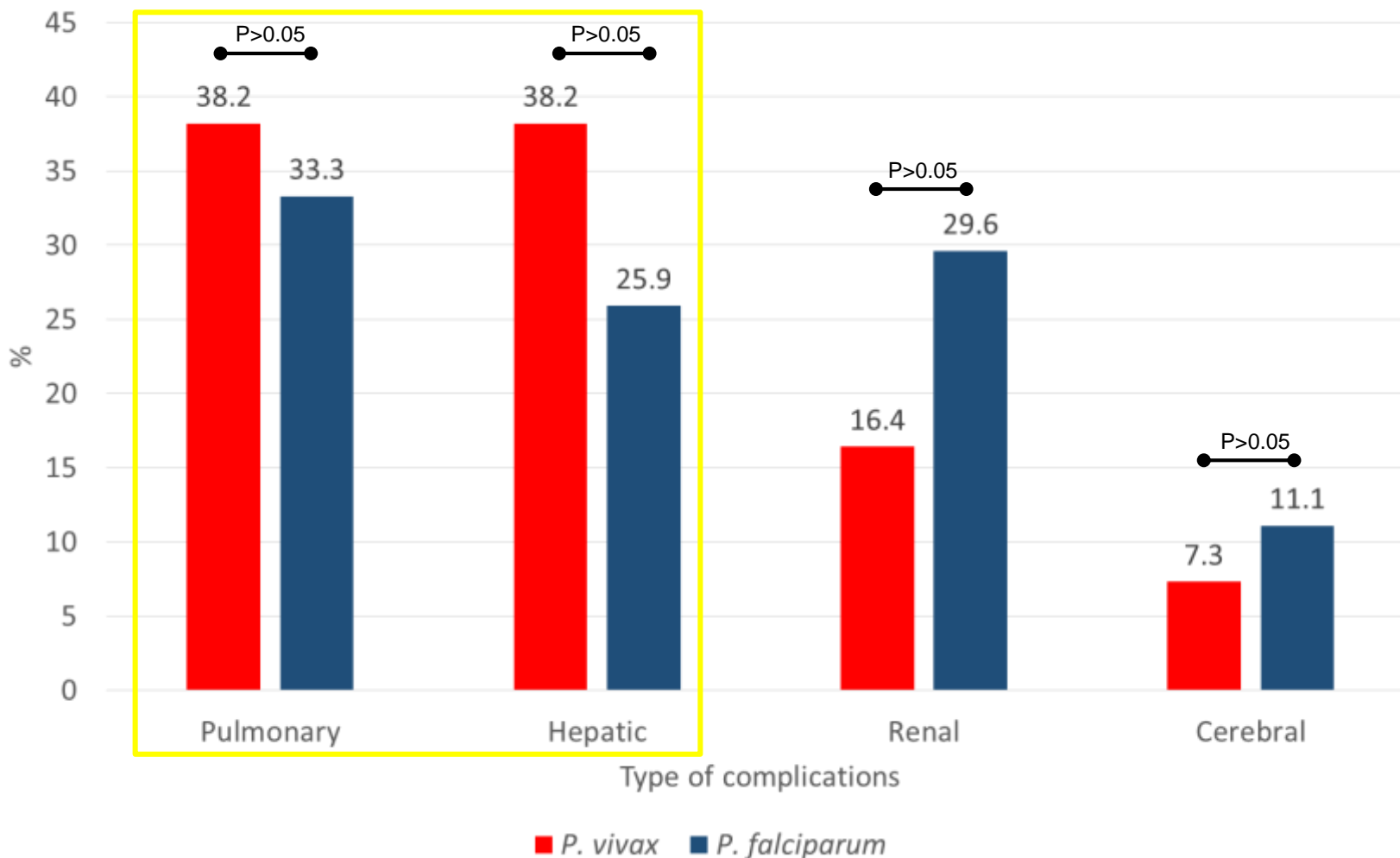
- 5,178 cases of malaria were reported, 82.2% were due to *P. vivax*.
- 1.27% (66) were classified as complicated cases.
 - 61.8% due to *Plasmodium vivax*
 - 30.3% due to *P. falciparum*
 - 5.6% due to *P. vivax/P. falciparum*
 - 1.1% due to *P. malariae*



Rodríguez-Morales AJ, Herrera AC, Botero S, Cabrera-Libreros J, Herrera-García PA, Puentes-Mahecha S, Willamil-Gómez W. **Severe or complicated malaria due to *Plasmodium vivax* in Risaralda, Colombia, 2008-2012.** FLAP 2013.

Epidemiology of *P. vivax* in Risaralda, Colombia

Comparison of complications between *P. vivax* and *P. falciparum*



RESEARCH

Open Access

Characterization of a malaria outbreak in Colombia in 2010

Pablo Chaparro^{1,2*}, Julio Padilla³, Andrés F Vallejo^{4,5} and Sócrates Herrera^{4,5}

Table 4 Complicated malaria cases by parasite species

	Parasite species		
	<i>P. vivax</i> (n = 293)	<i>P. falciparum</i> (n = 282)	mixed (n = 32)
Cerebral	44 (7,1%)	59 (9,5%)	6 (1,0%)
Renal	66 (10,6%)	88 (14,1%)	10 (1,6%)
Liver	130 (20,9%)	99 (15,9%)	14 (2,2%)
Pulmonary	34 (5,5%)	31 (5,0%)	1 (0,2%)
unreported	19 (3,0%)	5 (0,8%)	1 (0,2%)

Source: SIVIGILA.

