



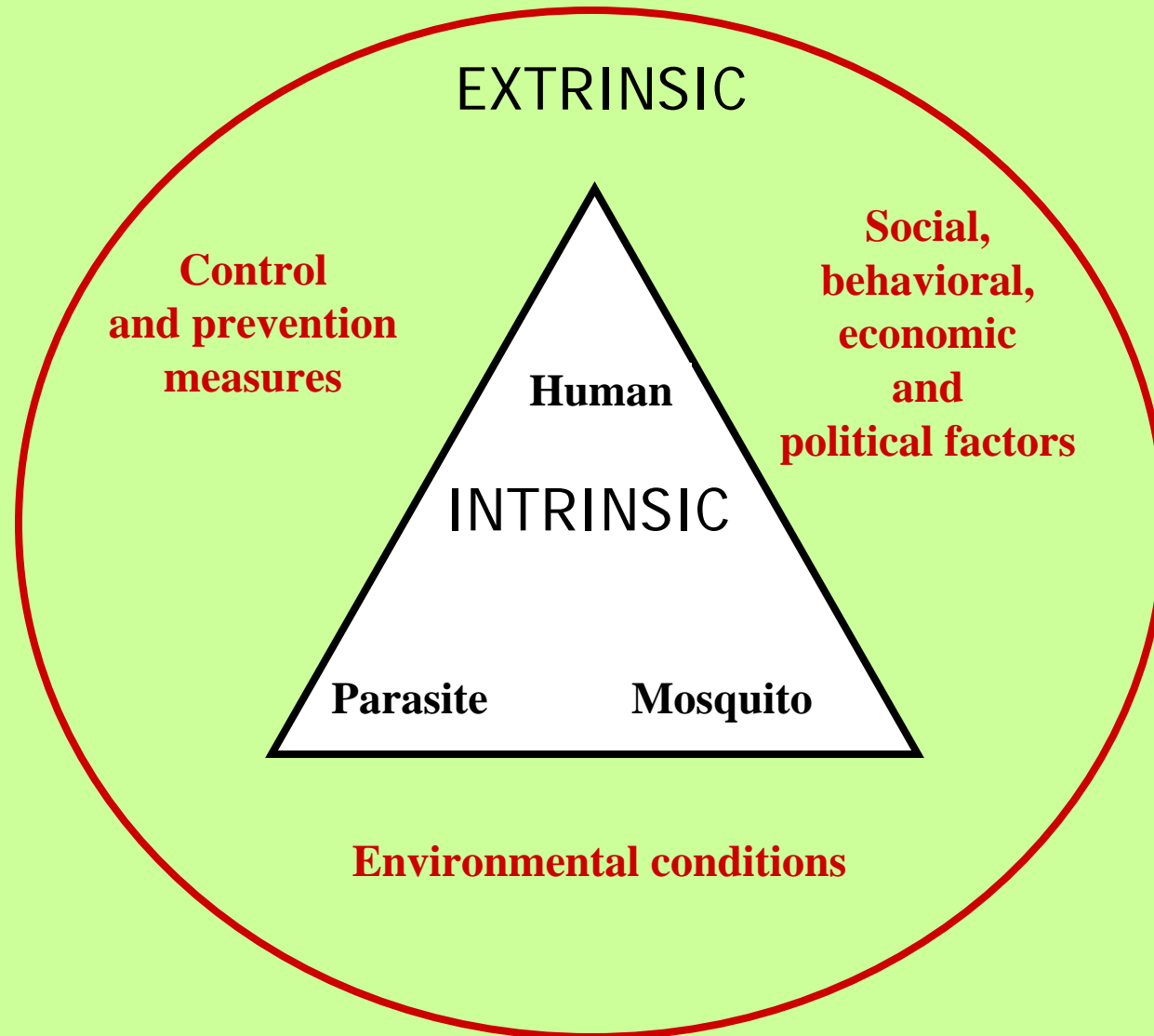
Malaria – The Peril and the Promise

Joel Breman, M.D., D.T.P.H.
Fogarty International Center
National Institutes of Health

Directors' Joint Consultative Committee Meeting

Arusha, Tanzania
July 25–28, 2006

Intrinsic and Extrinsic Factors Linked to the Malaria Burden





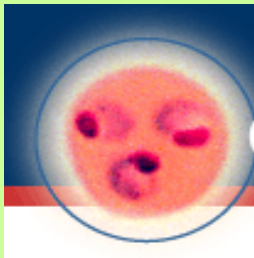
Malaria

- **Manifestations**
- **Burden**
- **Interventions**

Manifestations of the Malaria Burden



Infected Mosquito



Pregnancy



Severe illness

Acute febrile illness

Infected Human

Chronic effects

Fetus

Maternal

Anemia

Hypoglycemia

Respiratory distress

Hypovolemia

Cerebral malaria

Long-term sequelae

Death

Anemia

Neurologic

Cognitive

Developmental

Impaired growth and development

Malnutrition

Low birth weight

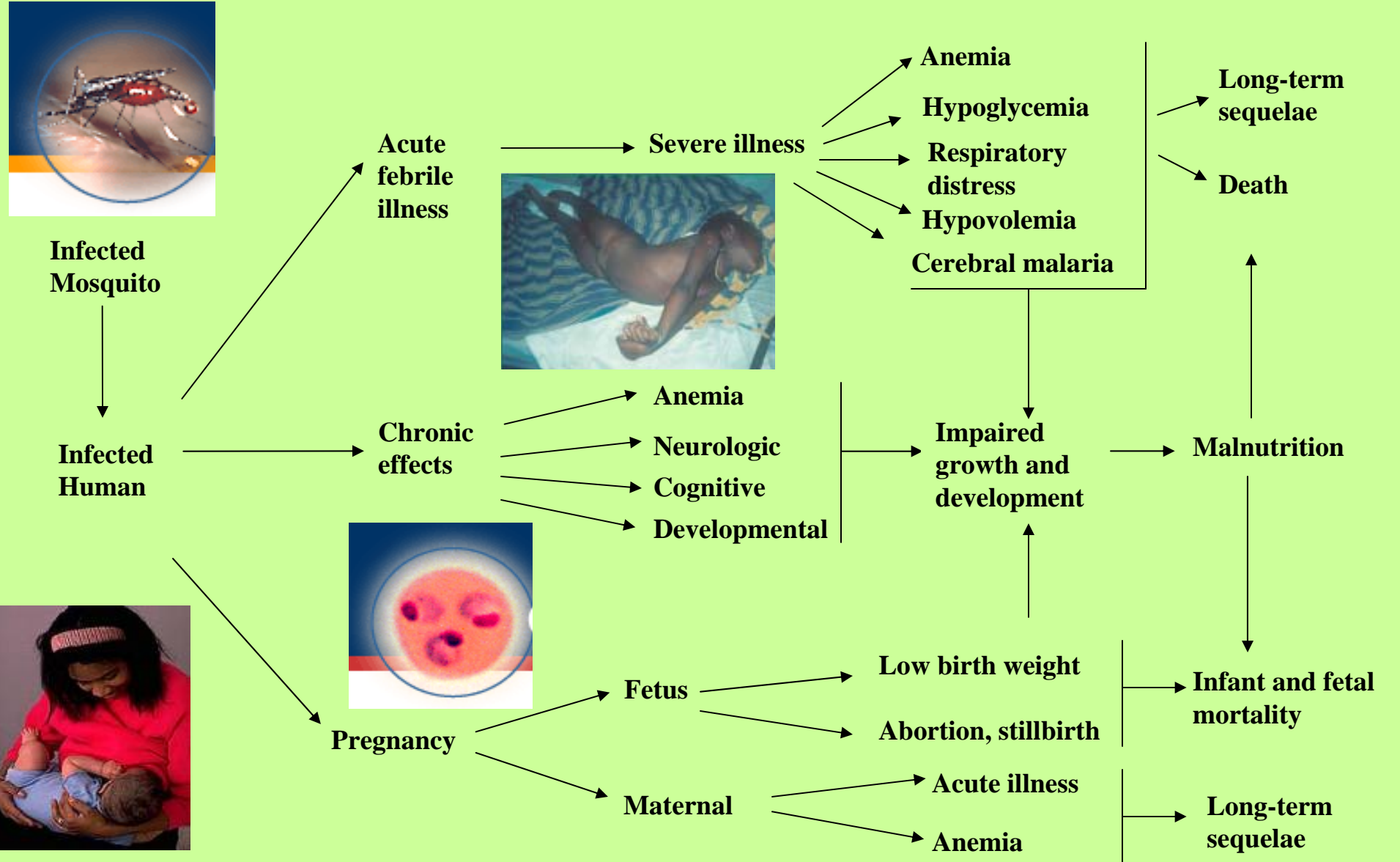
Abortion, stillbirth

Infant and fetal mortality

Acute illness

Anemia

Long-term sequelae



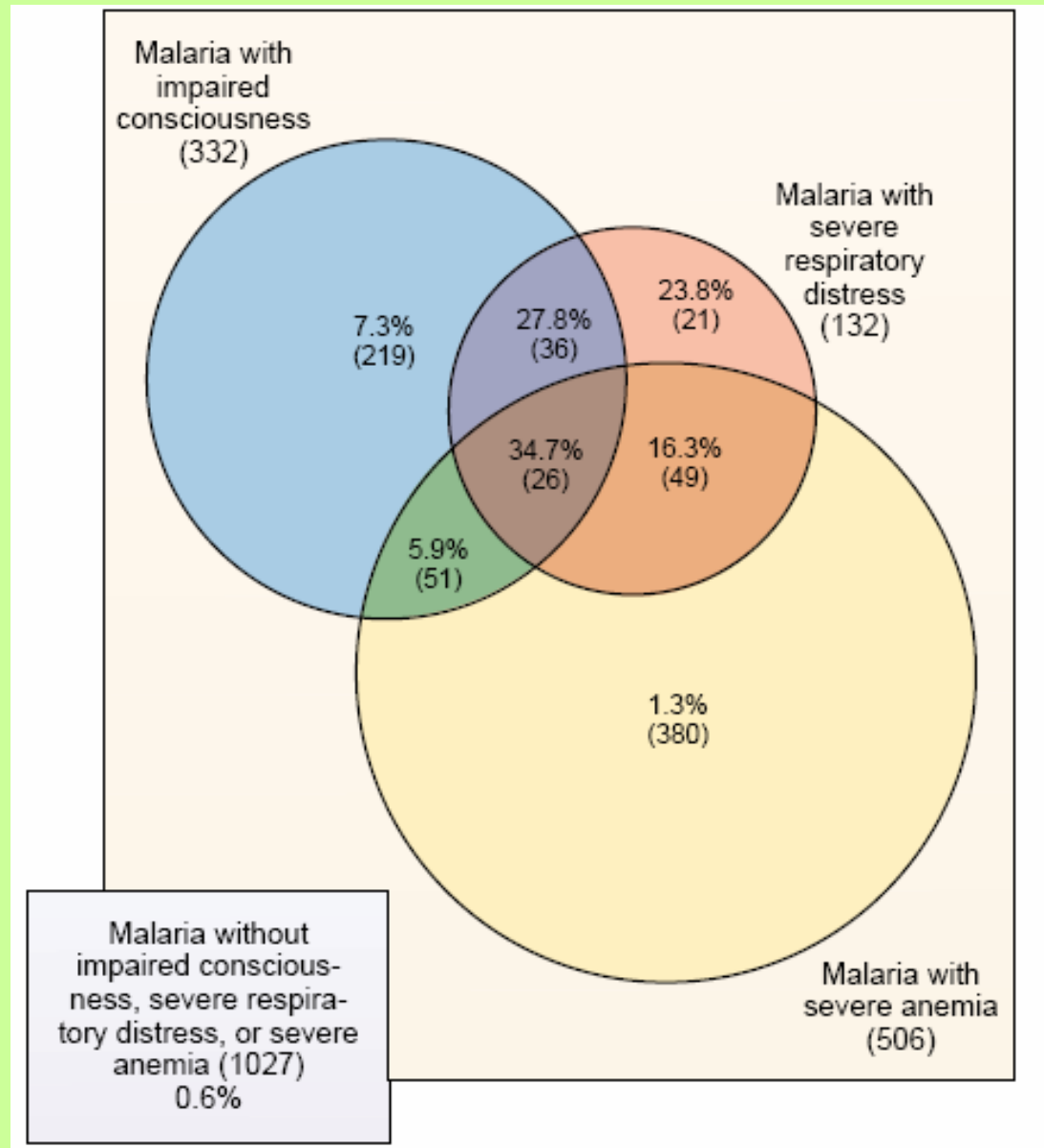
Deaths from Malaria: Children Under Five and Total, Africa 2001

