Malaria Control

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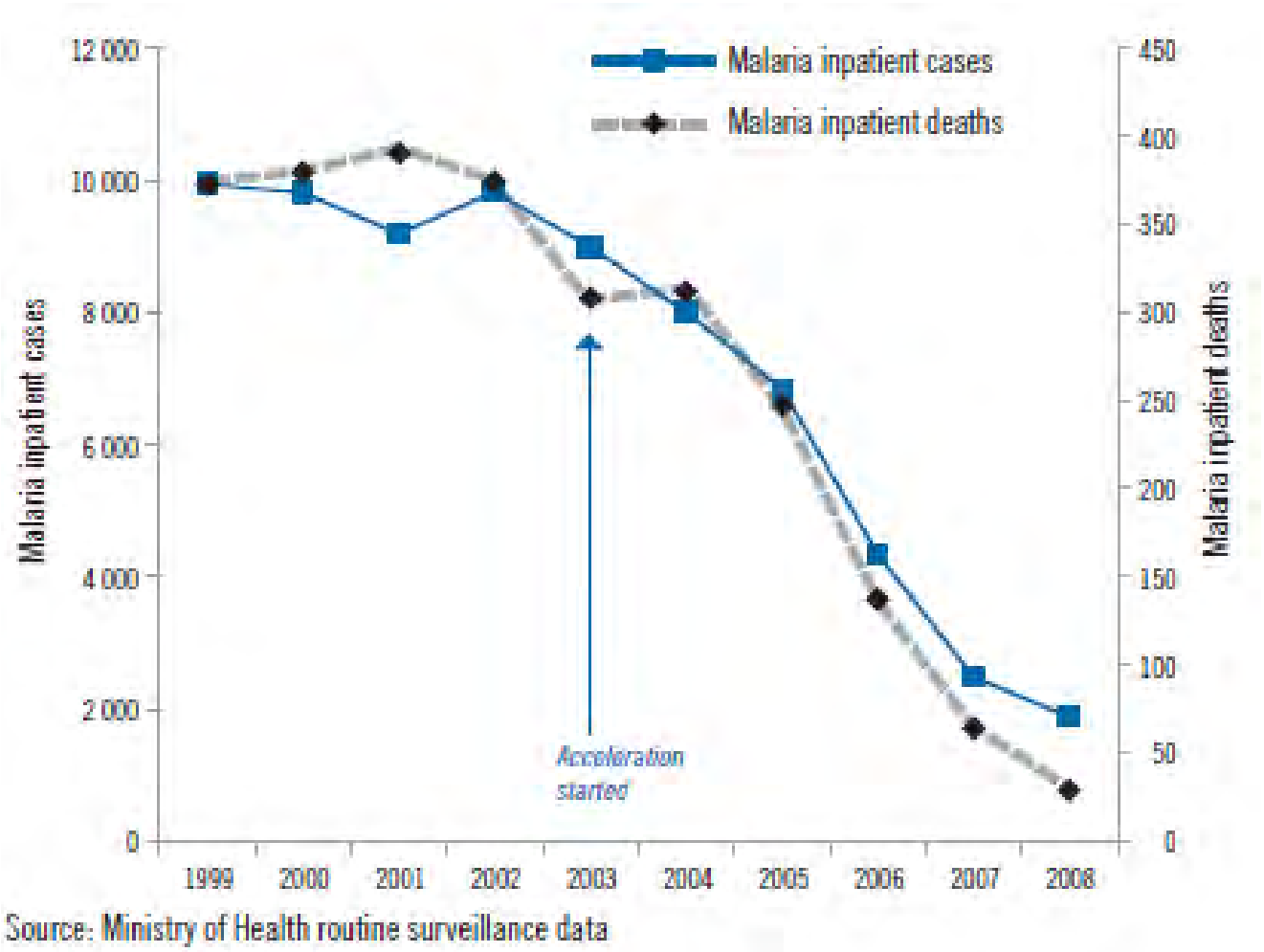
MRC The Gambia Unit
MRC Medical Research Council
CENTENARY 1913-2013

Zanzibar - hospitalizations et malaria deaths 1999-2008



Source: Ministry of Health routine surveillance data

The Gambia - slide positivity rates 2003-2009

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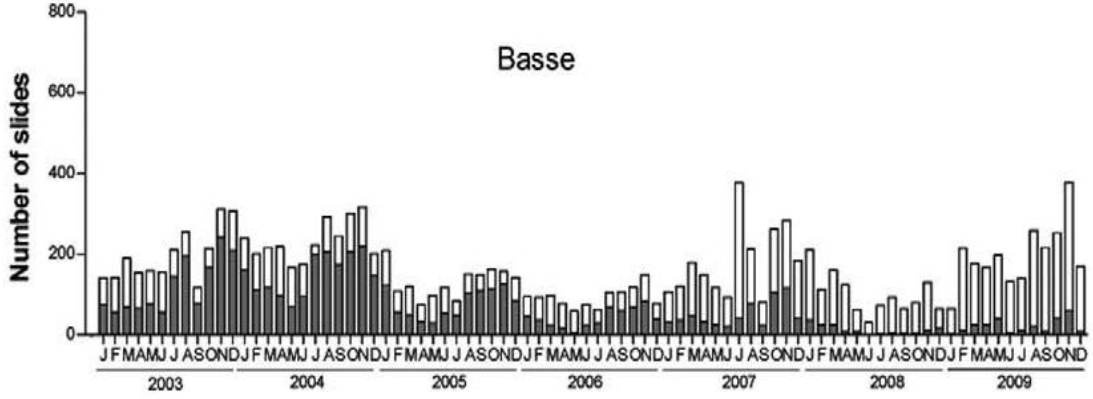