Case Report

Unusual Presentation of Vivax Malaria with Anaemia, Thrombocytopenia, Jaundice, Renal Disturbance, and Melena: A Report from Malang, a Nonendemic Area in Indonesia



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Correspondence

Anemia and thrombocytopenia in *Plasmodium vivax* malaria is not unusual in patients from endemic and non-endemic settings

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- Thrombocytopenia is a well-documented and frequent complication in *P. vivax malaria* [4], reported in almost **200 articles** in journals indexed on Medline, including some systematic reviews.
- Anemia in *P. vivax* malaria has been found in >80% of patients [1], [2] and [4]. In countries such as Brazil, numerous studies have documented anemia in patients with vivax malaria, and systematic reviews draw attention to this topic [5]. In a MEDLINE search for anemia in *P. vivax* malaria over **470 articles** were identified.
- With regard to jaundice, most patients with hepatocellular damage present increased liver transaminases with subsequent cholestasis and this has been reported in *P. vivax* malaria, and jaundice even the cause of hospitalization of patients with *P. vivax*. A MEDLINE search on jaundice in *P. vivax* malaria identified **over 80 papers**.

Thrombocytopenia in malaria: who cares?

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TABLE I

Systematic review of studies, estimating thrombocytopenia in malarial patients (1997-2011)

References	Study site	Type of patients	Age range	Species	n	Thrombocytopenia % [criterion (mm ³)]
Mohanty et al. (1997)	India	Inpatients and outpatients	All ages	<i>P.v.</i>	24	29 (< 150,000)
				<i>P.f.</i>	76	39 (< 150,000)
Noronha (1998)	Brazil	Inpatients and outpatients	< 14 y	<i>P.f.</i>	54	51.8 (< 150,000)
Kortepeter and Brown (1998)	USA	Inpatients and outpatients	> 18 y	<i>P.f./P.v.</i>	79	74 (< 150,000)
Murthy et al. (2000)	India	Inpatients	10-80 y	<i>P.f.</i>	158	40.5 (< 150,000)
				<i>P.f.</i>	113	33.6 (< 150,000)
Gonzalez et al. (2000)	Colombia	Inpatients	All ages	<i>P.v.</i>	128	39 (< 150,000)
				<i>P.v.</i>	73	91.8 (< 150,000)
Alecrim (2000)	Brazil	Inpatients	> 12 y	<i>P.v.</i>	319	60.8 (< 150,000)
		Outpatients	All ages	<i>P.v.</i>	429	46.6 (< 140,000)
Oh et al. (2001)	South Korea	Inpatients and outpatients	> 17 y	<i>P.v.</i>	101	85.1 (< 150,000)
Robinson et al. (2001)	Australia	Inpatients	NA	<i>P.f./P.v./P.o.</i>	246	71 (< 150,000)
Mourão et al. (2001)	Brazil	Inpatients	< 12 y	<i>P.f.</i>	255	73.7 (< 150,000)
Lacerda et al. (2001)	Brazil	Inpatients	> 12 y	<i>P.f.</i>	218	87.6 (< 150,000)
Ladhani et al. (2002)	Kenya	Inpatients	Children	<i>P.f.</i>	1,369	56.7 (< 150,000)
Park et al. (2002)	Brazil	Inpatients	All ages	<i>P.v.</i>	237	61.6 (NA)
Mohapatra et al. (2002)	India	Inpatients and outpatients	15-60 y	<i>P.v.</i>	110	3.6 (< 100,000)
Bashawri et al. (2002)	Saudi Arabia	Inpatients and outpatients	2 m-74 y	<i>P.v./P.f.</i>	727	55.6 (< 150,000)
Araújo Filho et al. (2003)	Brazil	Inpatients and outpatients	4-64 y	<i>P.v.</i>	68	20.6 (< 50,000)
Echeverri et al. (2003)	Colombia	Outpatients	All ages	<i>P.v.</i>	104	8 (< 130,000)
Jadhav et al. (2004)	India	Inpatients and outpatients	All ages	<i>P.v.</i>	973	65 (50,000-150,000)
				<i>P.f.</i>	590	50 (50,000-150,000)

TABLE I

Systematic review of studies, estimating thrombocytopenia in malarial patients (1997-2011)

References	Study site	Type of patients	Age range	Species	n	Thrombocytopenia % [criterion (mm ³)]
Rodríguez-Morales et al. (2005)	Venezuela	NA	NA	<i>P.v.</i>	116	87.6 (< 150,000)
Rodríguez-Morales et al. (2006)	Venezuela	Inpatients	< 12 y	<i>P.v.</i>	78	58.9 (< 150,000)
Casals-Pascual et al. (2006)	Kenya	Inpatients and outpatients	6 m-10 y	<i>P.f.</i>	120	34.4 (< 150,000)
Kumar and Shashirekha (2006)	India	Inpatients and outpatients	All ages	<i>P.v.</i>	27	88.8 (< 150,000)
Lacerda (2007)	Brazil	Outpatients	> 18 y	<i>P.v.</i>	142	71.8 (< 150,000)
				<i>P.f.</i>	26	65.4 (< 150,000)
Koltas et al. (2007)	Turkey	Outpatients	All ages	<i>P.v.</i>	90	NA
Taylor et al. (2008)	Indonesia	Outpatients	All ages	<i>P.v./P.f.</i>	151	78.8 (< 150,000)
Tan et al. (2008)	Thailand	Inpatients and outpatients	Pregnant women	<i>P.v.</i>	523	22 (< 75,000)
				<i>P.f.</i>	694	34 (< 75,000)
Silva (2009)	Brazil	Outpatients	All ages	<i>P.v.</i>	397	77.1 (< 150,000)
Rasheed et al. (2009)	Pakistan	Inpatients	All ages	<i>P.v./P.f.</i>	502	80 (< 150,000)
Shaikh et al. (2009)	Pakistan	Outpatients	All ages	<i>P.v./P.f.</i>	124	82.5 (< 150,000)
Prasad et al. (2009)	India	Inpatients	< 5 y	<i>P.f.</i>	40	85 (< 150,000)
Gonzalez et al. (2009)	Venezuela	Outpatients	3-67	<i>P.v.</i>	59	55.9 (< 150,000)
Poespoprođjo et al. (2009)	Indonesia	Inpatients	0-3 m	<i>P.v./P.f. and mixed</i>	179	61.3 (< 100,000)
Khan et al. (2009)	Qatar	Outpatients	All ages	<i>P.v.</i>	81	63 (< 150,000)
Maina et al. (2010)	Kenya	Outpatients	< 5 y	<i>P.f.</i>	523	49 (< 150,000)
Kochar et al. (2010)	India	Inpatients and outpatients	All ages	<i>P.v./P.f. and mixed</i>	1,064	24.6 (< 150,000)
George and Alexander (2010)	India	Inpatients	18-66 y	<i>P.v.</i>	30	93.3 (< 150,000)
Srivastava et al. (2011)	India	Inpatients	All ages	<i>P.v.</i>	50	82 (< 150,000)