Cause of malaria-related death	Number of malaria deaths
● Under fives	
Cerebral malaria	110,000
Severe anemia	190,000-974,000
Respiratory distress	110,000
Hypoglycemia	153,000-267,000
Low birth weight	62,000-363,000
Total deaths from malaria	625,000-1,824,000
● Total, all ages*	962,000-2,806,000

Sources Breman, Alilio and Mills, 2004; Murphy and Breman, 2001

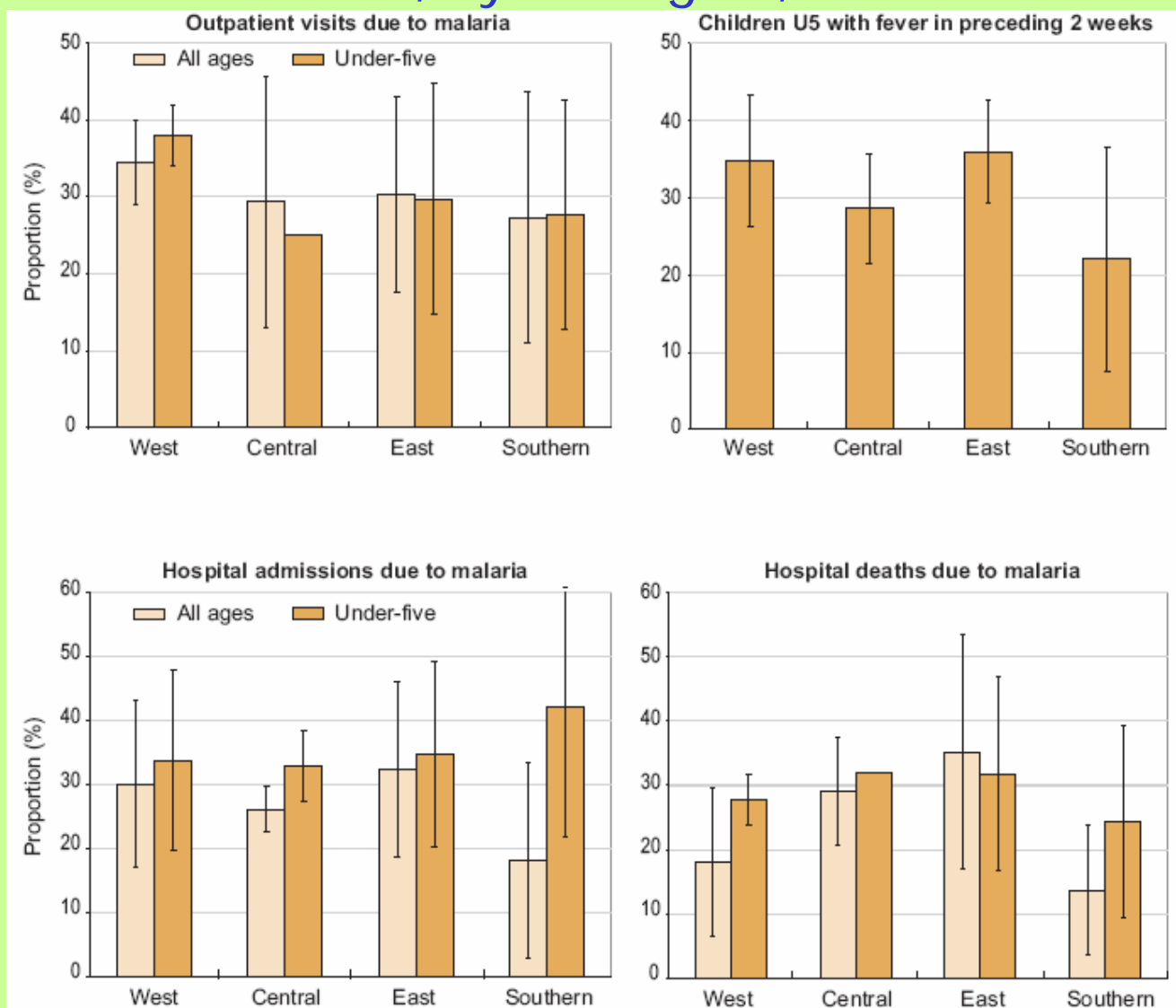
*Children under 5 represent 65 percent of all deaths in Africa as per Snow and others (2003).

Overlap for Major Clinical Subgroups of Severe Malaria



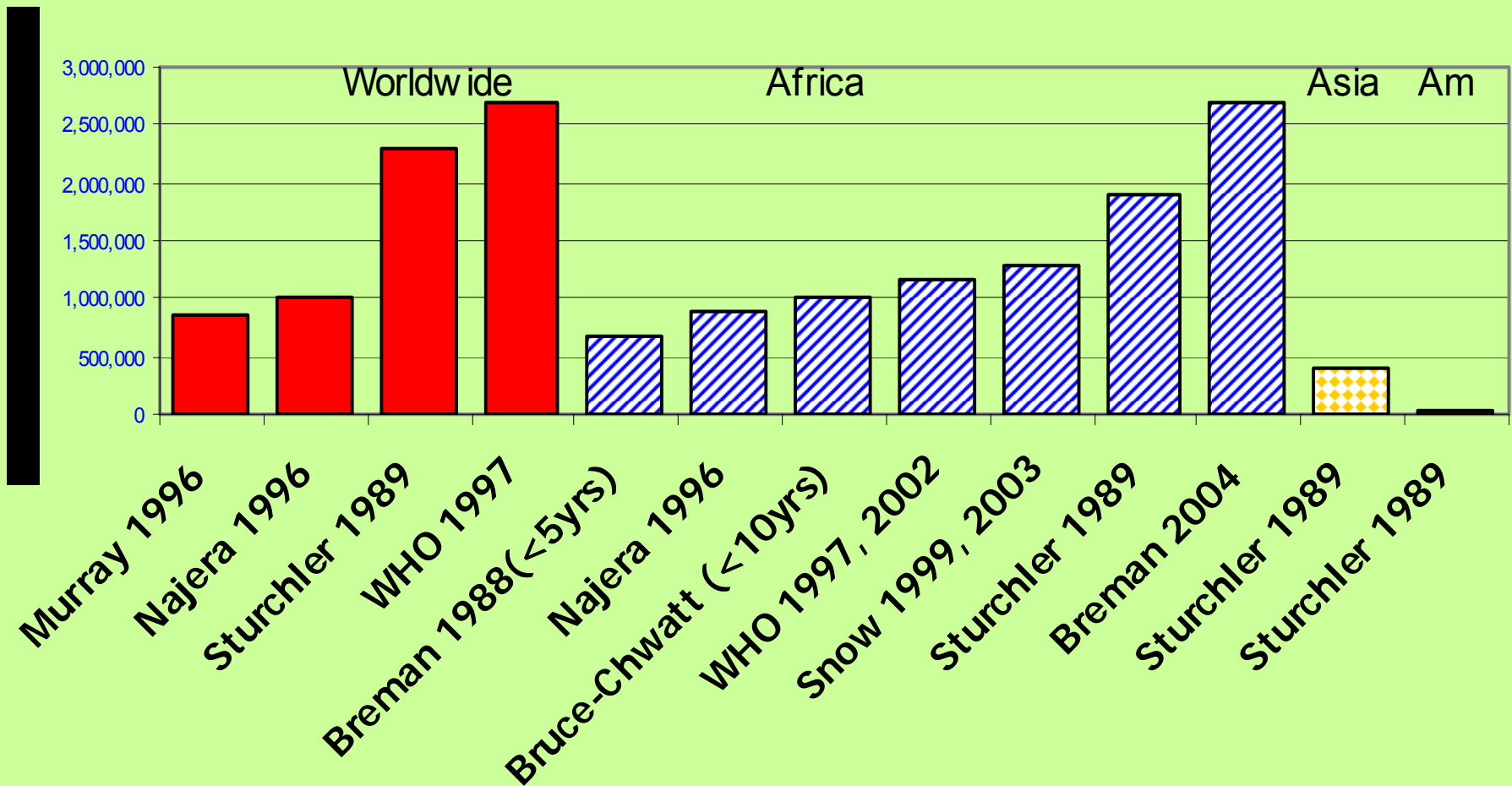
Marsh et al, NEJM 1995, () = number of patients

Figure 2. Burden of malaria on health systems in Africa south of the Sahara, by subregion, 1999-2004



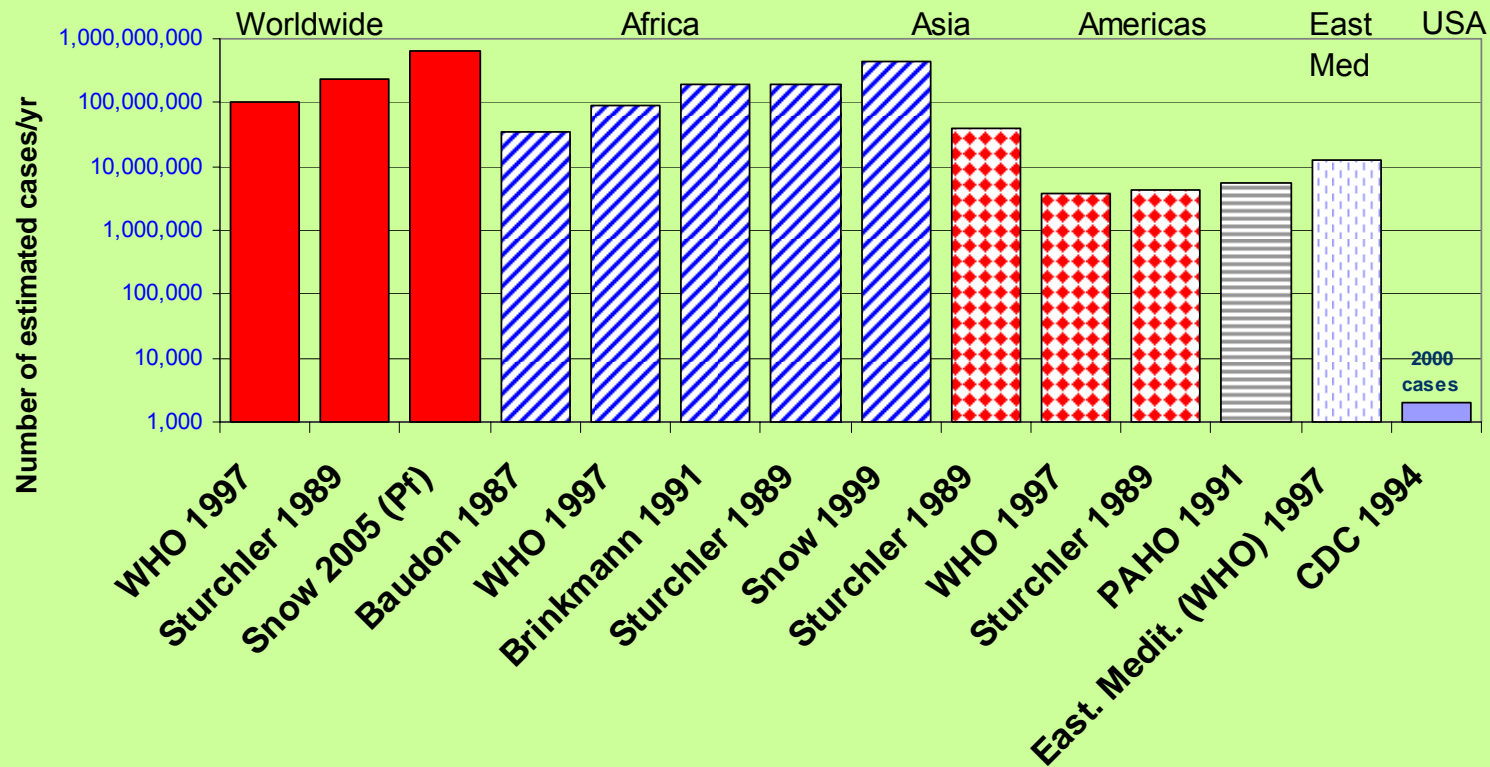
Proportion of outpatient visits, hospital admissions and hospital deaths due to malaria from national HIS data averaged from 2001 to 2003 or the 3 most recent years with available data since 1999 from countries in Africa south of the Sahara; proportion of children under 5 years of age with fever in the preceding 2 weeks from national DHS (11) and MICS (10) between 1999 and 2004 (median survey year 2000). Error bars indicate the standard deviation.