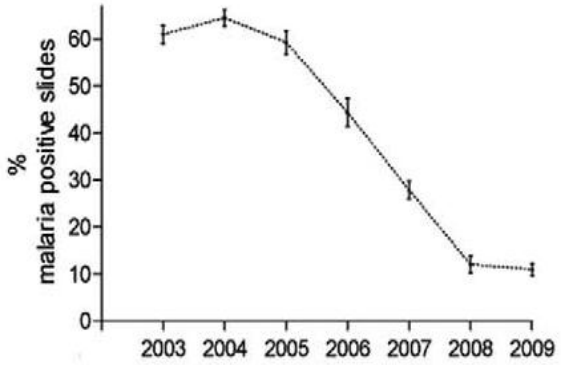

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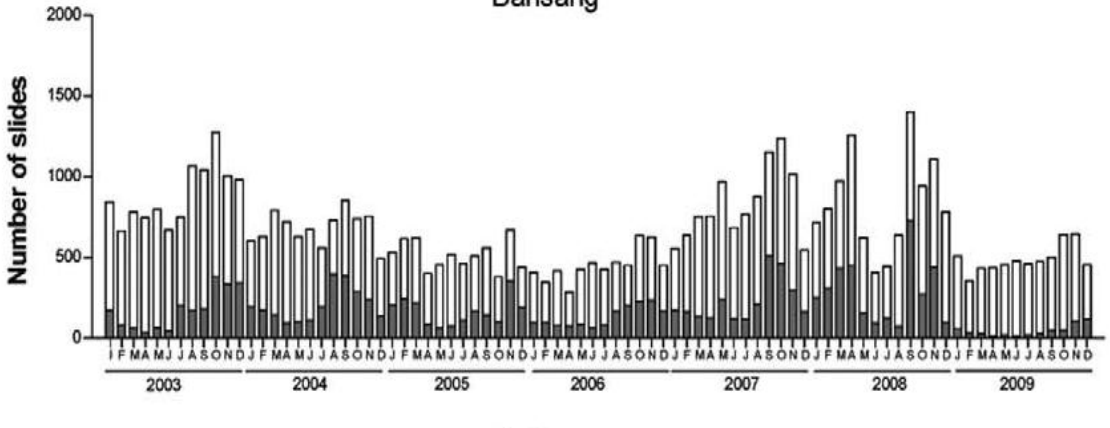
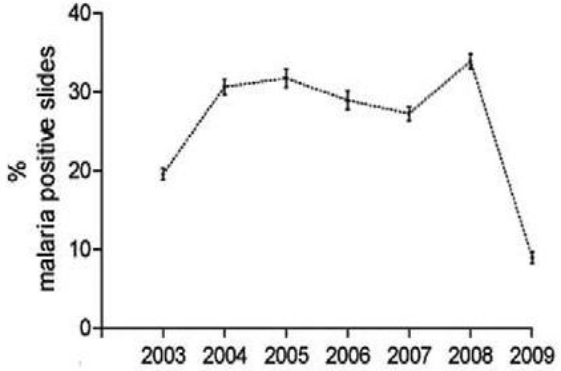
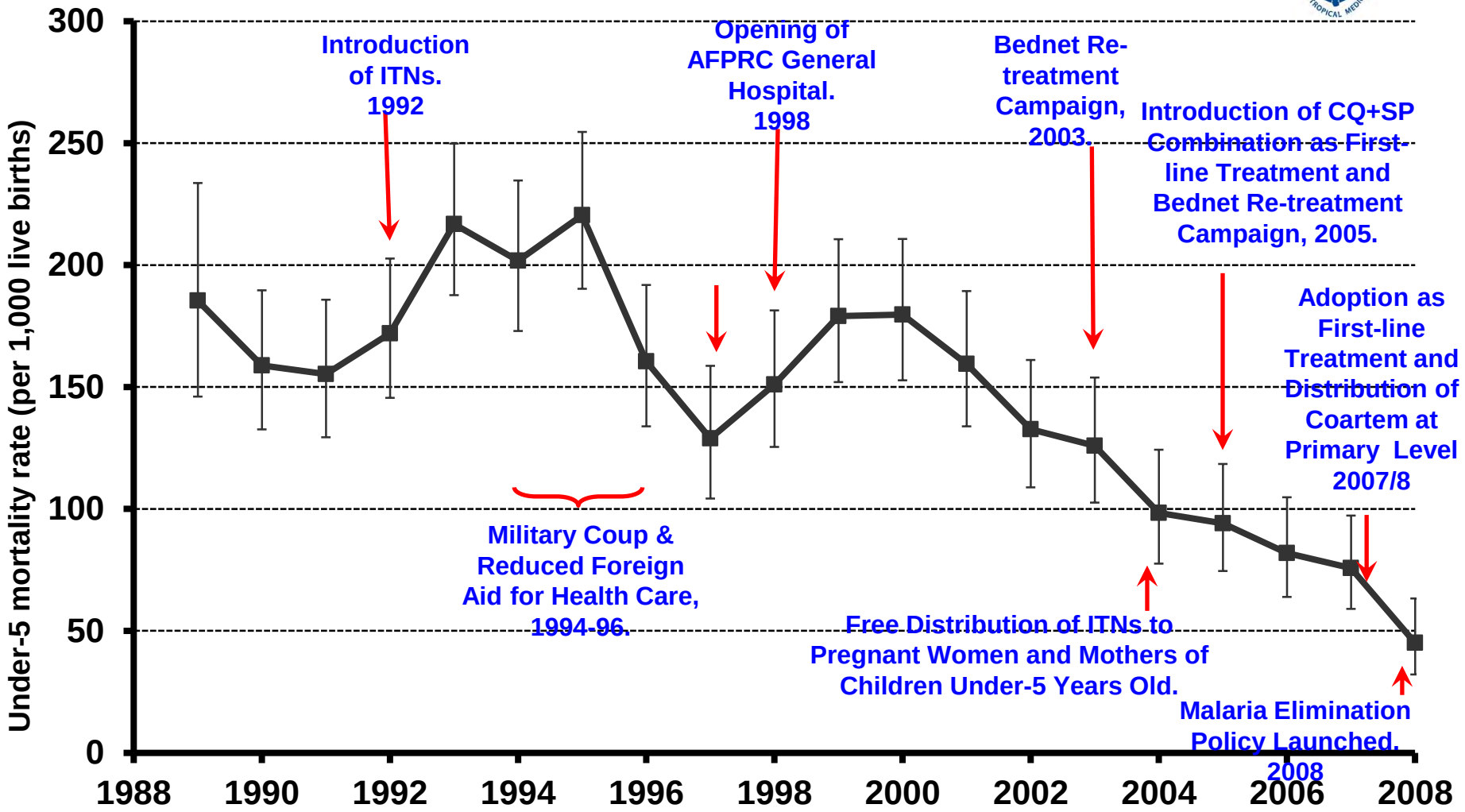




Farafenni – childhood mortality 1998-2008



Elimination: A Paradigm Shift for Surveillance

For elimination purposes, a malaria case is a person in whom, *regardless of the presence or absence of clinical symptoms*, **malaria parasites** have been confirmed by quality-controlled laboratory diagnosis.

Clinical Cases → **Infections**

Interventions during elimination programs are based on the concept of a **malaria focus**, assuming that transmission is focalized and no longer homogeneous across the country.

Universal Coverage → **Targeting Foci**

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Malaria control vs. malaria elimination

	CONTROL	ELIMINATION
GOAL	Reduction of the malaria burden to a level that it is no longer a major public health problem	Interruption of local mosquito-borne malaria transmission in a defined geographical area
Area of Operations	Malaria endemic areas: Universal coverage of prevention and treatment (SUFI)	Foci identified through epidemiological intelligence
Surveillance	May not be the best but is sufficient	Must be rapid and highly efficient

Adapted from WHO, 2007

PLoS MEDICINE

malERA a research agenda for malaria eradication

www.ploscollections.org/malERA2011

Produced with support from the Malaria Eradication Research Agenda (malERA) initiative, which was funded by a grant from the Bill & Melinda Gates Foundation.

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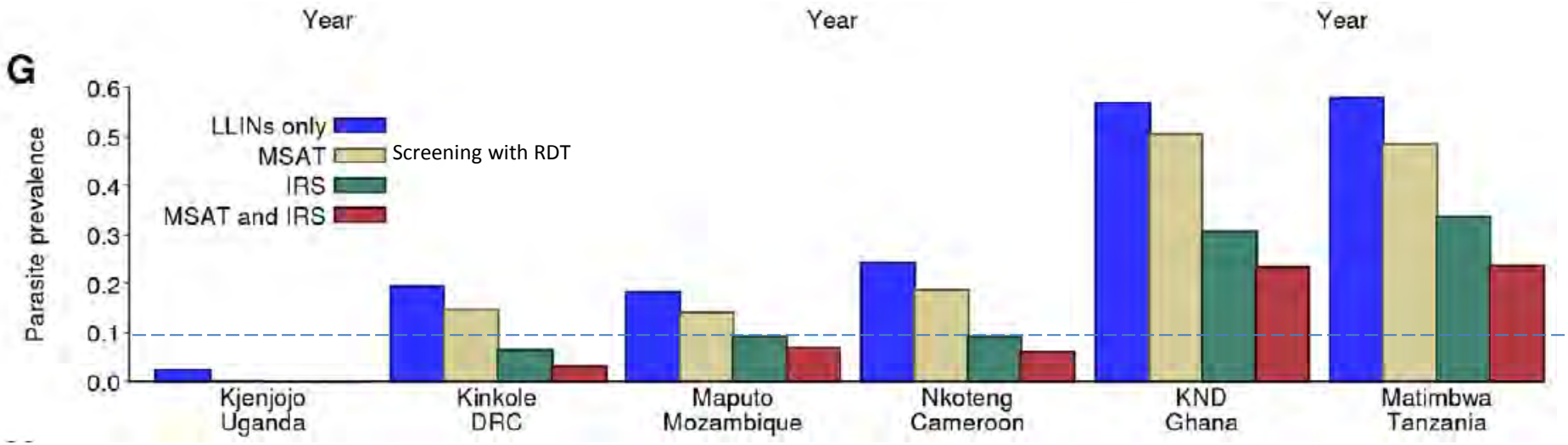
Image: Grassi, B. Studi di uno zoologo sulla malaria (1901), courtesy of the Biodiversity Heritage Library.