m: months; NA: non-available; *P.f.*: *Plasmodium falciparum*; *P.o.*: *Plasmodium ovale*; *P.v.*: *Plasmodium vivax*; y: years.

Complicated and Severe *P. vivax* Malaria

- Clinical data from these patients strongly indicate that *P. vivax* can cause both sequestration-related and non-sequestration-related complications of severe malaria:
 - Cerebral malaria
 - Uremic encephalopathy
 - **Severe anemia**
 - **Severe thrombocytopenia**
 - Haemophagocytic syndrome
 - **Leukopenia**
 - **Hypotension**
 - **Circulatory collapse**
 - Disseminated intravascular coagulation
 - Abnormal bleeding
 - **ARDS and ALI**
 - Hepatic dysfunction
 - **Jaundice**
 - Hemoglobinurea
 - Dyslipidemia
 - **Hypoglicemia**
 - Hydronephrosis
 - **Renal failure**
 - Spontaneous splenic rupture
 - **Miscarriage**
 - **Preterm delivery**
 - **Low birth weight**
 - Coma
 - **Death**

Major research priorities in the study of severe vivax disease.

Epidemiology

1. What is the real incidence of severe disease in population-based studies in Latin America?
2. Is the incidence of severe disease similar in distinct epidemiological scenarios? And what is the impact of the health system organization on this severity?
3. What is the prognosis and fatality rate of severe disease in hospitalized and non-hospitalized patients?
4. What is the role of host genetics (e.g. Duffy genotypes, G6PD deficiency) upon severity?



Major research priorities in the study of severe vivax disease.

Clinical aspects

1. Do the WHO criteria for severe *P. falciparum* malaria also apply for *P. vivax* severe disease?
2. Which clinical complications are able to predict death?
3. What is the contribution of co-morbidities to severe disease?
4. What is the contribution of concurrent infections (bacterial, viral, fungal, parasitic) to severe disease?
5. Are there specific severity presentation in some groups, e.g. pregnant women and children?
6. Which are the bad prognostic findings in obstetric ultrasounds in pregnant women with malaria?
7. What is the burden of clinical complications related more to drugs' side effects?



Major research priorities in the study of severe vivax disease.

Pathogenesis

1. Which are the microscopic findings of autopsies from patients who died with the diagnosis of vivax infection?
2. Do all the clinical complications, classified as 'severe', share the same mechanisms of disease?
3. Is severe disease linked to the existing evidence of *ex vivo* cytoadhesion of *P. vivax* infected RBCs? What triggers endothelial activation?
4. Which are the best biomarkers for severity?

Therapeutic aspects

1. Is clinical severity linked to CQ-resistance?
2. What should be the standard-of-care specific treatment for severe patients in areas where CQ-resistance is not high?
3. Antibiotics should be used systematically in which severe complications?
4. What type of adjunctive treatment should be initiated?





Plasmodium vivax

Neglected but not “benign”



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Tropical Medicine & International Health

Severe Malaria




**World Health
Organization**

Section 13: Severe vivax malaria

Plasmodium falciparum causes the majority of severe and fatal malaria cases and has overshadowed the public health importance of vivax malaria (Baird 2007; Price *et al.* 2007). *Plasmodium vivax* is less pathogenic than *P. falciparum* in otherwise healthy patients, but can cause complicated and severe disease (Price *et al.* 2007, 2009; Baird 2009; Bassat & Alonso 2011; Anstey *et al.* 2012). In the malaria therapy era, acute mortality during *P. vivax* therapy of neurosyphilis averaged 5–10% overall (Swellengrebel & De Buck 1938) and up to 10–14% with the Madagascar strain (James 1933), but these were debilitated patients with a fatal underlying disease. *Plasmodium vivax* infection has been associated with severe and fatal disease in endemic areas, including Indonesia (Barcus *et al.* 2007; Tjitra *et al.* 2008; Lampah *et al.* 2011; Nurleila *et al.* 2012), Papua New Guinea (Genton *et al.* 2008; Manning *et al.* 2011), India (Kochar *et al.* 2010; Yadav *et al.* 2012), Brazil (Andrade *et al.* 2010; Lacerda *et al.* 2012), Venezuela (Rodriguez-Morales *et al.* 2008), Thailand (Luxemburger *et al.* 1997), Malaysia (Barber *et al.* 2012) and Sudan (Mahgoub *et al.* 2012). Severe manifestations associated with *P. vivax* infection in these series include severe anaemia, respiratory distress and acute lung injury (ALI), acute kidney injury (AKI), splenic rupture, metabolic acidosis, jaundice, multiorgan dysfunction, shock and rarely coma.