Estimated World and Regional Malaria Deaths, 1952-2004



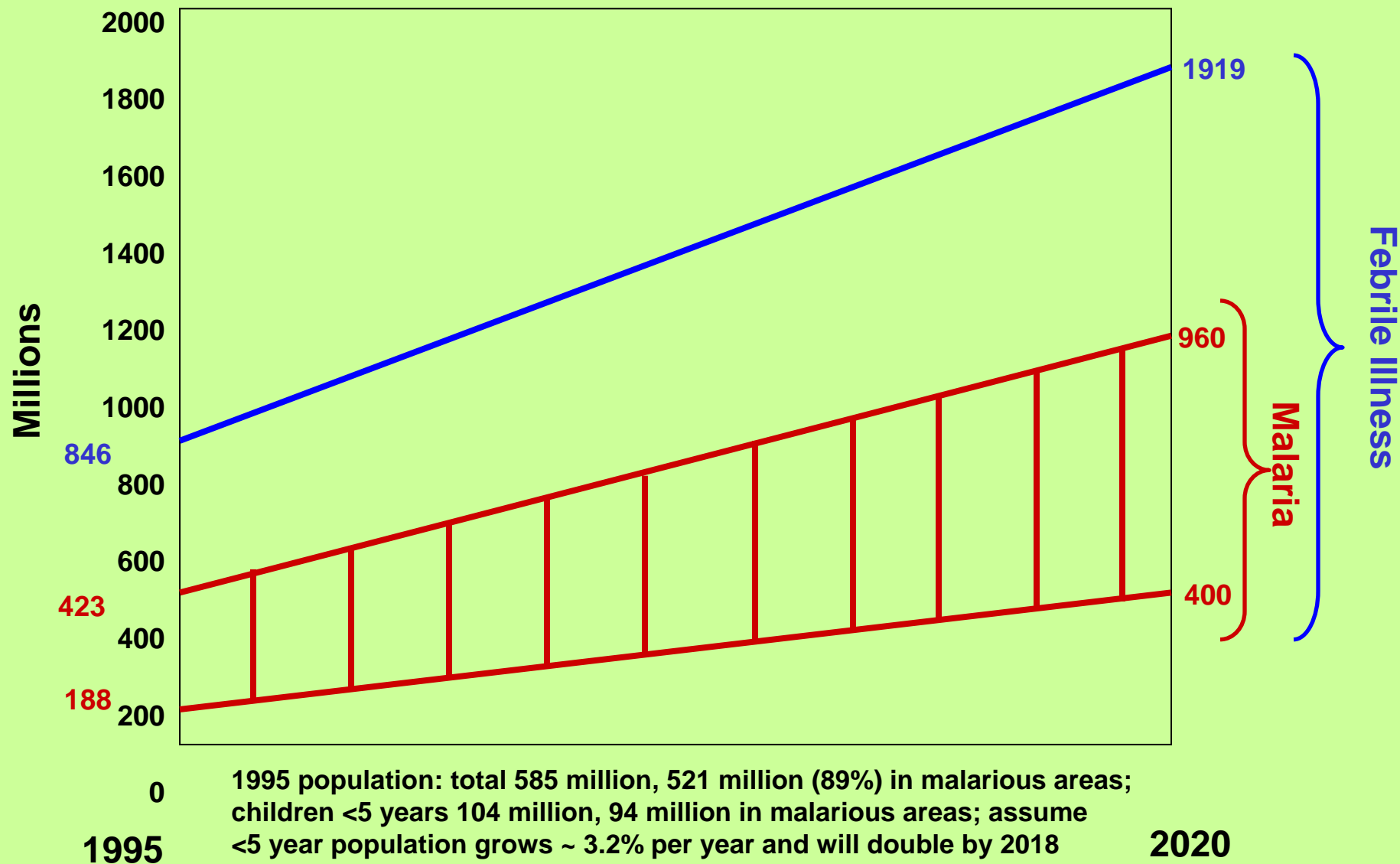
Breman, 2001, Breman, Alilio, Mills, 2004

Estimated World & Regional Malaria Cases, 1987-1999



Breman, 2001

Acute Febrile Episodes and Malaria-Associated Febrile Episodes in African Children 0-4 years Living in Endemic Areas, 1995-2020



Plasmodium falciparum in 2002

Clinical Cases

<u>Region</u>	Population at risk <u>(million)</u>	Cases (M) (%) <u>(million)</u>
Africa	521	365 (215 - 374) (57%)
Americas	55	4 (2 - 8) (1%)
South East Asia	1,314	119 (66 - 224) (34%)
Western Pacific	142	15 (9 - 26) (4%)
Eastern Med.	176	12 (5 - 25) (4%)
Europe	<u>4</u>	<u>1 (0 - 1) (<1%)</u>
Total	2,211	515 (298 - 659) (100%)

Snow et al, *Nature* 2005

Leading Causes of Disability-Adjusted Life Years (DALYs) in Sub-Saharan African Region, 2001

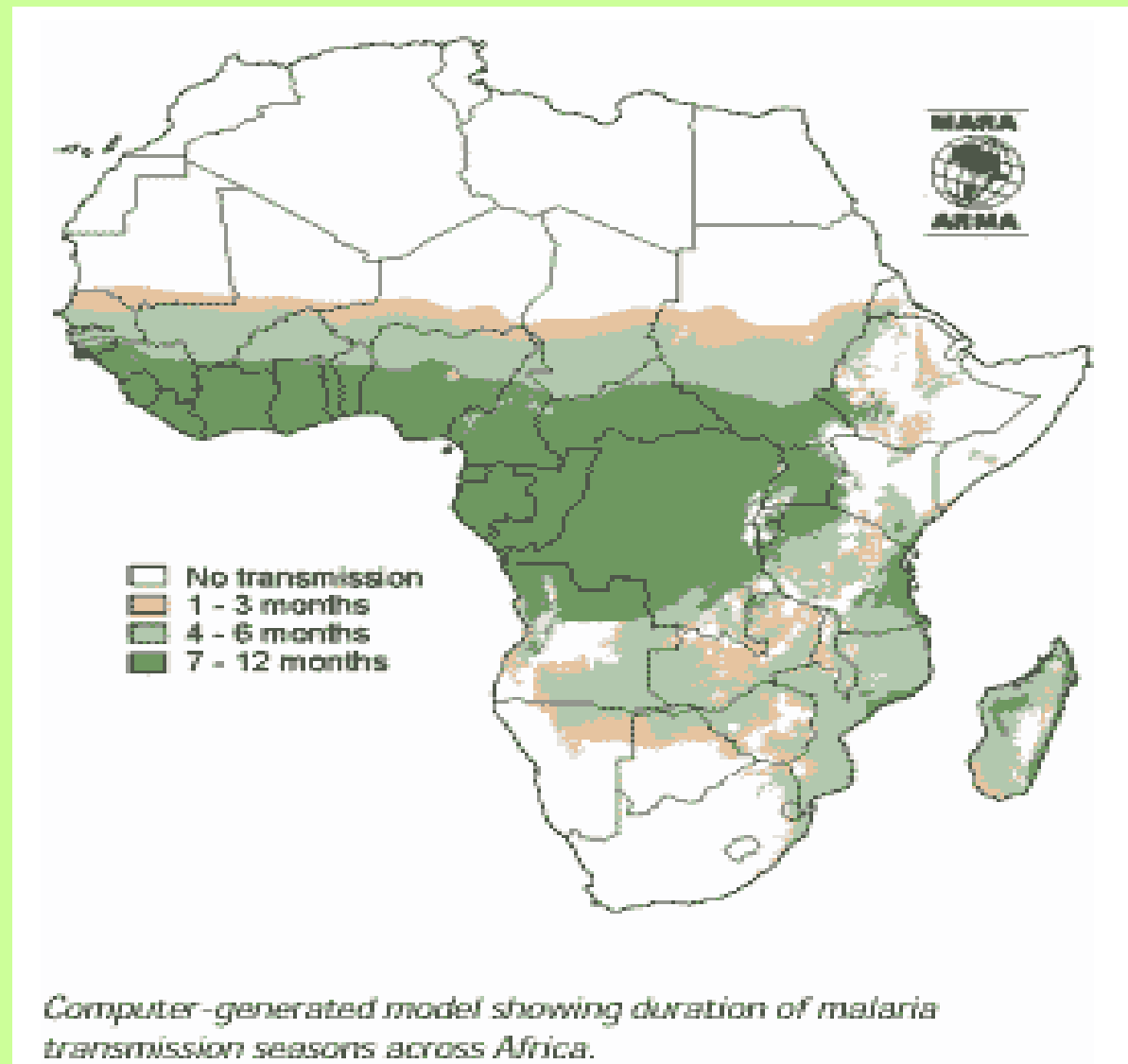
<u>Total DALYs</u>	<u>%</u>
1. HIV/AIDS	17.8
2. Malaria	10.3
3. Lower respiratory infections	8.4
4. Perinatal conditions	6.3
5. Diarrheal diseases	6.1
6. Measles	4.6
7. Tuberculosis	2.4
8. Whooping cough	1.9
9. Road traffic accidents	1.8
10. Protein-energy malnutrition	<u>1.6</u>
Total	61.2

Source: Mathers, et al., 2005 (DCPP Web site)