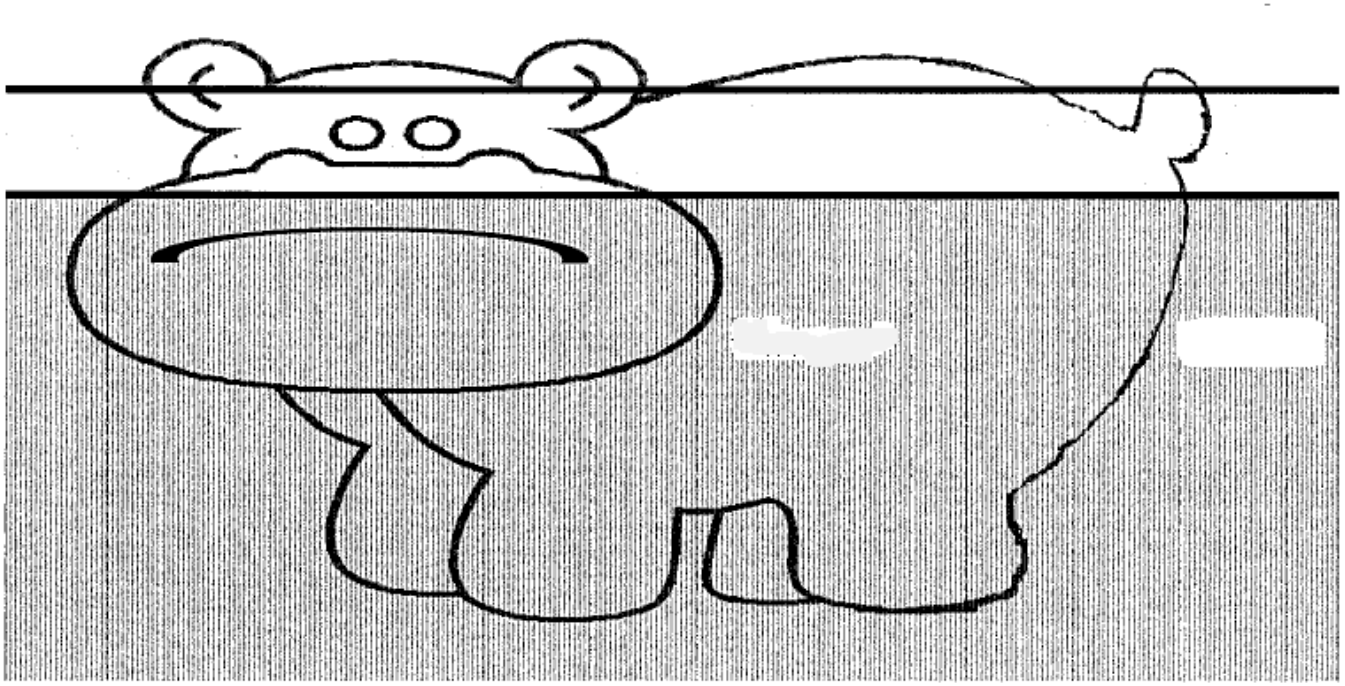
Griffin et al, PLoS Medicine, 2010



EIR	3	43	46	81	586	675

Elimination achievable with current methods only in areas with extremely low transmission

The hidden reservoir of malaria infection



Modified from Breman, AJTMH 2001

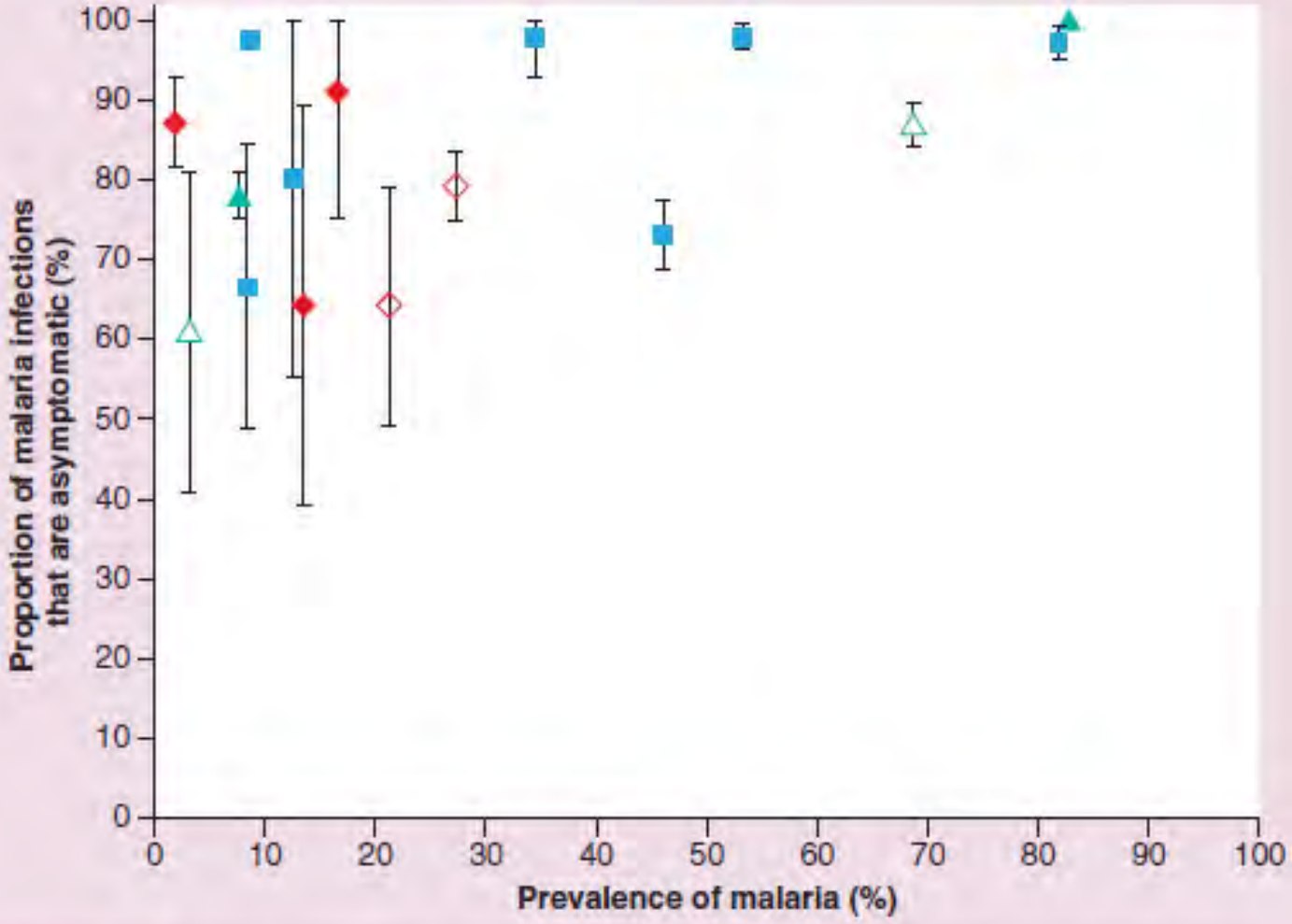


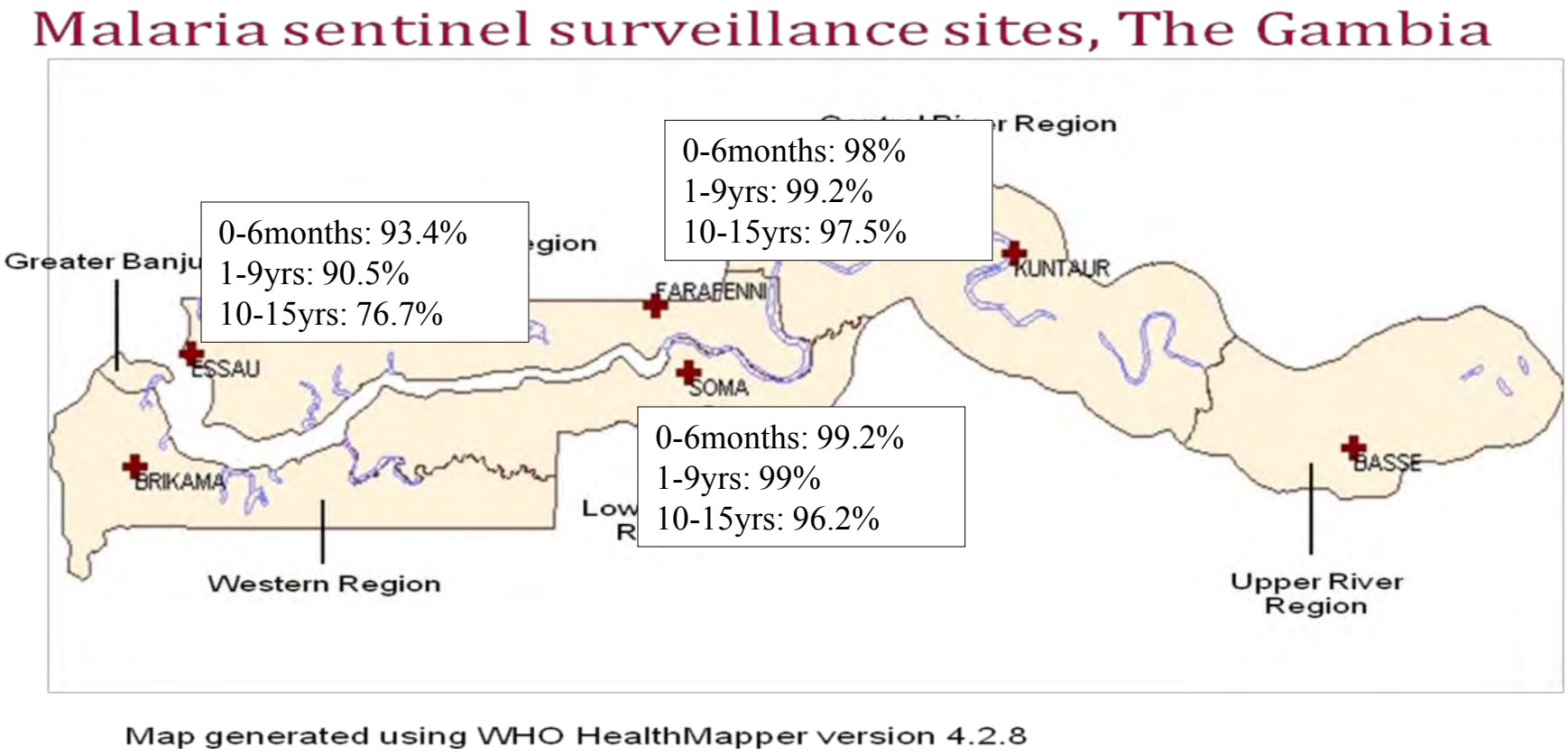
Figure 1. The proportion of malaria infections that are asymptomatic compared with population prevalence of malaria across 16 sites in 14 countries. Error bars correspond to the 95% CI. Hollow and filled shapes indicate diagnosis by microscopy and PCR, respectively. Diamonds, triangles and squares indicate surveys conducted in Asia, Latin America and Africa, respectively.