Epidemiology of complicated and severe vivax malaria

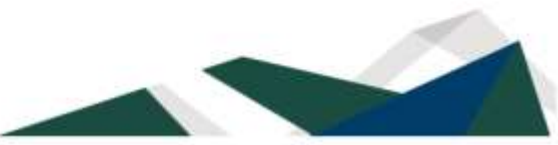

Outside of Africa, *P. vivax* causes almost half of all malaria cases, with 70–390 million clinical infections each year (Price *et al.* 2007). In countries endemic for both major *Plasmodium* species, *P. vivax* infection can account for up to 38% of patients hospitalised with malaria (Buck *et al.* 1983; Gopinathan & Subramanian 1986; Maitland *et al.* 1997; Carrara *et al.* 2006; Tjitra *et al.* 2008). In Indonesian Papua, *P. vivax* accounted for 24% of malaria admissions in all age groups, but 47% (415/887) of infants (Tjitra *et al.* 2008). The need for hospitalisation indicates significant morbidity and at least moderately severe disease (Anstey *et al.* 2012). This ranges from vomiting and inability to tolerate oral therapy, through to prostration and those with disease manifestations fulfilling the severity criteria described earlier for falciparum malaria (Section 2). The risk of severe disease from single *P. vivax* infections is very low in otherwise healthy adults and older children without comorbidities, with ready access to early diagnosis and effective treatment. (Price *et al.* 2009; Anstey *et al.* 2012). In endemic areas, the risk of severe disease is associated with young age, higher transmission intensity, early and frequent relapse, less access to early diagnosis and treatment and/or greater prevalence of comorbidities including bacterial co-infections and malnutrition (Price *et al.* 2009; Anstey *et al.* 2012).



Severe malaria syndromes

Series of severe vivax malaria have described a broad range of severe manifestations in children and adults, using criteria developed for severe falciparum malaria.

Severe anaemia. The major severe manifestation in most series of vivax malaria in children is severe anaemia, defined as a haemoglobin concentration of <5 g/dl in children and <7 g/dl in adults (Luxemburger *et al.* 1997; **Rodriguez-Morales *et al.* 2008**; Tjitra *et al.* 2008; Poespoprodjo *et al.* 2009; Alexandre *et al.* 2010; Kochar *et al.* 2010). There are few data on the confounding effects of other causes and the effect of successive episodes of malaria caused by reinfection and relapses. Despite these limitations, the association between vivax infection and severe anaemia is strong, particularly in infancy (Michon *et al.* 2007; Genton *et al.* 2008; Tjitra *et al.* 2008; Ladeia-Andrade *et al.* 2009; Poespoprodjo *et al.* 2009; Lin *et al.* 2010; Douglas *et al.* 2013). Among patients presenting to hospital in Indonesian Papua,





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Aspecto	<i>P. vivax</i>	<i>P. falciparum</i>
Fase pre-eritrocítica (días)	6 - 8	5.5 - 7
Periodo prepatente (días)	11 - 13	9 - 10
Periodo de incubación (días)	15d o hasta 6 - 12 meses	12 (9 - 14)
Gametocitemia (días postprepatente)	1 - 3 ¹⁹	7 - 15 ¹⁹
Ciclo eritrocítico (horas)	48	48
Parasitemia por ul (mm ³)		
Promedio	20.000	20.000 - 500.000
Máximo	50.000	2.000.000
Ataque primario	Moderado - severo	Severo en no inmunes
Paroxismos de fiebre (horas)	8 - 12	16 - 36 o más largos
Recaídas	Sí	No existen
Eritrocitos parasitados	Reticulocitos	Todos
Merozoitos por esquizonte	12 - 24	8 - 32

Tabla 1. Características de la infección en *P. vivax* y *P. falciparum*.

Síntomas de malaria no complicada

La malaria no complicada se define como la malaria sintomática sin signos de severidad o evidencia de disfunción de un órgano vital.

A continuación se explica la evolución de la sintomatología:

◆ Primeros síntomas

- Dolor de cabeza.
- Debilidad
- Fatiga
- Dolores en articulaciones y músculos.
- Malestar abdominal.
- 30 minutos: escalofríos, frío intenso y progresivo, seguido de temblor incontrolable.

◆ 6 - 8 horas

- Periodo febril
- Temperatura por encima de 38 grados.
- Sudoración profusa
- La temperatura baja a 36.8 grados.

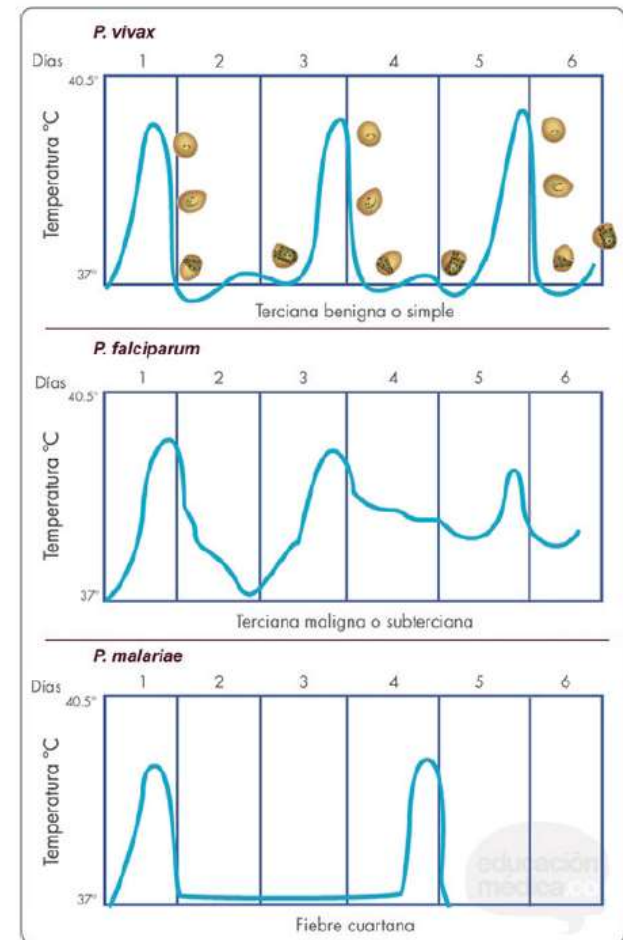


Figura 4. Comportamiento febril.