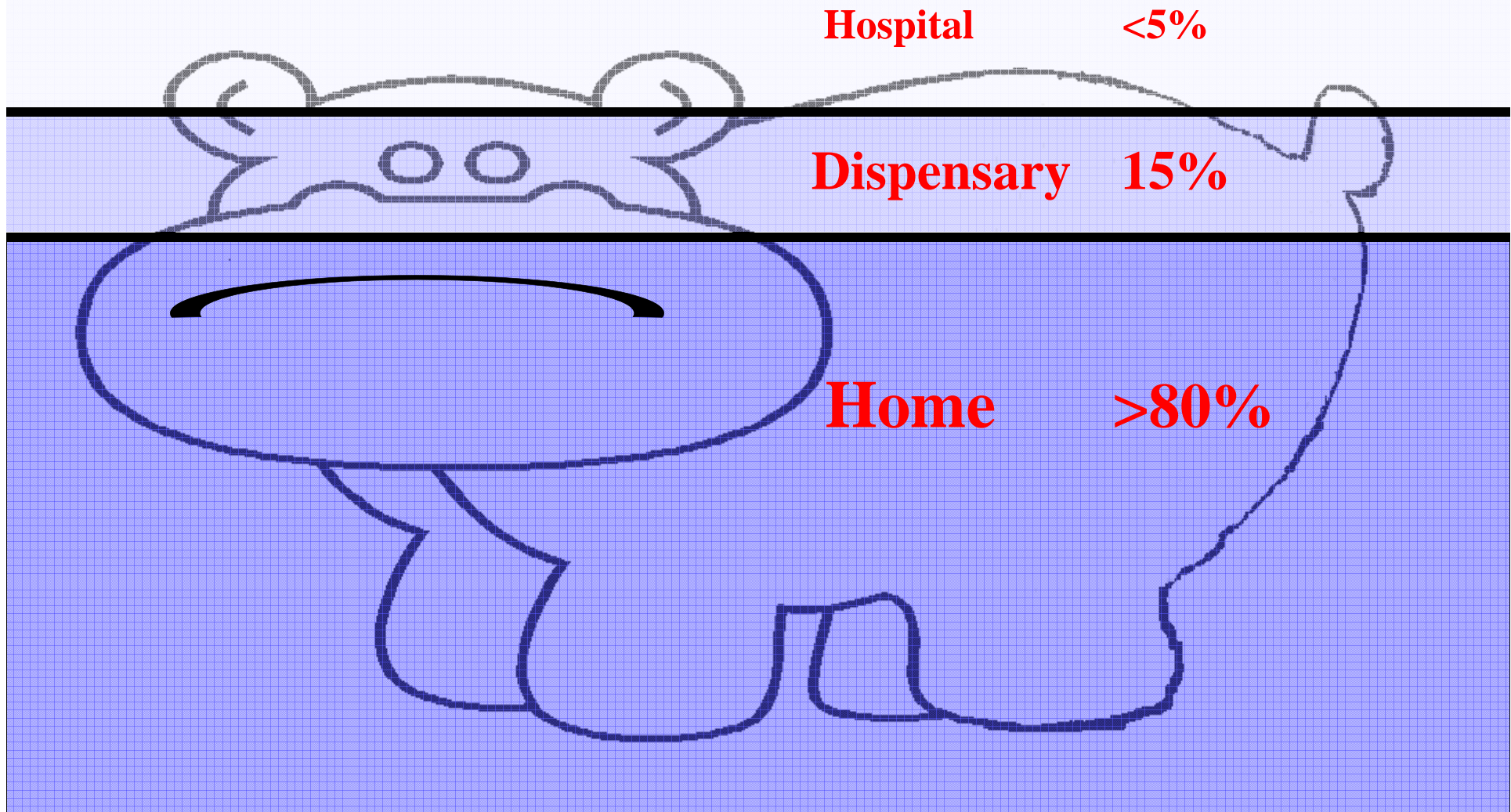


JOHN E. FOGARTY
INTERNATIONAL
CENTER

MARA/ARMA Model of Malaria Transmission, 2003

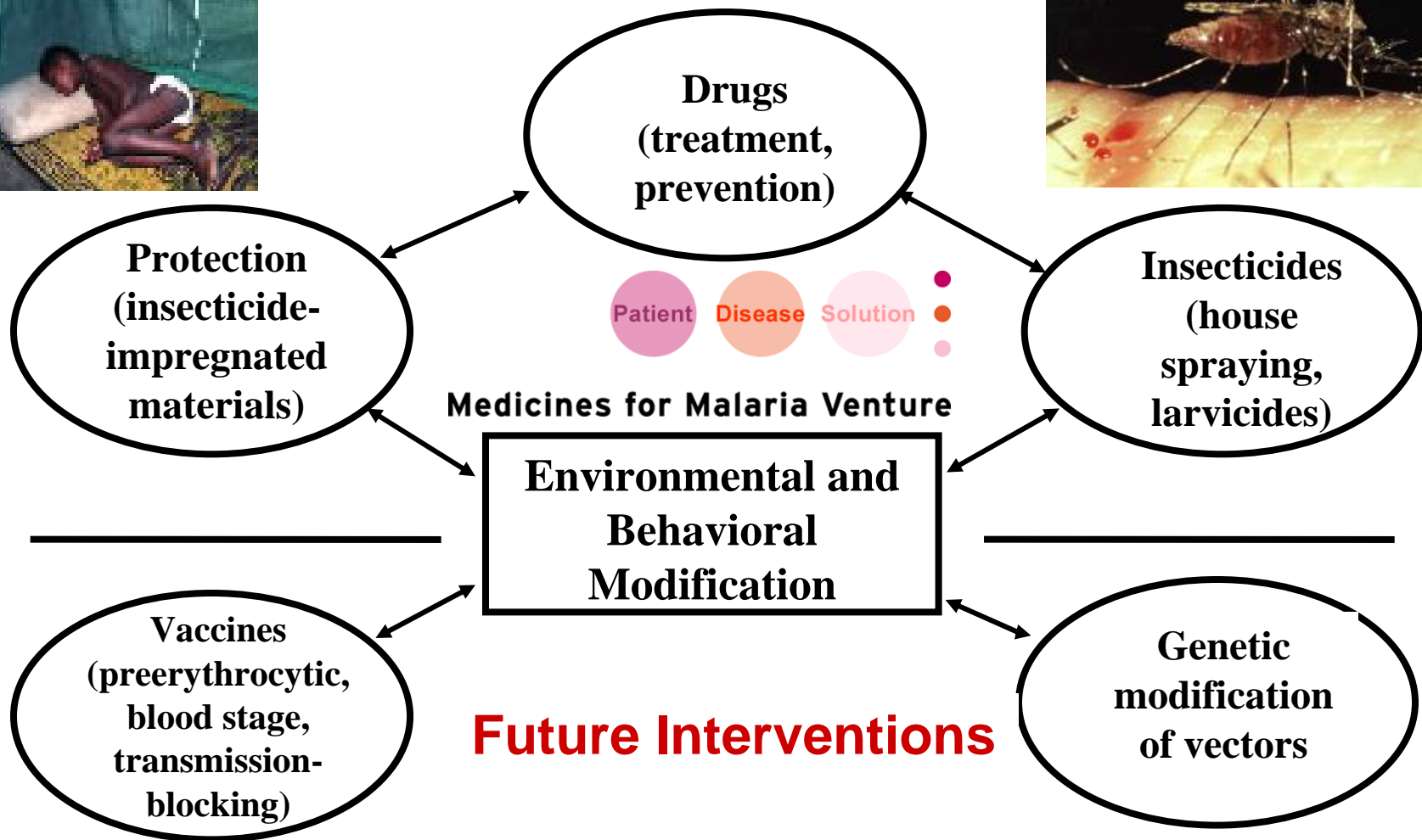
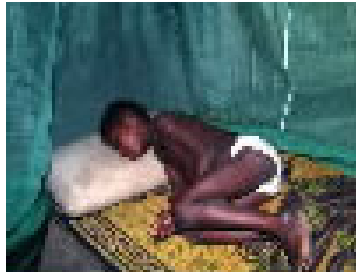


“The Ears of the Hippopotamus” Where Malaria Patients are Managed... and Die



Control of the Malaria Burden

Current Interventions



Roll Back Malaria's Strategy and Goals for 2005

Box 1: The goal of Roll Back Malaria is to halve the burden of malaria by 2010.

The following targets for specific intervention strategies were established at the Abuja Malaria Summit, April 2000

RBM strategy

- Prompt access to effective treatment
- Insecticide-treated nets (ITNs)

Abuja target (by 2005)

- 60% of those suffering with malaria should have access to and be able to use correct, affordable, and appropriate treatment within 24 hours of the onset of symptoms
- 60% of those at risk for malaria, particularly children under 5 years of age and pregnant women, will benefit from a suitable combination of personal and community protective measures, such as ITN

a: The original Abuja declaration included the recommendation for chemoprophylaxis as well, but present WHO and RBM policy strongly recommends IPT, and not chemoprophylaxis, for prevention of malaria during pregnancy.

Roll Back Malaria's Strategy and Goals for 2005

Box 1: The goal of Roll Back Malaria is to halve the burden of malaria by 2010.

The following targets for specific intervention strategies were established at the Abuja Malaria Summit, April 2000

RBM strategy

- Prevention and control of malaria in pregnant women

- Malaria epidemic and emergency response

Abuja target (by 2005)

- 60% of pregnant women at risk of malaria will be covered with suitable combinations of personal and community protective measures, such as ITN

- 60% of pregnant women at risk of malaria will have access to intermittent preventive treatment^a

- 60% of epidemics are detected within 2 weeks of onset

- 60% of epidemics are responded to within 2 weeks of detection

a: The original Abuja declaration included the recommendation for chemoprophylaxis as well, but present WHO and RBM policy strongly recommends IPT, and not chemoprophylaxis, for prevention of malaria during pregnancy.

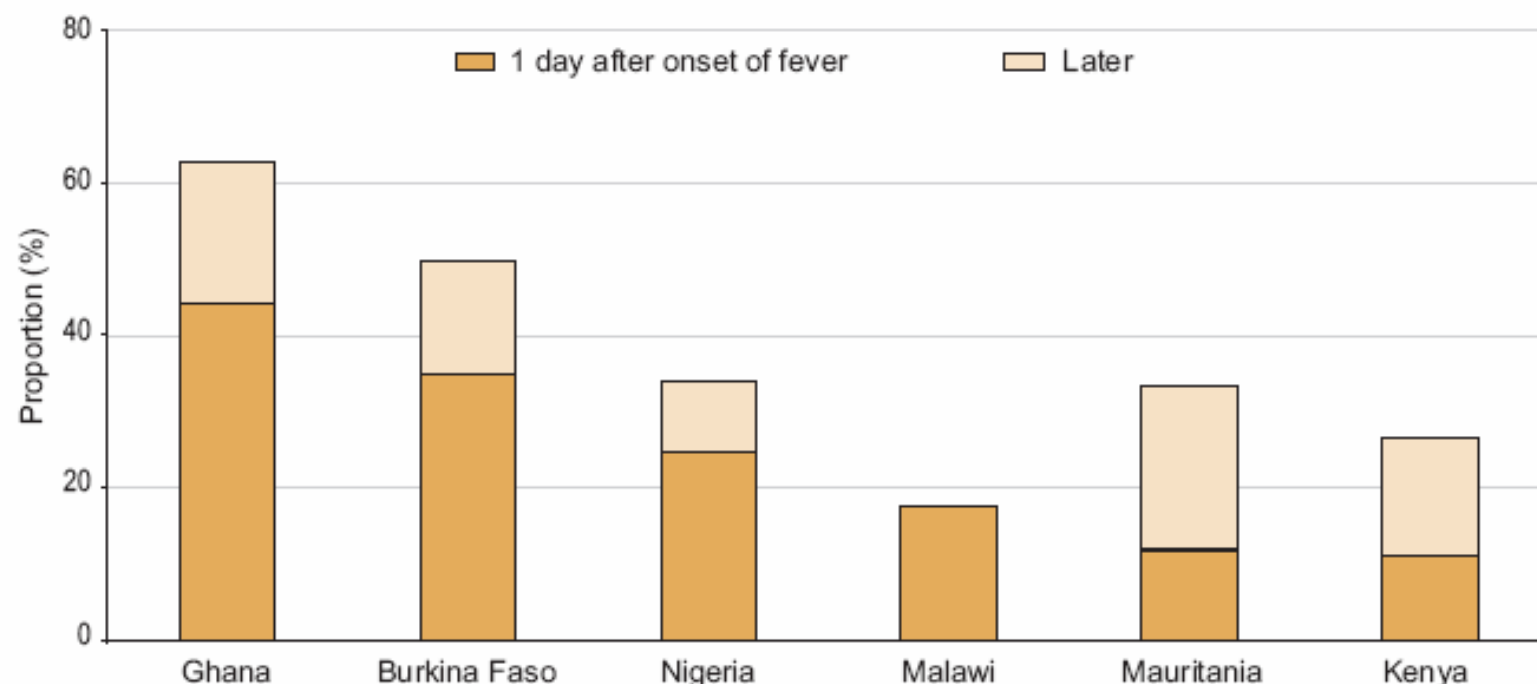
Table 5. Priority Malaria Control Strategies, by Epidemiological Setting

Epidemiological setting	Control strategy
<p>Stable endemic malaria</p> <p><i>Example:</i> large parts of East, Central and West Africa, Papua New Guinea, Solomon Islands and Vanuatu</p>	<p>Prevention</p> <ul style="list-style-type: none"> - ITNs for children under 5 years of age, pregnant women and people living with HIV/AIDS - IRS, where appropriate - IPT in pregnancy <p>Treatment</p> <ul style="list-style-type: none"> - Early and effective case management including presumptive treatment for suspected cases and home management where appropriate