Lindblade et al, 2013

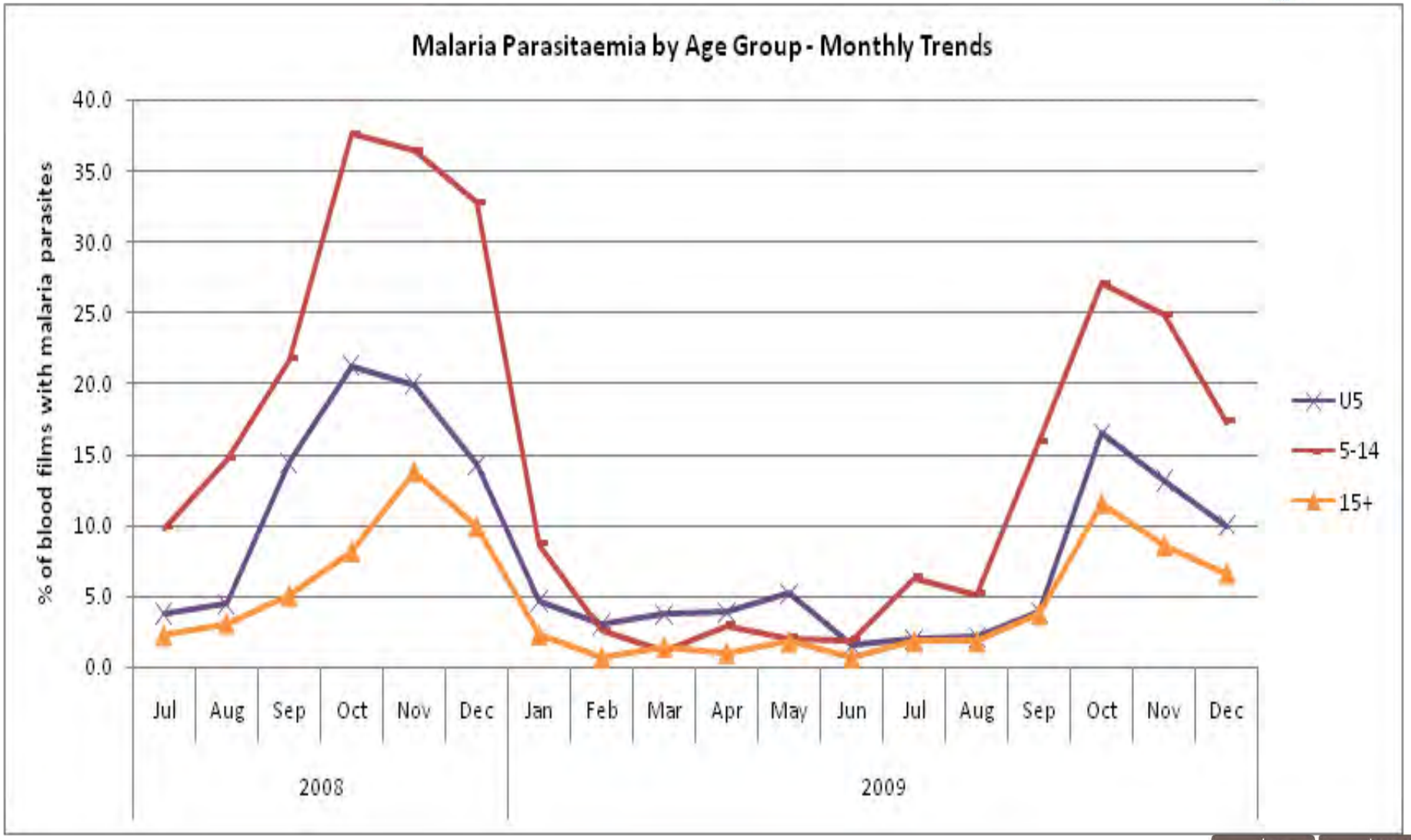
Asymptomatic malaria infections

- About half infections undetected by microscopy
- Difference is greatest in low transmission settings
- Many asymptomatic infections can persist for significant periods of time;
- *P. falciparum* gametocytes positively associated with no symptoms and low asexual parasite densities;
- Mosquitoes infected with gametocyte densities as low as 5 gametocytes/µl
- Children with undetectable gametocytaemia by molecular methods could still transmit to mosquitoes;
- Gametocyte carriers may be more attractive to mosquitoes than both uninfected individuals and individuals with only asexual parasites

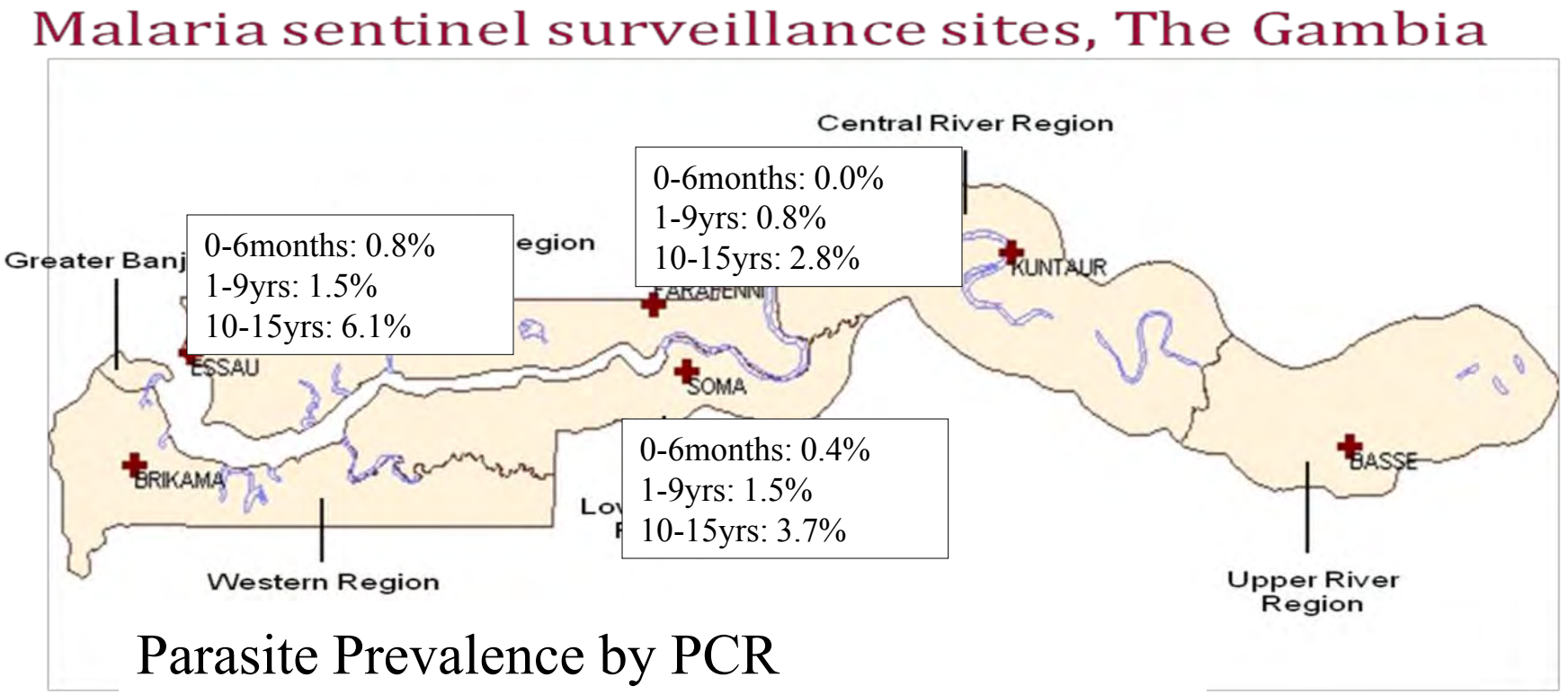
Bednet ownership, October 2011



The Gambia, SPR in all sentinel sites by age group (2008-2009)