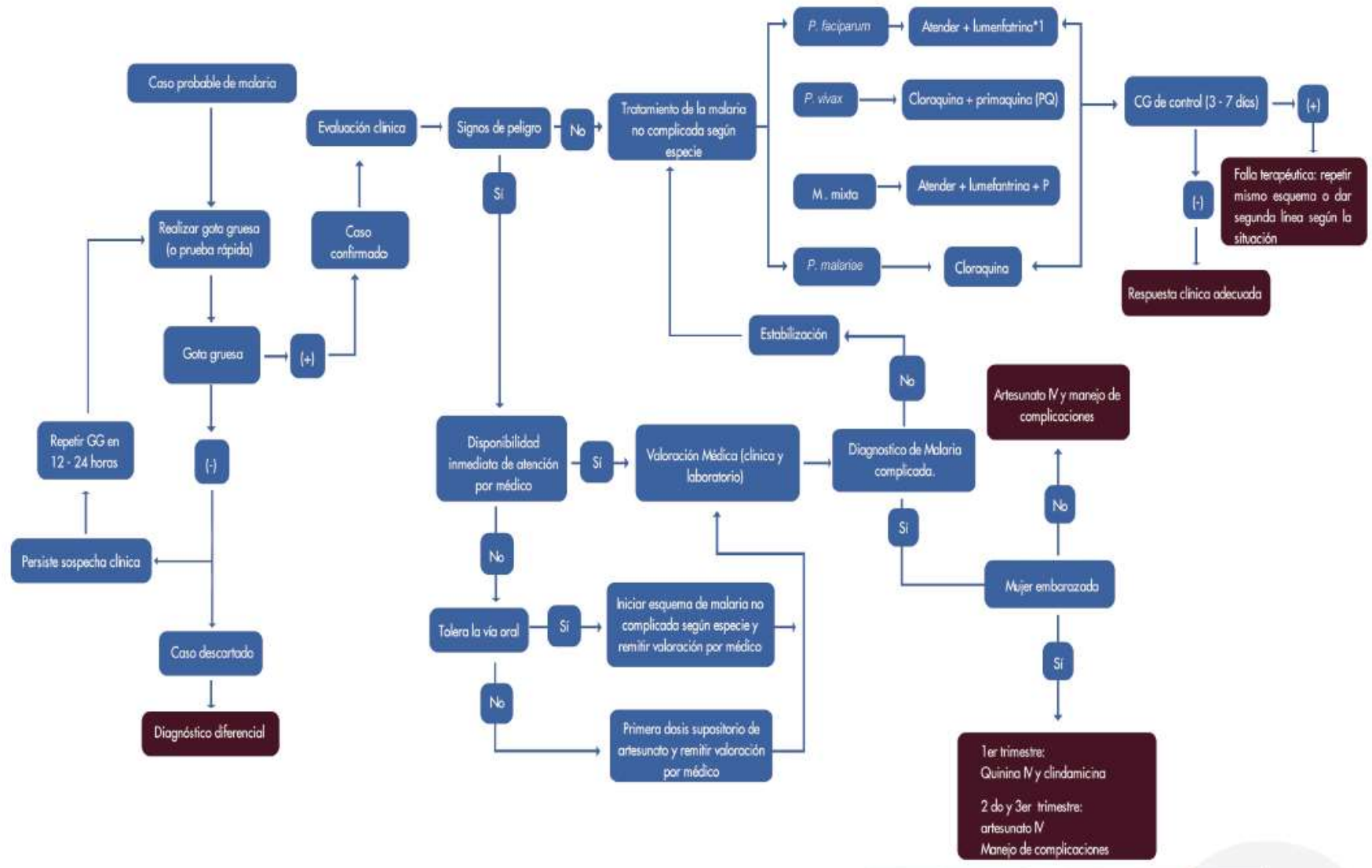
Fiebre baja o moderada	Fiebre alta	Hiperpirexia
Hepatitis por virus Tuberculosis pulmonar Tétano en fase inicial Heridas infectadas Cistitis Infarto del miocardio Hemorragia digestiva	Septicemias Leptospirosis Neumonías bacterianas Meningitis Malaria Colangitis Pielonefritis Abscesos viscerales	Tumores cerebrales Supuraciones del SNC Traumatismo craneoencefálico Tétano grave Hipertermia maligna Drogas Encefalitis

Tabla 2. Causas de fiebre según la intensidad. Con respecto a la duración de la fiebre, las enfermedades se pueden clasificar en cortas y prolongadas. Fiebres de corta duración son de menos de 3 semanas. La mayoría de las enfermedades febriles son de corta duración, evolución autolimitada y causadas por virus. Con respecto a la intensidad, la fiebre puede clasificarse como baja (hasta 37.9 °C); moderada (entre 38 y 38.9 °C), alta (entre 39 y 40.5 °C) e hiperpirexia (mayor de 40.5 °C)

Tipo de fiebre	Causa
Intermitente	Malaria, endocarditis bacteriana, uso de antitérmicos, tuberculosis miliar, anfotericina B.
Remitente	Malaria gravea por <i>P. falciparum</i> , neumonías bacterianas, septicemias, endocarditis bacteriana aguda, abscesos viscerales.
Continua	Fiebre tifoidea, malaria grave, brucelosis, fiebre por drogas, meningitis tuberculosa, fiebre maculosa.
Bifásica	Leptospirosis, dengue, enterovirus, fiebre amarilla, poliomielitis.
Recurrente	Colangitis, brucelosis, leishmaniasis visceral, linfomas, enfermedad de Still, fiebre del Mediterráneo.
Doble pico diario	Leishmaniasis visceral, malaria mixta, endocarditis bacteriana, tuberculosis miliar, enfermedad de Still.