Table 5. Priority Malaria Control Strategies, by Epidemiological Setting

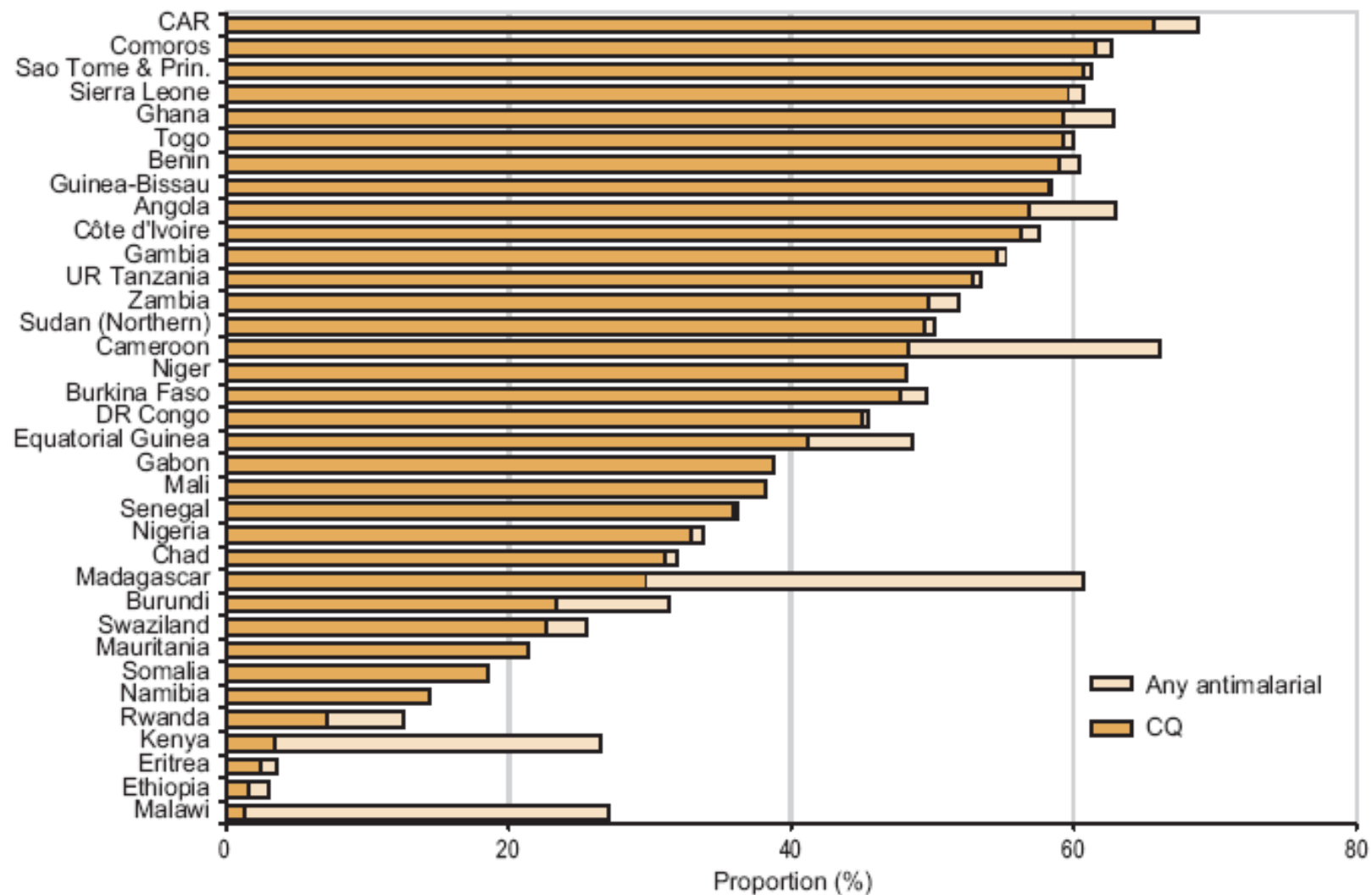
Epidemiological setting	Control strategy
Unstable malaria <i>Example:</i> parts of Southern Africa, Transcaucasia, Central Asia and the Americas; highland and desert fringe areas, some urban areas, plantations, irrigation schemes	Prevention - IRS - Larviciding - Environmental management - ITNs Treatment - Early and effective case management in suspected cases - Diagnostics to confirm cases, if possible before treatment

Figure 11. Proportion of children under 5 years of age in selected African countries treated with an antimalarial starting within 1 day after onset of fever or later, 2003-2004



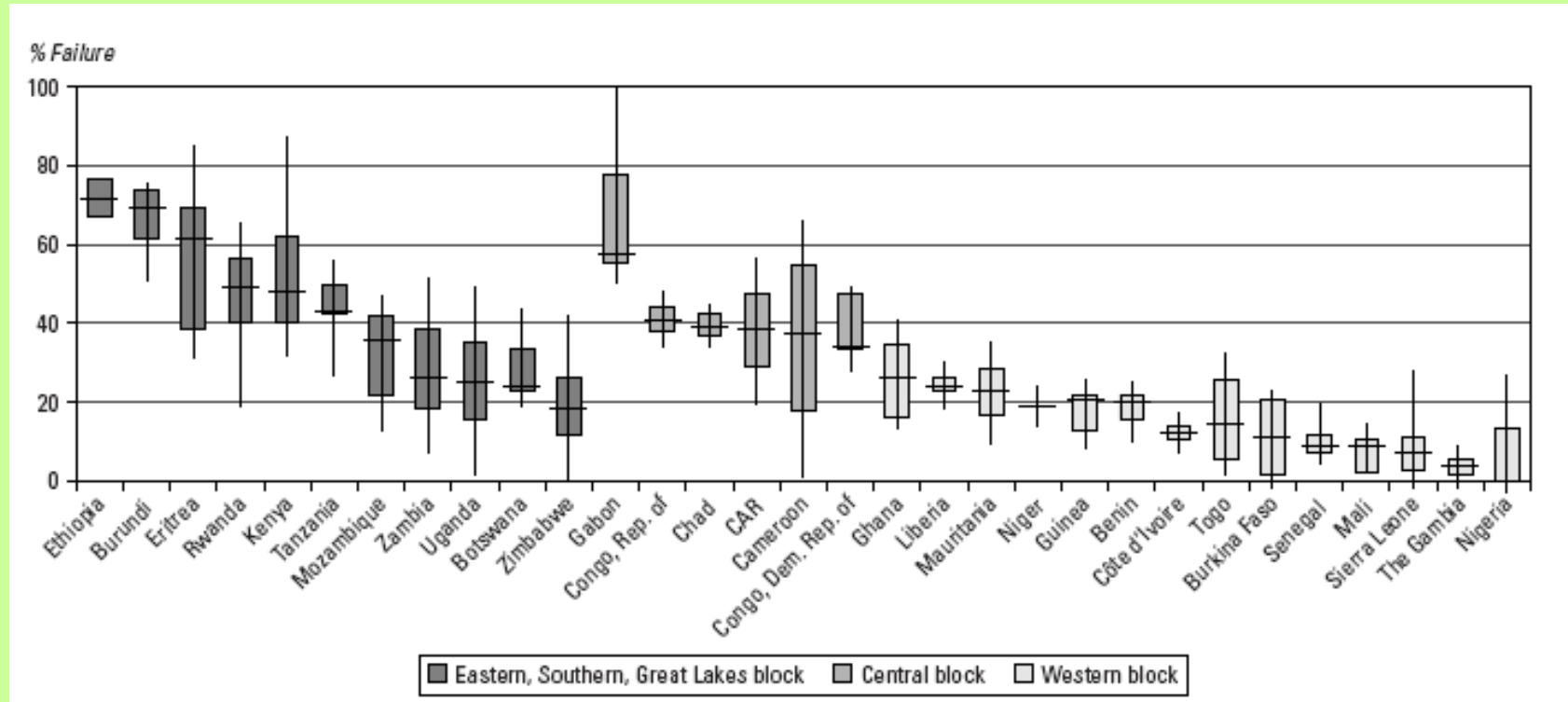
Data from most recent national household survey, either DHS (11) conducted in 2003 or 2004, and a survey by the MoH in 2004 for Malawi. In the Malawi survey, the coverage of antimalarial treatment starting more than one day after onset of fever was not measured.

Figure 10. Proportion of children under 5 years of age with fever treated with any antimalarial or with chloroquine in countries in Africa south of the Sahara, 1999-2004



Data from most recent national household survey either DHS (11) or MICS (11). Median survey year is 2001.

Figure 21.2 Chloroquine Treatment Failure in Africa, 1997-2002



Source: WHO 2005.

Note: WHO has established 126 sentinel sites in 36 African countries that monitor the efficacy of locally used antimalarial drugs by following patients in clinics.

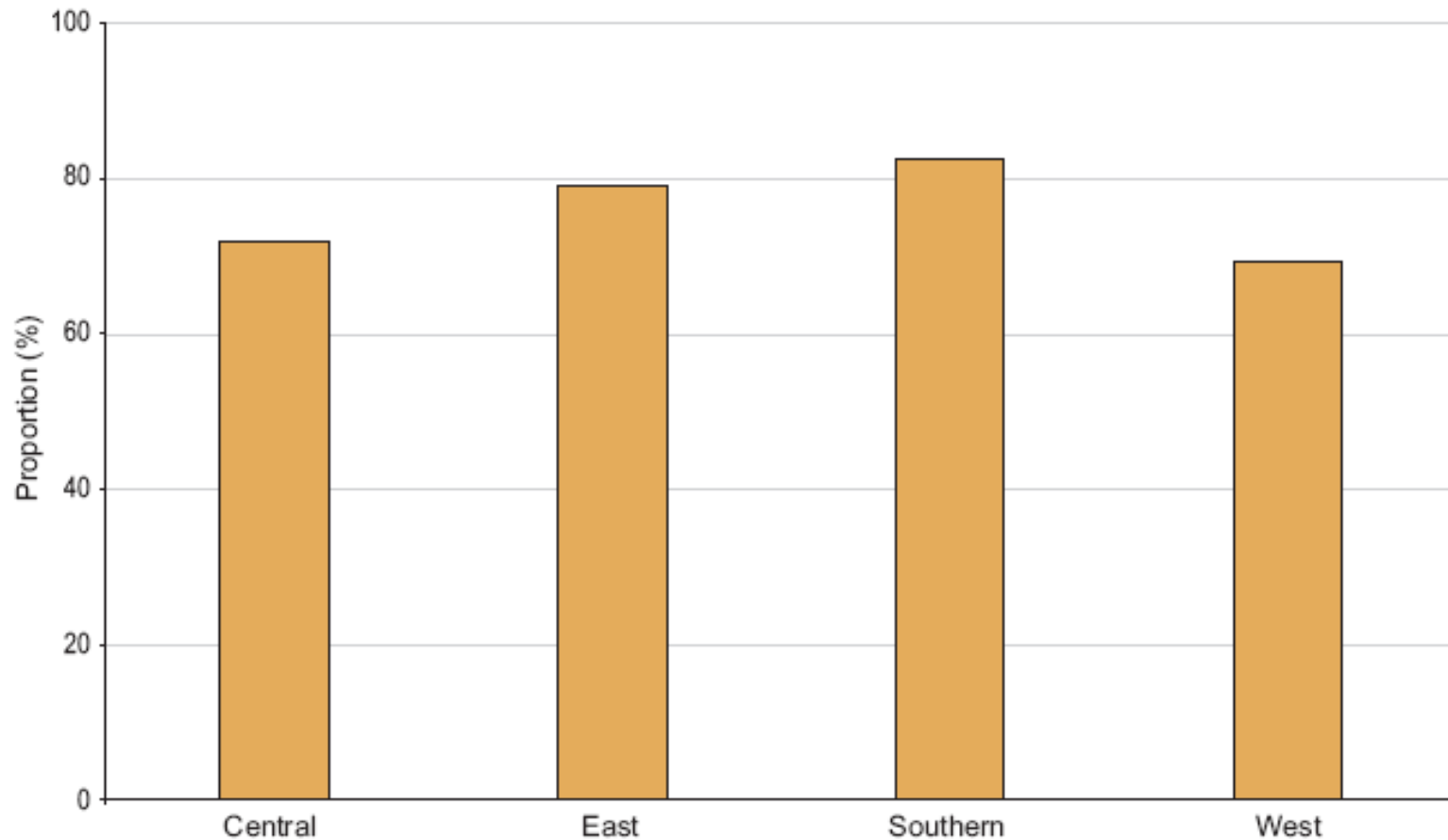
The box indicates the 25th-75th percentile, the vertical line the lower and upper values, and where the lines cross the median.