% RDT positives, October 2011



Parasite Prevalence by PCR

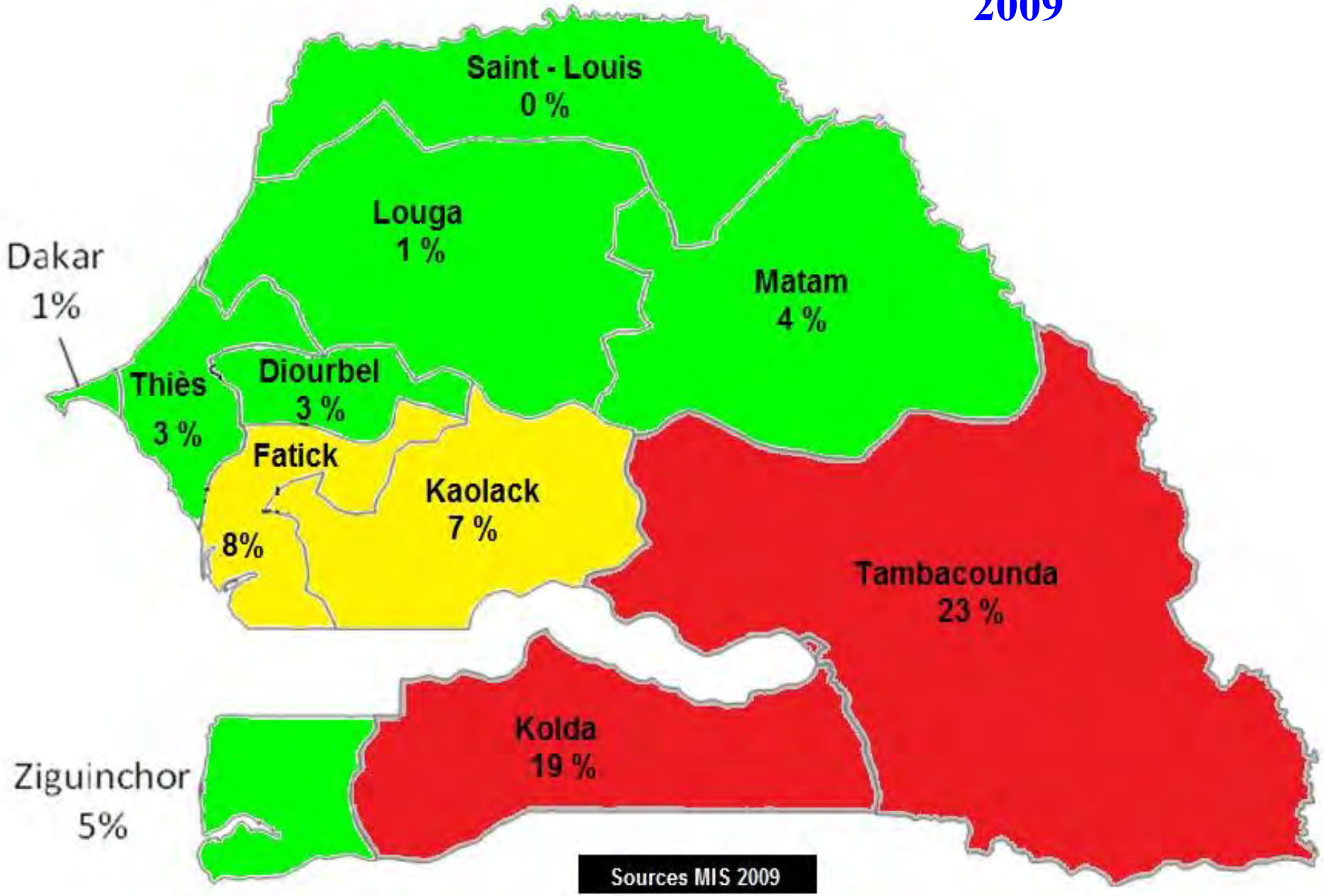
0-6m: 13.7%

1-9yrs: 9.3%

10-15yrs: 11.3%

Prévalence parasitaire du paludisme

Résultats MIS 2009



Two broad different approaches

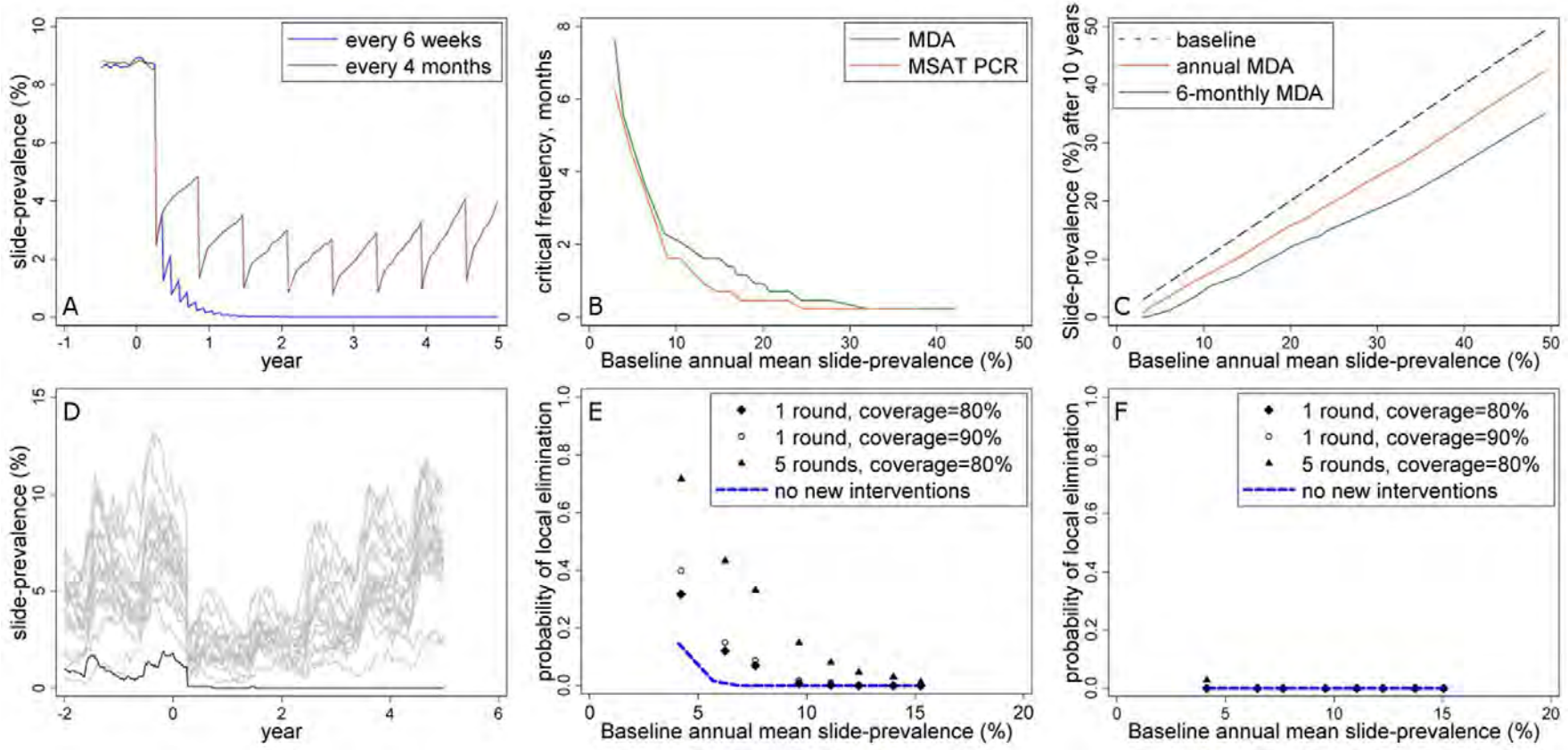
Active case detection (ACD)

- Reactive
  - Screening people around a passively detected clinical case
  - No studies on impact on transmission
- Proactive
  - Screening of high risk populations
  - Low sensitivity of diagnostic tests