Tabla 3. Causas de fiebre según tipo de curva febril. En este cuadro se presenta una clasificación de enfermedades según el comportamiento de la curva de la fiebre.

ANEXO 4. DIAGNÓSTICO



*1 Quinina + clindamicina es la primera opción en mujeres en primer trimestre de embarazo con malaria por *P. falciparum*.
 *2 La primaquina (PQ) está contraindicada en el embarazo y en menores de 2 años.



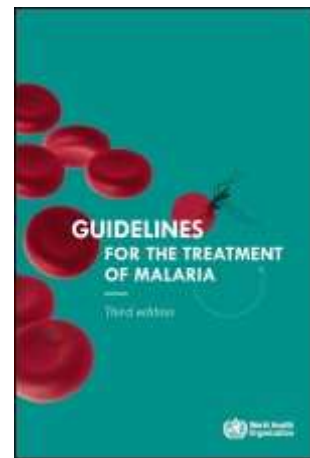
Tipo de antimalárico	Mecanismo de acción	Medicamento
Esquizonticidas tisulares contra formas hísticas primarias	<ul style="list-style-type: none"> Contra las formas hísticas primarias de los Plasmodia en hígado, que darán lugar a la etapa eritrocítica de la infección. Evitan la maduración de los esquizontes hepáticos en el ciclo pre-eritrocítico. 	<p>Cloroguanida (proguanil): utilizada para la profilaxis causal del paludismo por <i>P. falciparum</i>.</p> <p>NO son de uso en Colombia.</p>
Esquizonticidas tisulares contra formas hísticas latentes	Actúan en las formas hísticas latentes de <i>P. vivax</i> y <i>P. ovale</i> que persisten después de que pasaron a la circulación las formas hísticas primarias.	<p>Primaquina: utilizado para evitar recaídas.</p> <p>Se usa en Colombia.</p>
Esquizonticidas hemáticos	Actúan en las etapas eritrocíticas asexuadas de los parásitos del paludismo para interrumpir la esquizogonia circulante.	<p>Dos grupos:</p> <ul style="list-style-type: none"> De acción rápida: cloroquina, quinina y sus derivados similares, quinidina, mefloquina, holo-fantrina y los derivados de la artemisinina. De acción más lenta (menos eficaces): pirimetamina, cloroguanida y antibióticos antipalúdicos. <p>En Colombia se usan para tratamiento <i>P. falciparum</i>: derivados de artemisininas, lumefantrine, quinina, clindamicina.</p> <p>Para tratamiento <i>P. vivax</i>: cloroquina.</p>
Gametocidas	Actúan contra las formas eritrocíticas sexuales de los Plasmodia y así evitan la infección de los mosquitos.	<p>Cloroquina y quinina: poseen actividad gametocida contra <i>P. vivax</i>, <i>P. ovale</i> y <i>P. malariae</i>.</p> <p>Primaquina tiene actividad potente contra <i>P. falciparum</i>.</p> <p>Los antimaláricos rara vez se utilizan en seres humanos solo por sus acciones gametocidas.</p>
Esporonticidas	Evitan o inhiben la formación de oocistos y esporozoitos palúdicos en mosquitos infectados.	<p>Cloroquina</p> <p>Los antimaláricos no se utilizan en seres humanos para este fin.</p>

Tabla 4. Tipos de antimaláricos según las formas del parásito y la fase del ciclo.





Guidelines for the treatment of malaria. Third edition

April 2015



The Guidelines include recommendations on the diagnosis and treatment of uncomplicated and severe malaria by all species, including in special at-risk populations (such as **young children, pregnant women, TB or HIV/AIDS patients and non-immune travellers**) and situations (**such as epidemics and humanitarian emergencies**), and on the use of drugs to prevent malaria in groups at high risk.



Treating uncomplicated *P. falciparum* malaria

Treatment of uncomplicated P. falciparum malaria

Treat children and adults with uncomplicated *P. falciparum* malaria (except pregnant women in their first trimester) with one of the following recommended ACTs:

- artemether + lumefantrine
- artesunate + amodiaquine
- artesunate + mefloquine
- dihydroartemisinin + piperazine
- artesunate + sulfadoxine–pyrimethamine (SP).

Strong recommendation, high-quality evidence

Duration of ACT treatment

ACT regimens should provide 3 days' treatment with an artemisinin derivative.

Strong recommendation, high-quality evidence

Revised dose recommendation for dihydroartemisinin + piperazine in young children

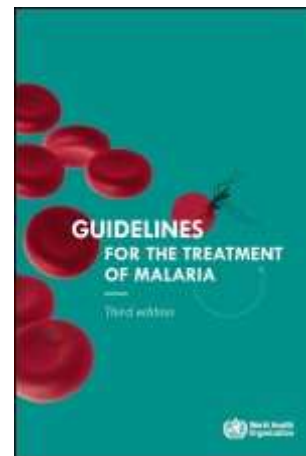
Children weighing <25kg treated with dihydroartemisinin + piperazine should receive a minimum of 2.5 mg/kg bw per day of dihydroartemisinin and 20 mg/kg bw per day of piperazine daily for 3 days.

Strong recommendation based on pharmacokinetic modelling

Reducing the transmissibility of treated P. falciparum infections

In low-transmission areas, give a single dose of 0.25 mg/kg bw primaquine with ACT to patients with *P. falciparum* malaria (except pregnant women, infants aged < 6 months and women breastfeeding infants aged < 6 months) to reduce transmission. G6PD testing is not required.