Table 21.5. Change in First-Line Drug

Scenario	Current drug policy			New drug policy		
	First-line drug	Second-line drug	Third-line drug	First-line drug	Second-line drug	Third-line drug
A	Chloroquine	SP	Quinine	SP	Amodiaquine	Quinine
B	Chloroquine	SP	Quinine	ACT	Amodiaquine	Quinine
C	SP	Amodiaquine	Quinine	ACT	Amodiaquine	Quinine

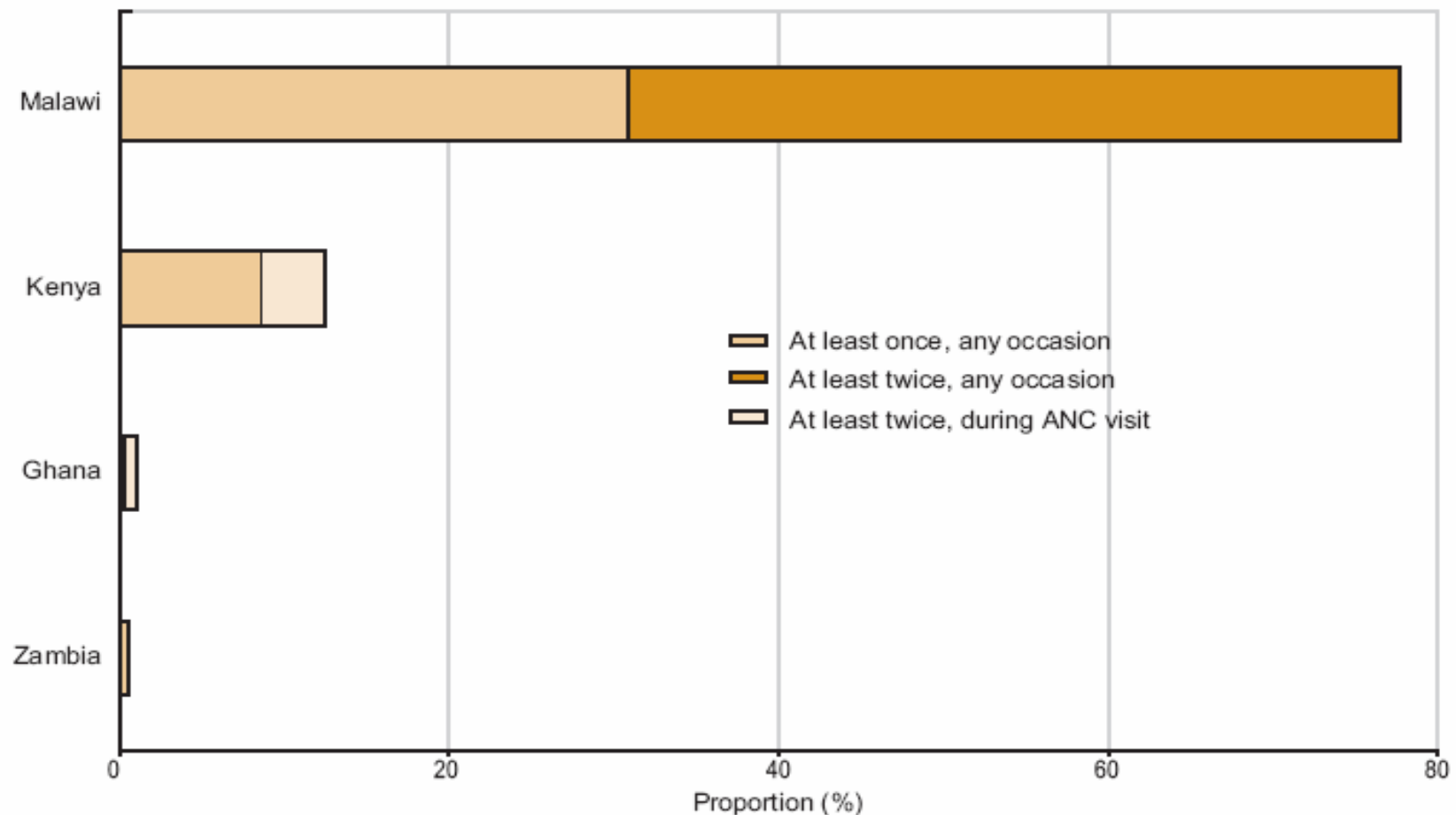
Source: Authors.

Figure 12. Proportion of pregnant women in Africa who receive antenatal care at least twice, based on national surveys, by subregion, 1995-2004



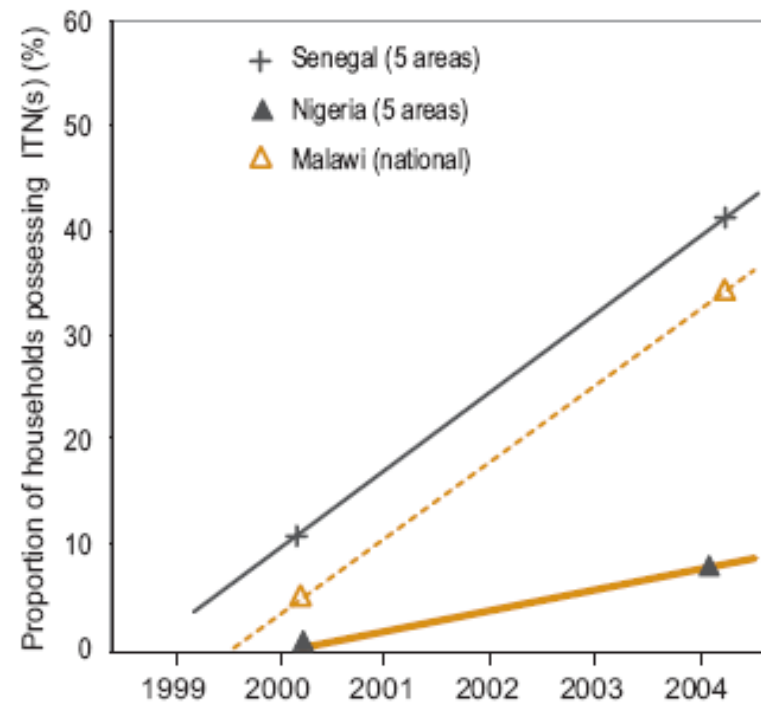
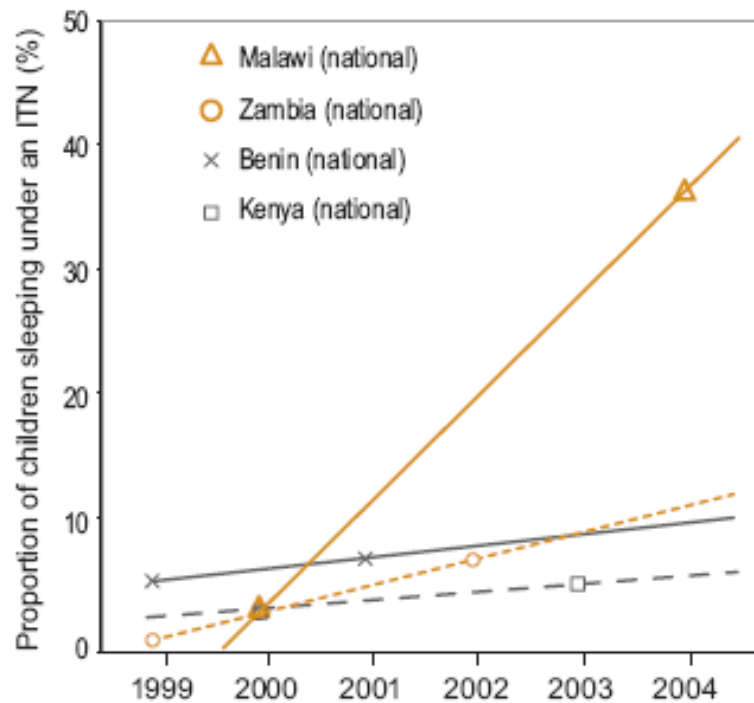
Data are from the most recent DHS ($n = 29$ surveys); median survey year is 2000.

Figure 13. Proportion of pregnant women receiving sulfadoxine-pyrimethamine based on national surveys conducted in African countries, 2002-2004



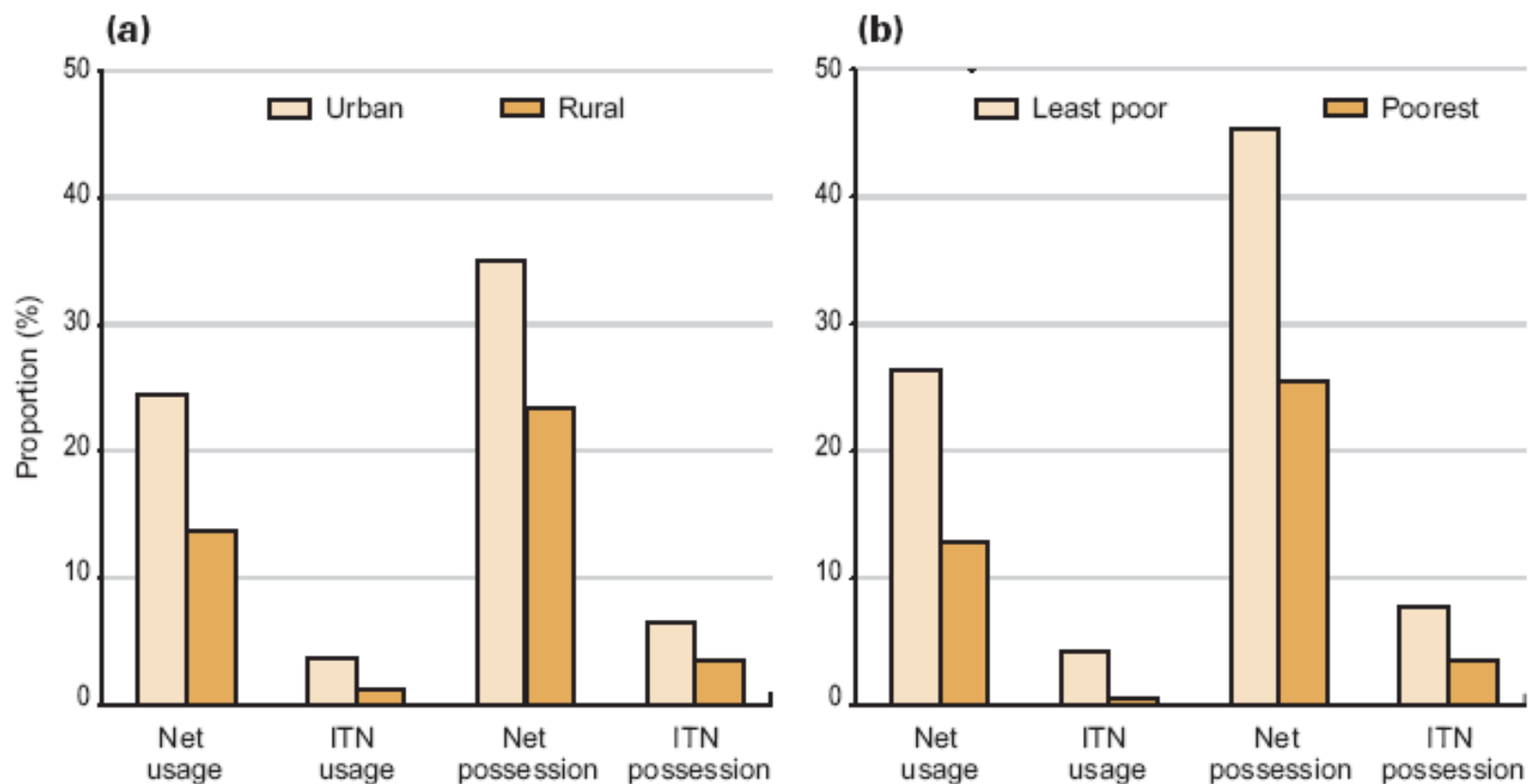
Median survey year is 2003 and includes countries where IPT implementation is currently underway or planned for the whole country. Surveys reflect DHS 2002 (Zambia), DHS 2003 (Ghana, Kenya) and MoH 2004 (Malawi). IPT was adopted in Ghana in 2004 and implementation began at the end of the year.