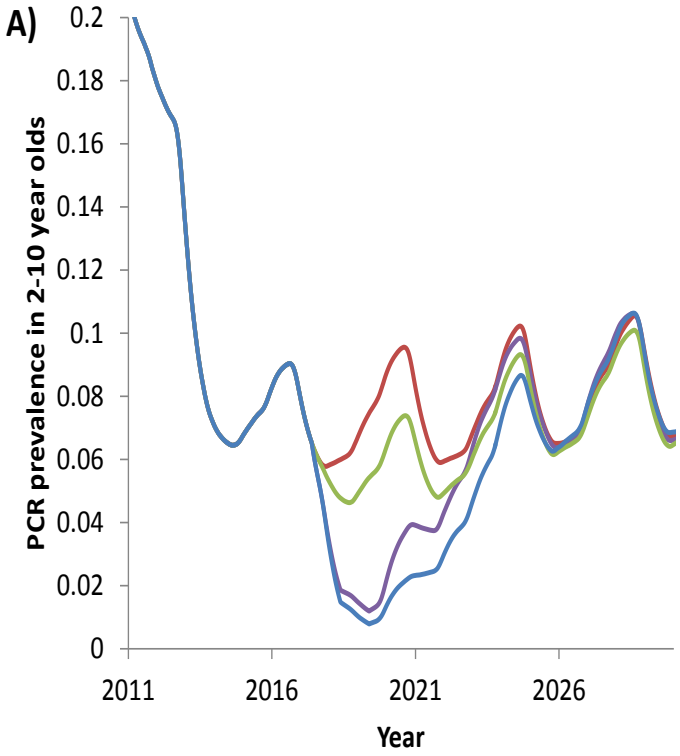
Presumptive treatment

- Mass drug administration (MDA)
  - Whole population
  - Targeted to high risk groups
    - IPT/SMC

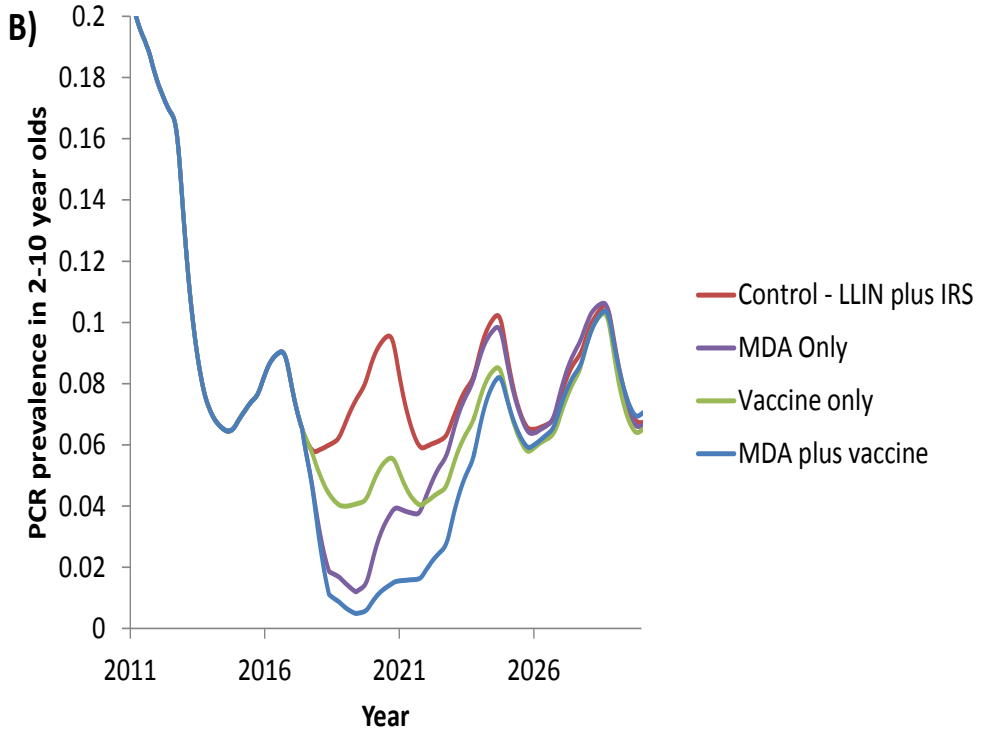
Potential for elimination by MDA (Okell et al, 2010)