Strong recommendation, low-quality evidence



Treating uncomplicated *P. falciparum* malaria in special risk groups

First trimester of pregnancy

Treat pregnant women with uncomplicated *P. falciparum* malaria during the first trimester with 7 days of quinine + clindamycin.

Strong recommendation, very low- quality evidence

Infants less than 5kg body weight

Treat infants weighing < 5 kg with uncomplicated *P. falciparum* malaria with an ACT at the same mg/kg bw target dose as for children weighing 5 kg.

Strong recommendation, very low- quality evidence

Patients co-infected with HIV

In people who have HIV/AIDS and uncomplicated *P. falciparum* malaria, avoid artesunate + SP if they are also receiving co-trimoxazole, and avoid artesunate + amodiaquine if they are also receiving efavirenz or zidovudine.

Good practice statement

Non-immune travellers

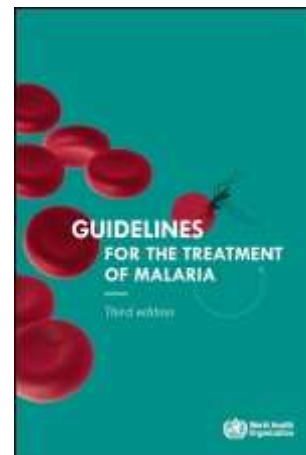
Treat travellers with uncomplicated *P. falciparum* malaria returning to non-endemic settings with an ACT.

Strong recommendation, high-quality evidence

Uncomplicated hyperparasitaemia

People with *P. falciparum* hyperparasitaemia are at increased risk of treatment failure, severe malaria and death so should be closely monitored, in addition to receiving an ACT.

Good practice statement



Treating uncomplicated *P. vivax*, *P. ovale*, *P. malariae* or *P. knowlesi* malaria

Blood stage infection

If the malaria species is not known with certainty, treat as for uncomplicated *P. falciparum* malaria.

Good practice statement

In areas with chloroquine-susceptible infections, treat adults and children with uncomplicated *P. vivax*, *P. ovale*, *P. malariae* or *P. knowlesi* malaria with either an ACT (except pregnant women in their first trimester) or chloroquine.

Strong recommendation, high-quality evidence

In areas with chloroquine-resistant infections, treat adults and children with uncomplicated *P. vivax*, *P. ovale*, *P. malariae* or *P. knowlesi* malaria (except pregnant women in their first trimester) with an ACT.

Strong recommendation, high-quality evidence

Treat pregnant women in their first trimester who have chloroquine-resistant *P. vivax* malaria with quinine.

Strong recommendation, very low-quality evidence

Preventing relapse in *P. vivax* or *P. ovale* malaria

The G6PD status of patients should be used to guide administration of primaquine for preventing relapse.

Good practice statement

To prevent relapse, treat *P. vivax* or *P. ovale* malaria in children and adults (except pregnant women, infants aged < 6 months, women breastfeeding infants aged < 6 months, women breastfeeding older infants unless they are known not to be G6PD deficient, and people with G6PD deficiency) with a 14-day course of primaquine in all transmission settings.

Strong recommendation, high-quality evidence

In people with G6PD deficiency, consider preventing relapse by giving primaquine base at 0.75 mg/kg bw once a week for 8 weeks, with close medical supervision for potential primaquine-induced adverse haematological effects.

Conditional recommendation, very low-quality evidence

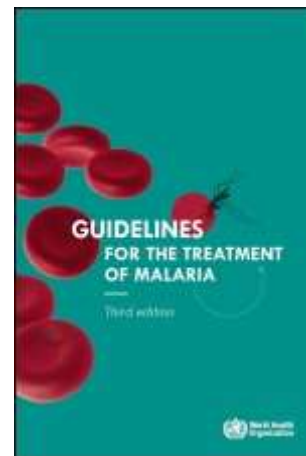
When the G6PD status is unknown and G6PD testing is not available, a decision to prescribe primaquine must be based on an assessment of the risks and benefits of adding primaquine.

Good practice statement

Pregnant and breast feeding women

In women who are pregnant or breastfeeding, consider weekly chemoprophylaxis with chloroquine until delivery and breastfeeding are completed, then, on the basis of G6PD status, treat with primaquine to prevent future relapse.

Conditional recommendation, moderate-quality evidence



Treating severe malaria

Treat adults and children with severe malaria (including infants, pregnant women in all trimesters and lactating women) with intravenous or intramuscular artesunate for at least 24 h and until they can tolerate oral medication. Once a patient has received at least 24 h of parenteral therapy and can tolerate oral therapy, complete treatment with 3 days of an ACT.

Strong recommendation, high-quality evidence

Revised dose recommendation for parenteral artesunate in young children

Children weighing < 20 kg should receive a higher dose of artesunate (3 mg/kg bw per dose) than larger children and adults (2.4 mg/kg bw per dose) to ensure equivalent exposure to the drug.

Strong recommendation based on pharmacokinetic modelling

Parenteral alternatives when artesunate is not available

If parenteral artesunate is not available, use artemether in preference to quinine for treating children and adults with severe malaria.