Figure 4. Time trends in ITN coverage in selected African countries with multiple data points, 1999-2004



Data for Benin, Kenya and Zambia from national DHS or MICS (10, 11); data for Nigeria and Senegal from Netmark surveys in selected areas with malaria (12); data for Malawi from DHS in 2000 (11) and a nationally representative survey by the MoH in 2004. Symbols indicate survey data; lines indicate estimated linear time trends based on the survey data.

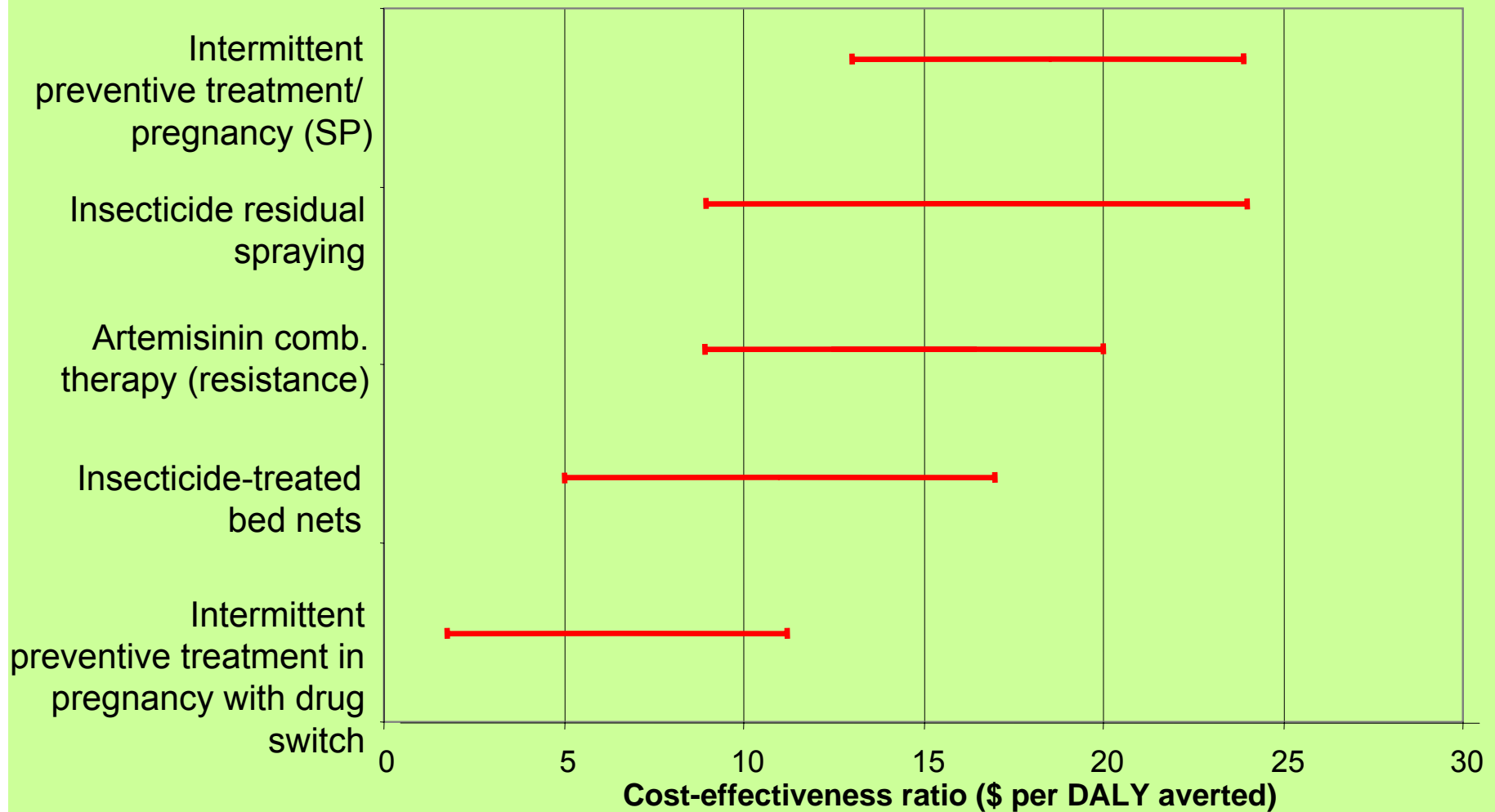
Figure 6. Median net and ITN possession (as % of households) or usage (as % of children under 5 years of age that slept under a net or ITN the night before a survey) in selected African countries by urban and rural division (a) and among the 20% poorest and 20% least poor households (b)



Data from national household surveys conducted between 1999 and 2004: urban/rural: net usage from 36 surveys, ITN usage from 34 surveys, net possession from 17 surveys, ITN possession from 8 surveys; poorest/least poor households: net usage from 25 surveys, ITN usage from 25 surveys, net possession from 6 surveys, ITN possession from 4 surveys.



Cost-Effectiveness of Interventions Against Malaria in Sub-Saharan Africa



Laxminarayan et al (DCPP authors), 2006, in Jamison et al, *Disease Control Priorities in Developing Countries*, 2nd ed.

Table 21.6. CERs for ITNs, IRS, and IPT

Intervention	Mean cost per DALY averted	90 percent range
<i>ITNs (net + insecticide treatment)</i>		
Deltamethrin	11	5-21
Permethrin (1 treatment)	12	6-20
Permethrin (2 treatments)	17	9-31
<i>ITNS (without provision of nets)</i>		
Deltamethrin	5	2-7
Permethrin (1 treatment)	6	3-9
Permethrin (2 treatments)	11	6-17
<i>IRS (1 round)</i>		
Malathion	12	8-18
DDT	9	5-13
Deltamethrin	10	6-14
Lambda-cyhalothrin	10	6-14

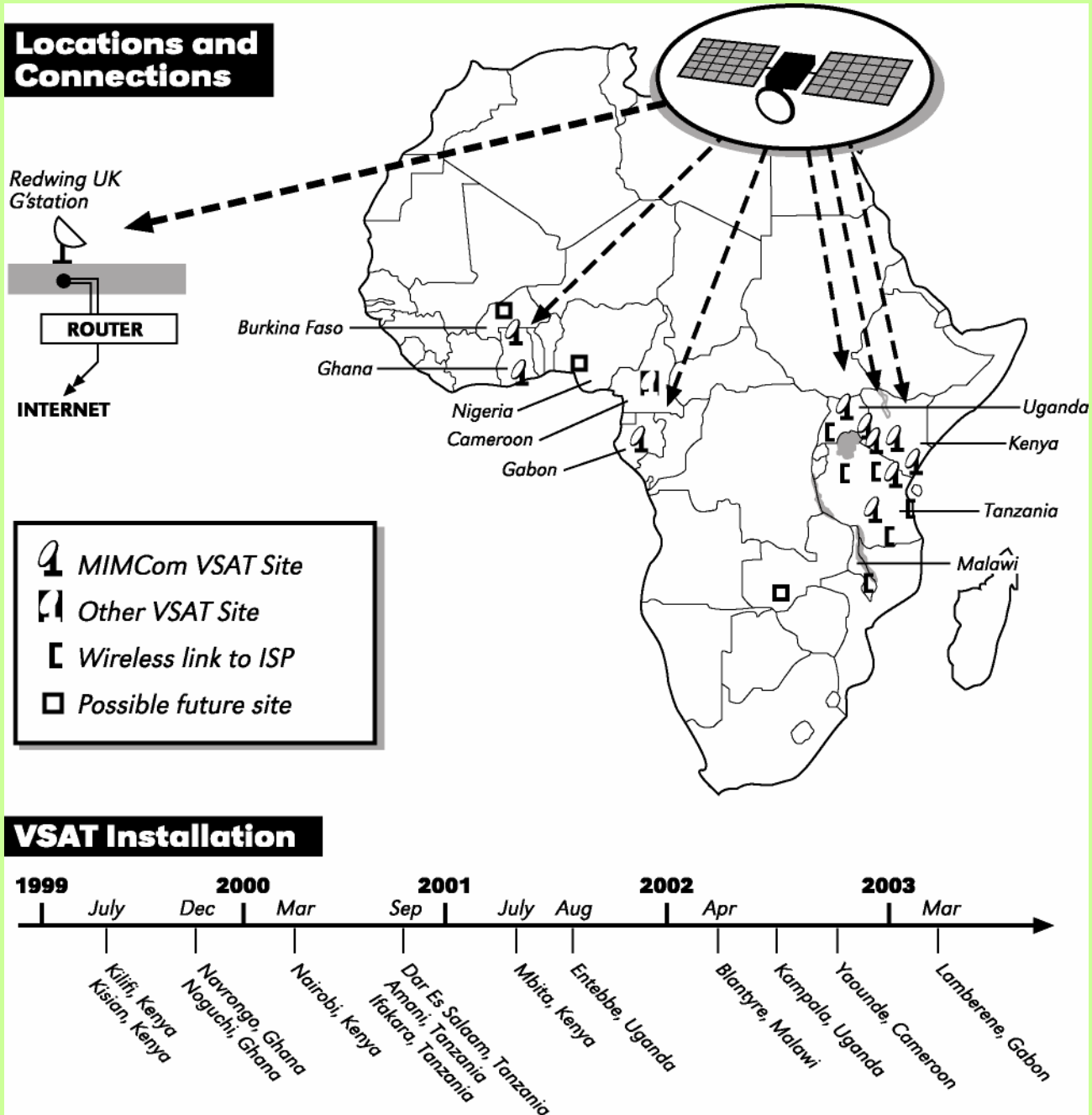
Table 21.6. CERs for ITNs, IRS, and IPT (2)

Intervention	Mean cost per DALY averted	90 percent range
<i>IRS (2 rounds)</i>		
Malathion	24	15-34
DDT	17	11-24
Deltamethrin	18	12-27
Lambda-cyhalothrin	19	12-28
<i>IPT</i>		
Incremental costs	13	9-21
Average costs	24	16-35

Table 6. Initiative to scale up ITN coverage started between 2001 and 2004

Togo, Zambia	Free distribution to children under 5 years of age during broader health campaigns including measles immunization (Box 4)
Malawi	Social marketing and distribution of highly subsidized ITNs through mother and child health clinics (Box 5)
United Republic of Tanzania	Subsidies in the form of discount vouchers delivered to pregnant women through antenatal clinics, in collaboration with the commercial sector
Benin, Eritrea, Ghana, Mali, Nigeria, Senegal	Distribution of free and highly subsidized ITNs through routine antenatal clinics and routine child-immunization (Expanded Programme on Immunization) clinics (Box 6); free mass (re-)treatment campaigns in Eritrea
Ghana, Malawi, Uganda, Zambia	National Child Health Days for distribution of ITNs and (re-)treatment, along with Vitamin A and/or deworming medication
Benin, Kenya, Madagascar, Mali, Nigeria, Rwanda, United Republic of Tanzania	Social marketing