MDA (1 yearly round for 2 years) plus RTS,S/AS01



VE=30%



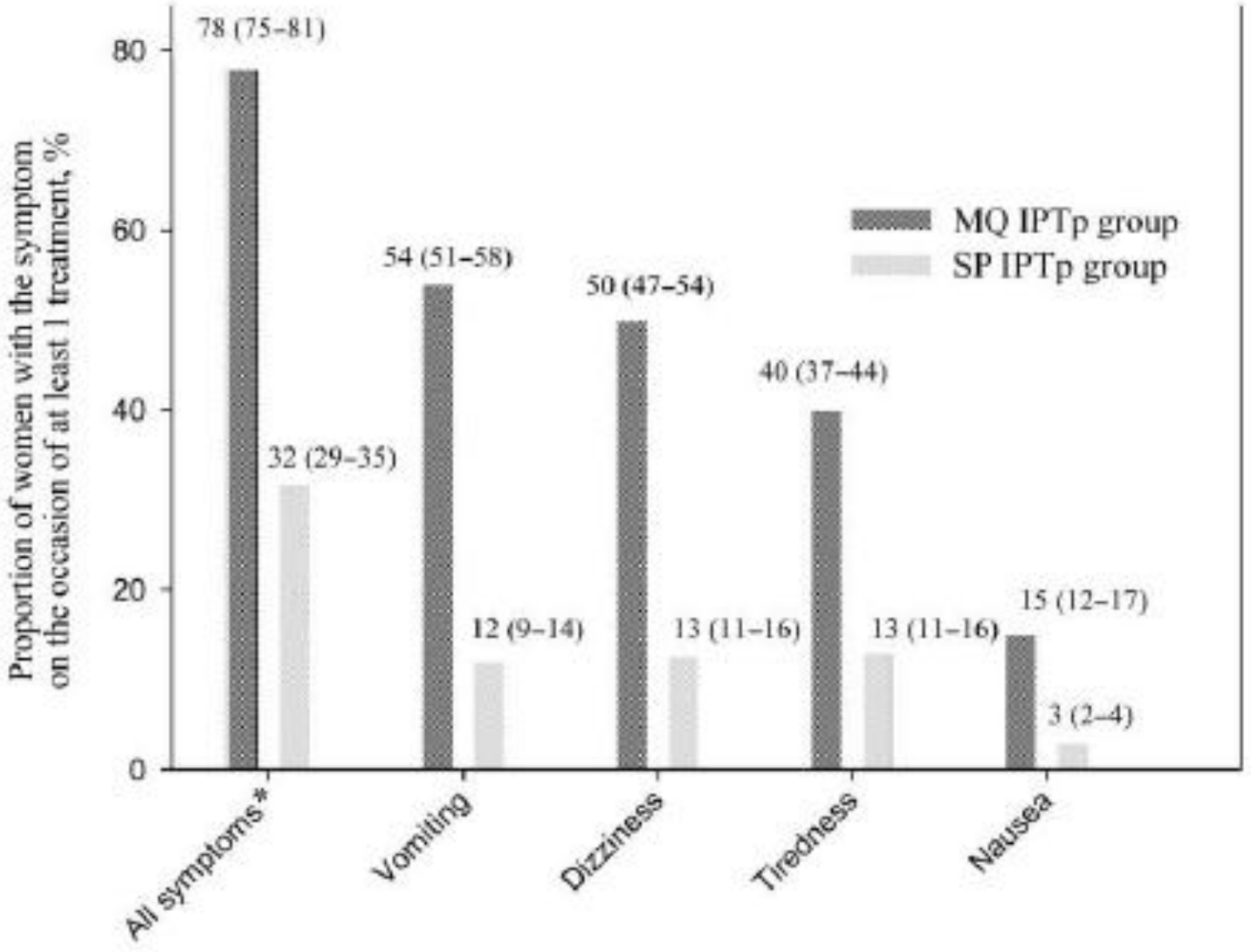
VE=50%

IPTp-MQ, Briand et al, 2009

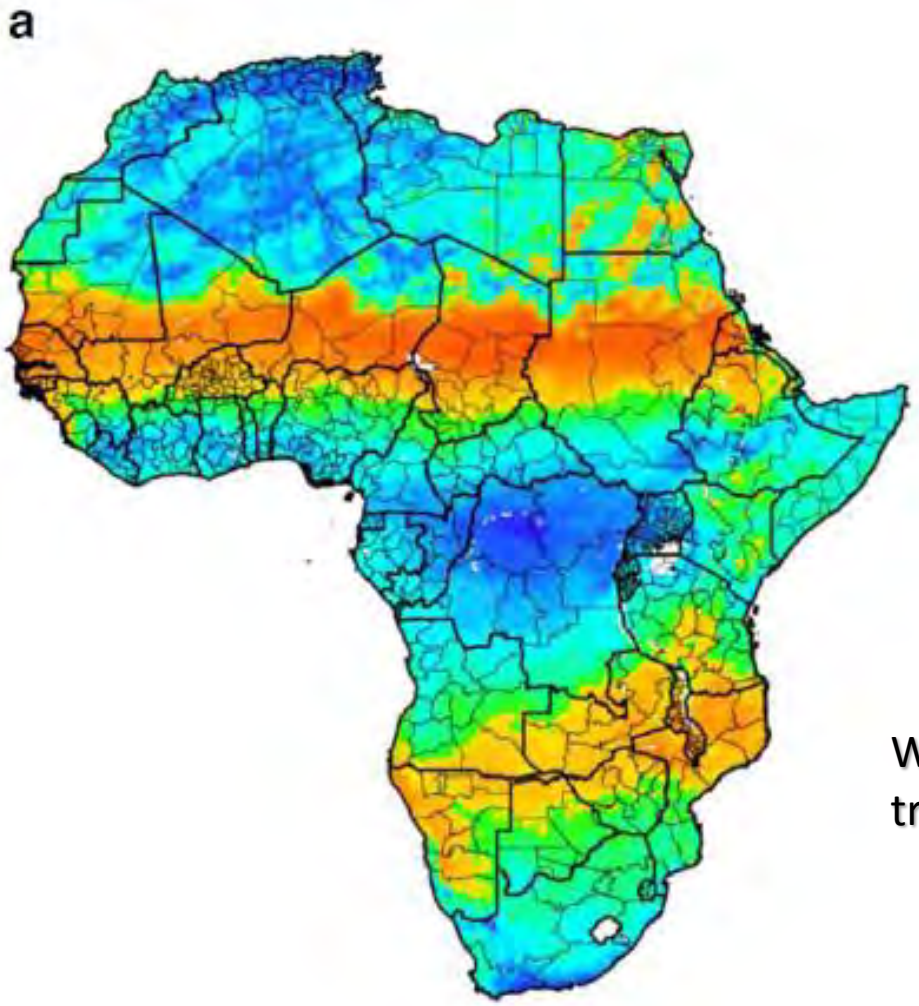
Table 3. Proportion of Placental Infection and Maternal Anemia at Delivery, by Treatment Group, According to Crude Analysis

Condition, analysis	MQ IPTp	SP IPTp	RR (95% CI)	*P*
Placental malaria[a]				
ITT	11/663 (1.7)	29/656 (4.4)	0.38 (0.19–0.74)[b]	.004[b]
PP	10/584 (1.7)	25/619 (4.0)	0.42 (0.21–0.88)[b]	.02[b]
Anemia[c] at delivery				
ITT	103/626 (16)	129/640 (20)	0.82 (0.65–1.03)	.09
PP	94/553 (17)	124/604 (21)	0.83 (0.65–1.05)	.12
Severe anemia[d] at delivery				
ITT	16/626 (2.6)	15/640 (2.3)	1.09 (0.54–2.19)	.81
PP	15/553 (2.7)	14/604 (2.3)	1.17 (0.57–2.40)	.67

IPTp-MQ, Briand et al, 2009



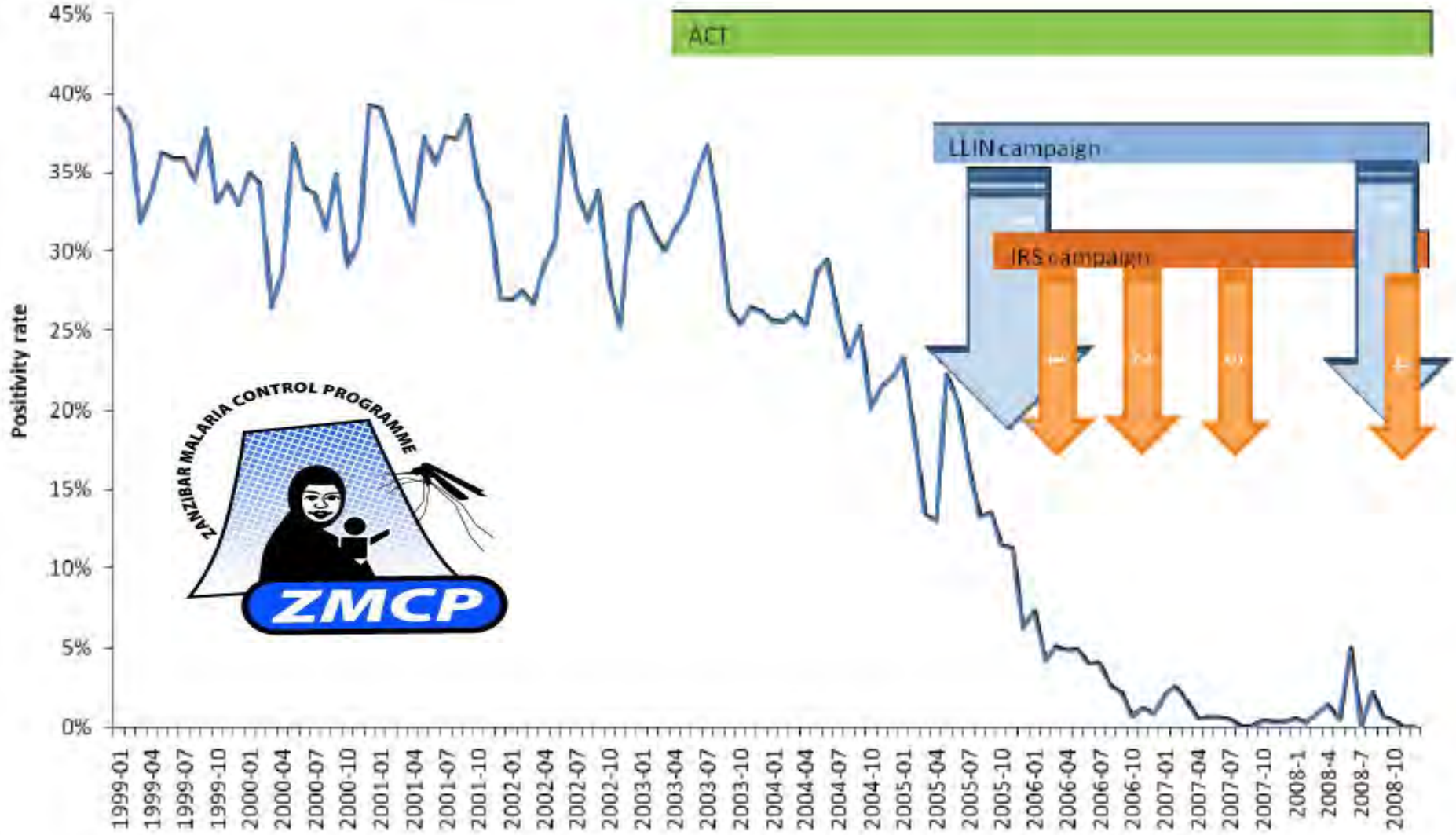
Seasonal Malaria Chemoprevention (Cairns et al, 2012)



Orange-red areas identified as adequate for SMC on the basis of >60% of rains in 3 months, i.e. 60% annual incidence in 3 consecutive months

What to do in areas of perennial transmission?

Zanzibar – spectacular reduction in slide positivity rates



Haji et al, 2013

Figure 2 Damaged LLINs being examined on a plastic frame showing distribution of large holes (>5 cm) and knots as a method of net repair.

Increasing resistance to pyrethroids in Pemba island (Haji et al, 2013)

Table 1 Species identification and insecticide susceptibility tests for mosquitoes collected on Pemba Island in December 2010

		An. arabiensis	*An. merus*	Unidentified	Total	% 24 hr mortality
Lambda-cyhalothrin 0.05%	Dead	26	5	3	74	46
	Alive	36	0	4		
Deltamethrin 0.05%	Dead	40	0	2	100	42
	Alive	48	7	3		
Permethrin 0.75%	Dead	28	16	7	89	57
	Alive	37	1	0		
Bendiocarb 0.1%	Dead	80	0	2	82	100
	Alive	0	0	0		
DDT 4%	Dead	95	0	3	98	100
	Alive	0	0	0		
Control	Dead	0	0	0	111	0
	Alive	101	5	5		

Primaquine

Figure 1: Countries that contain primaquine in first line treatment for *P. falciparum* guidelines worldwide[3]