Conditional recommendation, low-quality evidence

Treating cases of suspected severe malaria pending transfer to a higher-level facility (pre-referral treatment)

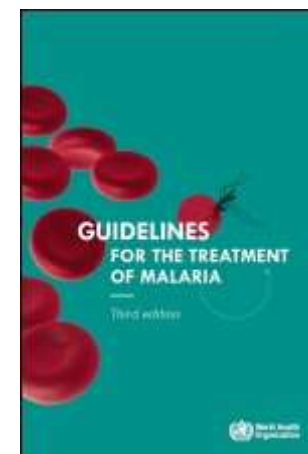
Pre-referral treatment options

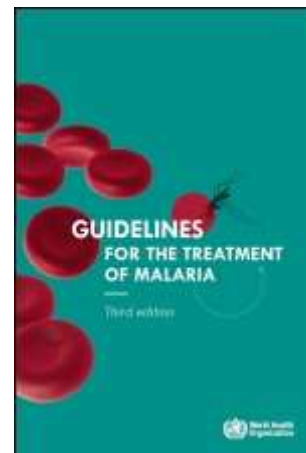
Where complete treatment of severe malaria is not possible but injections are available, give adults and children a single intramuscular dose of artesunate, and refer to an appropriate facility for further care. Where intramuscular artesunate is not available use intramuscular artemether or, if that is not available, use intramuscular quinine.

Strong recommendation, moderate-quality evidence

Where intramuscular injections of artesunate are not available, treat children < 6 years with a single rectal dose (10 mg/kg bw) of artesunate, and refer immediately to an appropriate facility for further care. Do not use rectal artesunate in older children and adults.

Strong recommendation, moderate-quality evidence





7.1.2 | SEVERE VIVAX AND KNOWLESI MALARIA

Severe vivax malaria is defined as for falciparum malaria but with no parasite density thresholds.

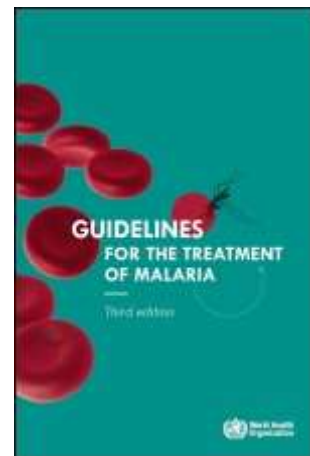
Severe knowlesi malaria is defined as for falciparum malaria but with two differences:

- *P. knowlesi* hyperparasitaemia: parasite density > 100 000/ μ L
- Jaundice and parasite density > 20 000/ μ L.

7.1.1 | SEVERE FALCIPARUM MALARIA

For epidemiological purposes, **severe falciparum malaria** is defined as one or more of the following, occurring in the absence of an identified alternative cause and in the presence of *P. falciparum* asexual parasitaemia.

- *Impaired consciousness*: A Glasgow coma score < 11 in adults or a Blantyre coma score < 3 in children
- *Prostration*: Generalized weakness so that the person is unable to sit, stand or walk without assistance
- *Multiple convulsions*: More than two episodes within 24 h
- *Acidosis*: A base deficit of > 8 mEq/L or, if not available, a plasma bicarbonate level of < 15 mmol/L or venous plasma lactate \geq 5 mmol/L. Severe acidosis manifests clinically as respiratory distress (rapid, deep, laboured breathing).
- *Hypoglycaemia*: Blood or plasma glucose < 2.2 mmol/L (< 40 mg/dL)
- *Severe malarial anaemia*: Haemoglobin concentration \leq 5 g/dL or a haematocrit of \leq 15% in children < 12 years of age (< 7 g/dL and < 20%, respectively, in adults) with a parasite count > 10 000/ μ L
- *Renal impairment*: Plasma or serum creatinine > 265 μ mol/L (3 mg/dL) or blood urea > 20 mmol/L
- *Jaundice*: Plasma or serum bilirubin > 50 μ mol/L (3 mg/dL) with a parasite count > 100 000/ μ L
- *Pulmonary oedema*: Radiologically confirmed or oxygen saturation < 92% on room air with a respiratory rate > 30/min, often with chest indrawing and crepitations on auscultation
- *Significant bleeding*: Including recurrent or prolonged bleeding from the nose, gums or venepuncture sites; haematemesis or melaena
- *Shock*: Compensated shock is defined as capillary refill \geq 3 s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure < 70 mm Hg in children or < 80 mm Hg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill).
- *Hyperparasitaemia*: *P. falciparum* parasitaemia > 10%



Malaria

World Malaria Day: new guidelines on the treatment of malaria



The Global Fund / John Rae

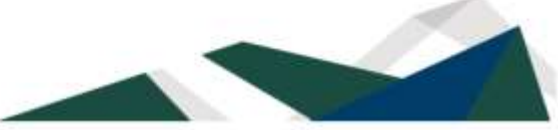

22 April 2015 – On the occasion of World Malaria Day 2015 (25 April), WHO is releasing the third edition of the *Guidelines for the treatment of malaria*. The updated guidelines provide evidence-based recommendations on the diagnosis and treatment of uncomplicated and severe malaria, and on the use of medicines to prevent malaria in high-risk groups.

[Download the updated guidelines](#)

[Read more about World Malaria Day](#)



¿Día Mundial de la lucha contra la Malaria?

- El Día Mundial de la **Malaria** (25 de abril) es una ocasión para destacar la necesidad de que se mantenga *el compromiso político* y se siga *invirtiendo en el control y la eliminación de la enfermedad*.
 - Asimismo, es una oportunidad para que nuevos donantes se unan a la *lucha* mundial contra la enfermedad y para que las *instituciones académicas y de investigación* den a conocer sus trabajos científicos.
 - Este año la OMS presentará nuevas directrices sobre el tratamiento de la malaria y pondrá en destaque su proyecto de estrategia técnica para **2016-2030**, cuya adopción será sometida a la consideración de la **Asamblea Mundial de la Salud en mayo de 2015**.
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Arnoldo Gabaldón

*Invertir en
el Futuro.
Vencer a la
Malaria.*



Sornchai Looareesuwan

Diapositivas disponibles en:
<http://blog.utp.edu.co/arodriguezm>

Thanks Gracias

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