Figure 2: MIMCom Sites





THE AMERICAN JOURNAL OF
***Tropical Medicine
and Hygiene***

Official Journal of the American Society of Tropical Medicine and Hygiene

Volume 71

August 2004

No. 2 Supplement

**The Intolerable Burden of Malaria:
II. What's New, What's Needed**

Sponsors:

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Disease Control Priorities in Developing Countries Project**

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Co-morbidity from Malaria

Mama Yemo Hospital, DR Congo 1985-1986

Admissions to pediatrics: 6,280

Diagnosis malaria 2,374 (38.2%)

Ages	<1 yr	1-4 yrs	5-9 yrs	10-13 yrs
%	21.4	49.2	23.0	5.6

Confirmed by blood smear + 74%
- 17
No slide 9

Co-morbidity from Malaria

Mama Yemo Hospital, DR Congo 1985-1986

Diagnosis only malaria	42.8%			
With anemia	22.2	} 42.6%		
“ gastroenteritis	10.6			
“ pneumonia	9.8			
Case fatality rate	21.1%			
Ages	<1 yr	1-4 yrs	5-9 yrs	10-13 yrs
%	31.8	20.4	14.8	13.5

* 62% of deaths occur in emergency ward

Table 1. Basic Malaria Monitoring and Evaluation Framework

Level	Area	Available information
Inputs (strategies, policies, guidelines, financing)	Policy and strategies Financing and disbursements	Policy, guidelines and strategies for malaria control put in place at national level (NMCPs, MoHs)
Processes (human resources, knowledge, attitudes, and practice)	Malaria-related commodities, including drugs	ACT procurement (UNICEF/WHO) Net/ITN/insecticide procurement (UNICEF/WHO)
Outputs (services delivered, knowledge, attitudes, and practice)	Services delivered	Insecticides used for malaria vector control (WHOPES from NMCPs) Drug efficacy and insecticide resistance (research studies, sentinel sites) Nets/ITNs sold or distributed (NMCPs) Nets (re-)treated (NMCPs) Antimalarial drugs distributed/used (NMCPs)

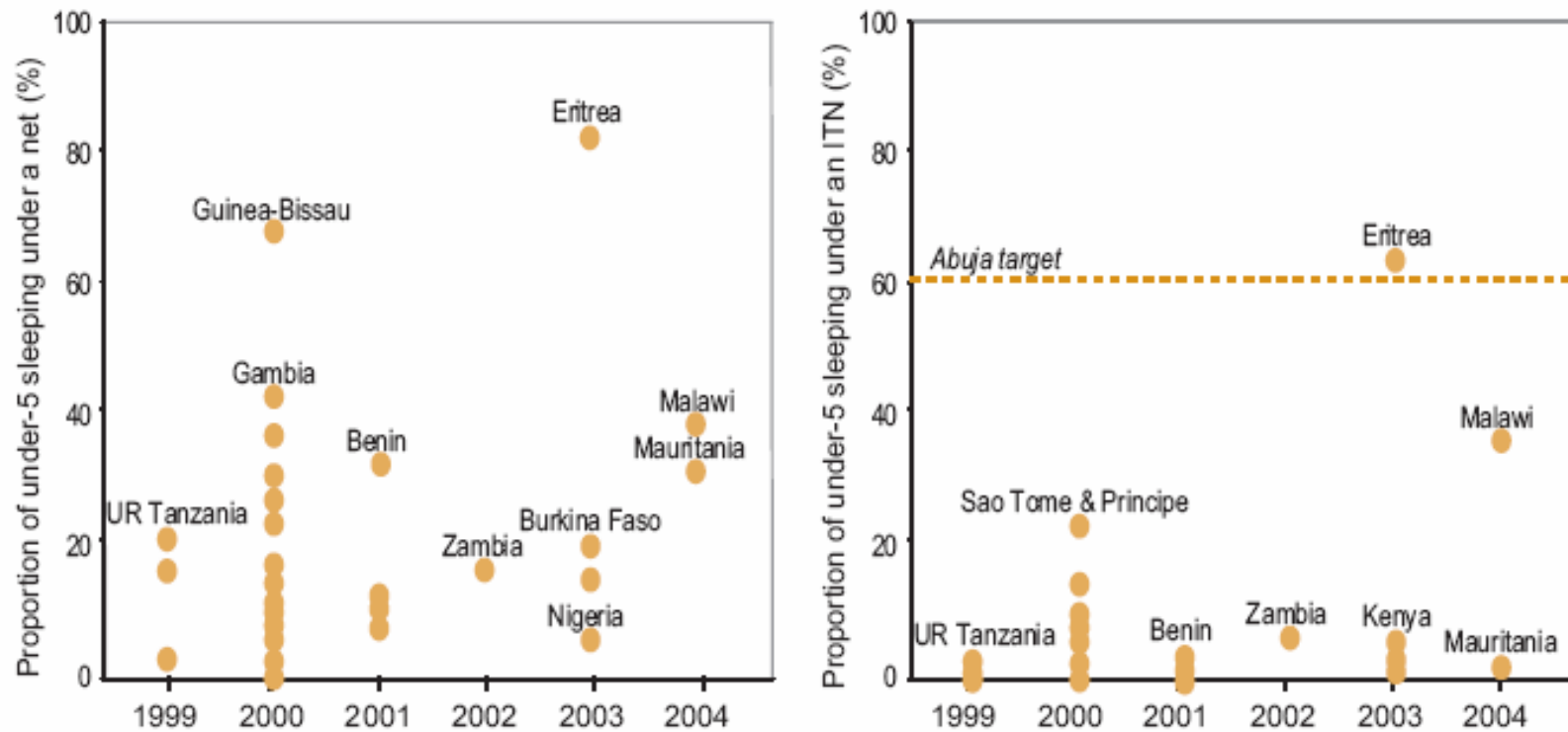
Table 1. Basic malaria monitoring and evaluation framework

Level	Area	Available information
Outcomes (changed behaviours, coverage)	Target populations benefiting from interventions, behavioural changes	Coverage of antimalarial treatment for fevers in children under 5 years of age (household surveys) Household ITN possession and usage (household surveys) Use by pregnant women of IPT (household surveys) Malaria epidemics detected and properly controlled
Impact (health status, biology) quality of life	Morbidity, mortality, socioeconomic status	Malaria case and death reports from health information systems (HIS) Proportional outpatient visits, hospital admissions and hospital deaths due to malaria (HIS in Africa) All-cause under-5 mortality (household surveys) Prevalence of childhood anaemia (household surveys)

Table 5. Priority malaria control strategies, by epidemiological setting

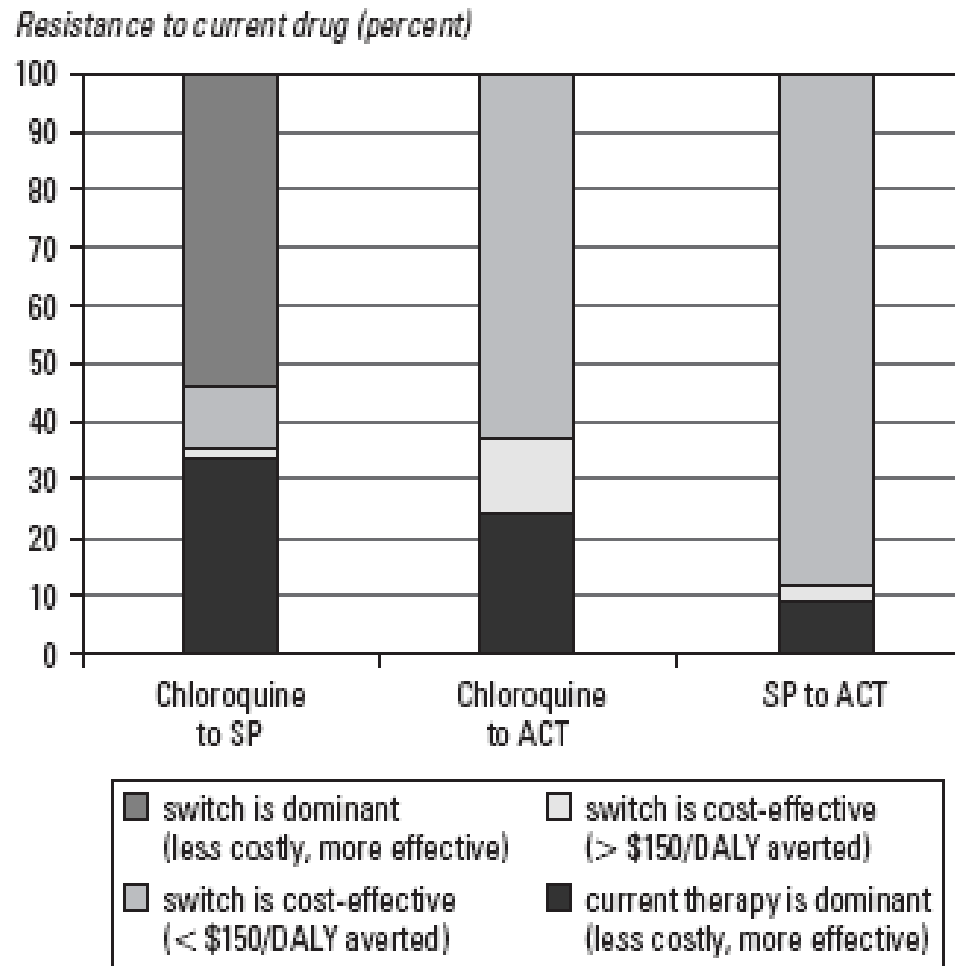
Epidemiological setting	Control strategy
Free of malaria <i>Example:</i> parts of Southern and North Africa, Ethiopian and Eritrean highlands and Transcaucasia	Prevention - For travelers going to malarious areas, chemoprophylaxis and personal protective measures against mosquitoes Treatment - Early and effective case management in suspected cases - Diagnostics to confirm cases, if possible before treatment

Figure 5. Proportion of children under 5 years of age sleeping under mosquito nets and ITNs in African countries, by year of survey, 1999-2004



Data from national household surveys, except for Eritrea, which had a representative household sample survey in the three zobas with risk of malaria (39). For each country, the most recent national datapoint is presented.

Figure 21.3. Cost-Effectiveness of Switching the First-Line Drug



Source: Authors.

Table 2. Aspects included in annual reporting from countries and territories to WHO regional offices

Region	Subregion	Reported malaria cases by:				Malaria-related services delivered			Malaria financing	
		Laboratory confirmation status	Age	Sex	Sub-national area	ITNs distributed or sold	Nets (re-)treated	Households sprayed during IRS campaigns	Budgeted expenses	Actual funding received
Africa	Central	–	✓	–	–	✓	✓	✓	✓	✓
	East	–	✓	–	–	✓	✓	✓	✓	✓
	North	✓	–	–	✓	–	–	✓	✓	✓
	Southern	–	✓	–	–	✓	✓	✓	✓	✓
	West	–	✓	–	–	✓	✓	✓	✓	✓

Malaria Burden: Major Gaps and Controversies Requiring Attention

■ Co-morbidity

- Anemia
- Low birthweight
- Malnutrition
- HIV

■ *Plasmodium*

- *falciparum*
- *vivax*
- Antigenic diversity
- Drug resistance

Malaria Burden: Major Gaps and Controversies Requiring Attention

■ *Anopheles*

- Transmission dynamics
- Correlation of EIR with clinical manifestations

■ Special conditions

- Epidemics
- Urbanization
- Migration

Current Surveillance Methods

- WHO Measures
 - Demographic surveillance systems (DSS)
 - Cross sectional surveys
 - Disease and health surveys (DHS) including verbal autopsies
 - Health information systems (HIS) including epidemic prone areas
 - Passive and active case finding
 - Household surveys

Current Surveillance Methods

- Often missing: specific areas and syndromes
 - Vital statistics and autopsies
 - Hospital-based surveillance
 - Inclusion of private sector, missionary, NGO, military reporting sites
 - Specific clinical syndromes; low birth weight, anemia, hypoglycemia
- Health policy and strategy development