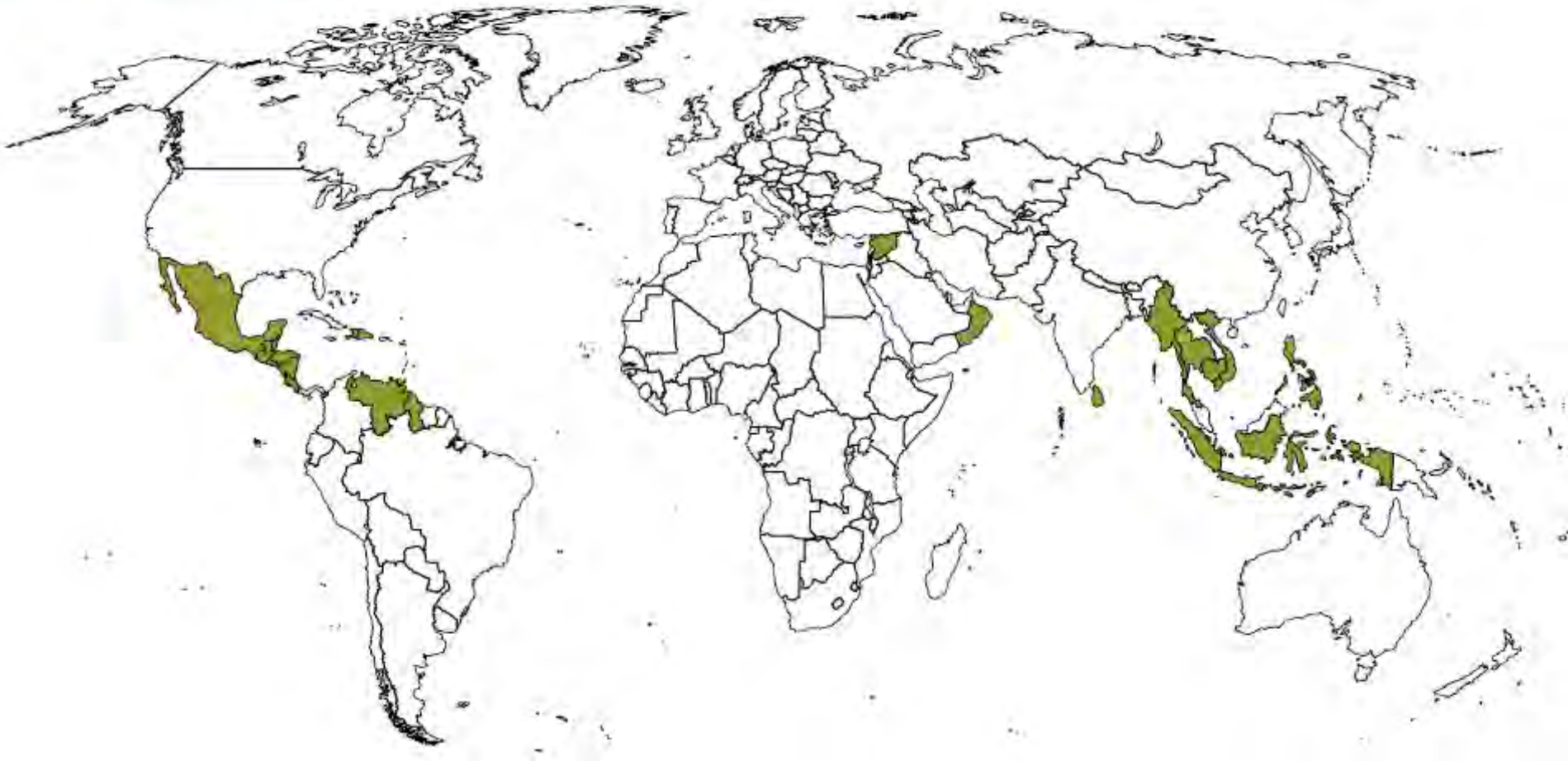
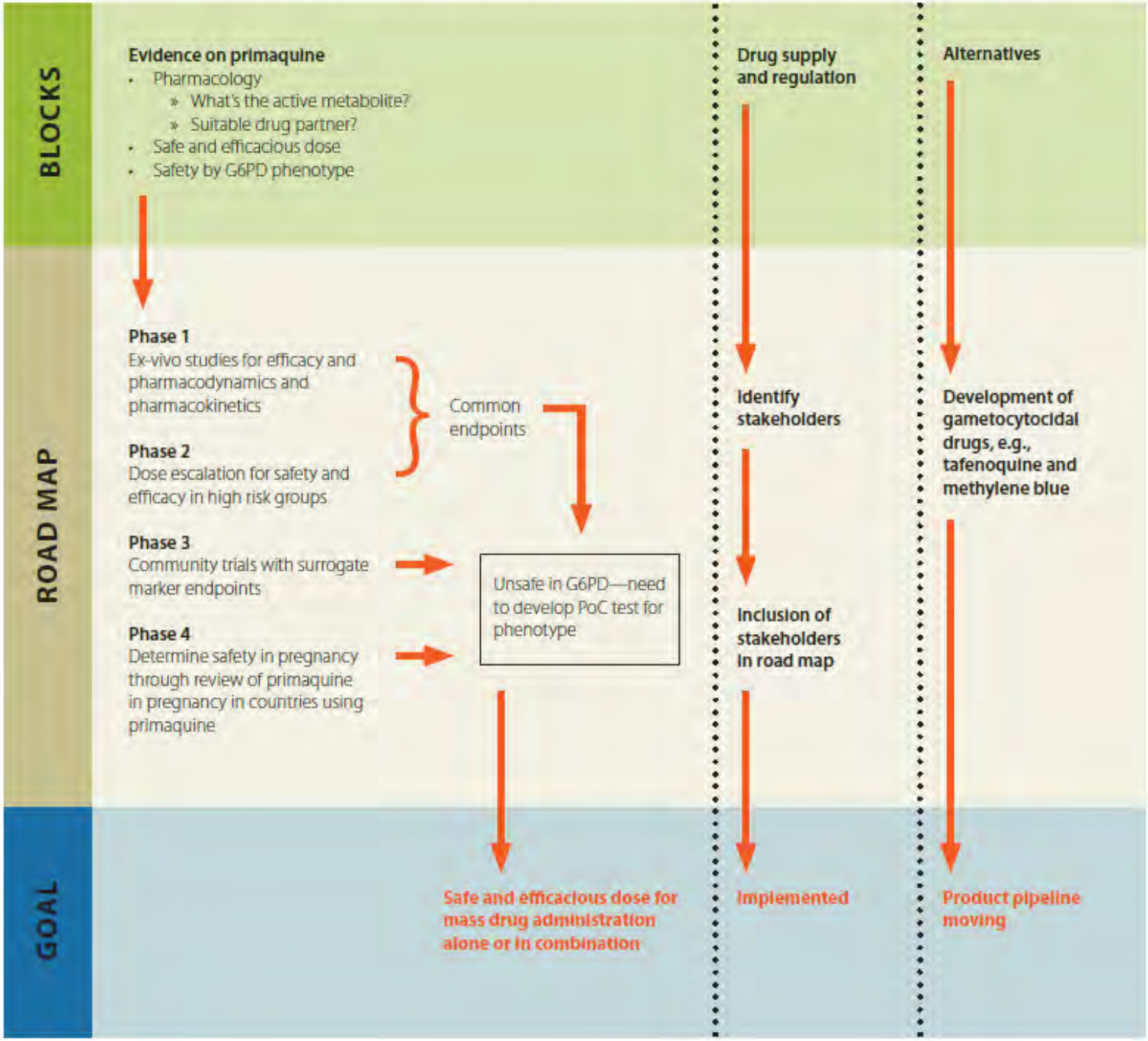


Figure 2: The roadmap for implementation of short course primaquine to reduce transmission of *P. falciparum* in Africa



Research Brief: Outputs from the meeting on short course primaquine for the treatment for *P. falciparum* in Africa

Study	ID	Comments
Primaquine as gametocytocidal		
Primaquine Pharmacokinetics in Lactating Women and Their Infants	NCT01780753	Recruiting
Pharmacokinetic and in Vitro Transmission Blocking Activities Study of Primaquine Compare to Methylene Blue in Healthy Volunteer Both G6PD Normal and G6PD Deficiency	NCT01668433	Recruiting
Evaluation of the Gametocytocidal Efficacy and Safety of Primaquine in Uncomplicated Falciparum Malaria in Uganda	NCT01365598	Completed
Pharmacokinetic Study of Primaquine and Pyronaridine-Artesunate in Healthy Subjects	NCT01552330	Completed
Phase2a Primaquine Dose Escalation Study	NCT01743820	Not recruiting yet, testing decreasing doses
Gametocytocidal Efficacy in Malaria Asymptomatic Carriers (PRINOGAM)	NCT01838902	Recruiting
Low Dose Primaquine for Clearance of Gametocytes (LOPRIM)	NCT01935882	Recruiting

Decreasing doses of PQ in asymptomatic carriers (PRINOGAM)

RDT positive

AS ≥ 20/µL

G6PD Neg

Day	0	1	2	3	7	10	14	21	28	35	42
DHA-PPQ											
PQ											
Clinical reviews											
Gametocytaemia (QT-NASBA)											
DMFA											
AEs/ SAEs											

Conclusions

- ACD strategies adopted by a number of malaria control programs worldwide
- Different approaches poorly defined and evaluated
- Factors affecting effectiveness not well understood
- How different interventions (e.g. MDA and RTS,S/AS01) can be combined
- Community-based cluster randomized trials to determine effectiveness of a package the best way forward

Thank you for your attention