

MALARIA CONTROL AND VACCINATION



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Gates Malaria Partnership

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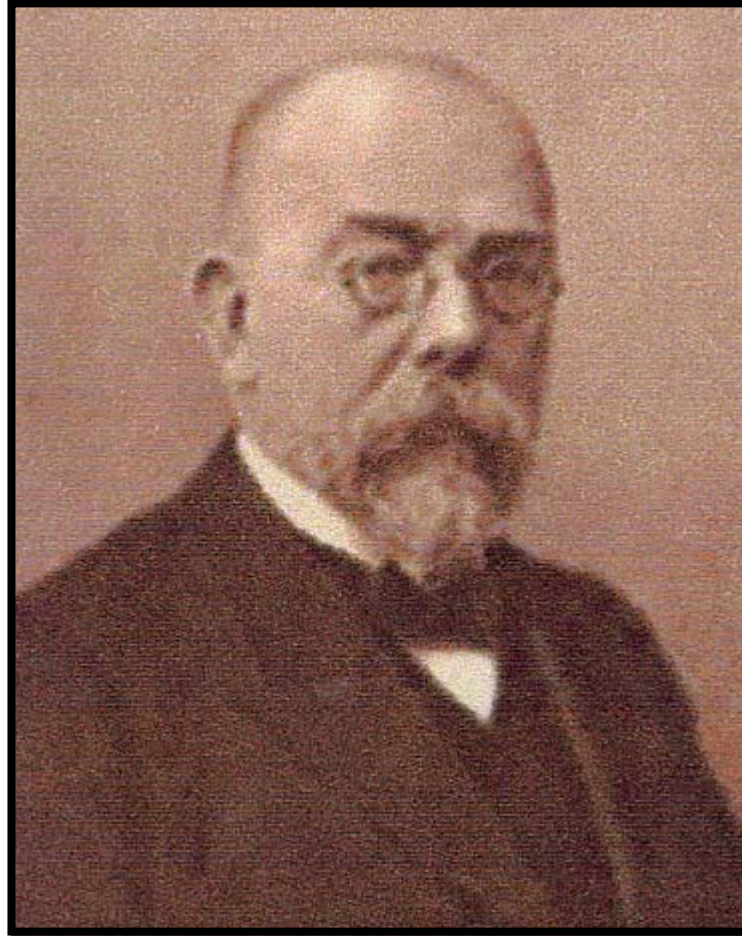
Montreux, June 10th 2004

ADMINISTRATION OF ANTIMALARIAL DRUGS THROUGH THE EPI PROGRAMME



**Robert
KOCH
(1843-90)**

**Advocated
extensive use
of quinine to
prevent malaria
(‘Koch Method’)**



WAYS OF USING ANTIMALARIA DRUGS TO PREVENT MALARIA IN ENDEMIC COUNTRIES

1. Treatment of clinical attacks of malaria with a gametocidal drug
2. Mass drug administration
3. Chemoprophylaxis
4. Intermittent preventive treatment (IPT)

TREATMENT OF CLINICAL ATTACKS WITH A GAMETOCIDAL DRUG

**Clinic on the
Thai-Burmese
border**



MASS DRUG ADMINISTRATION (MDA)

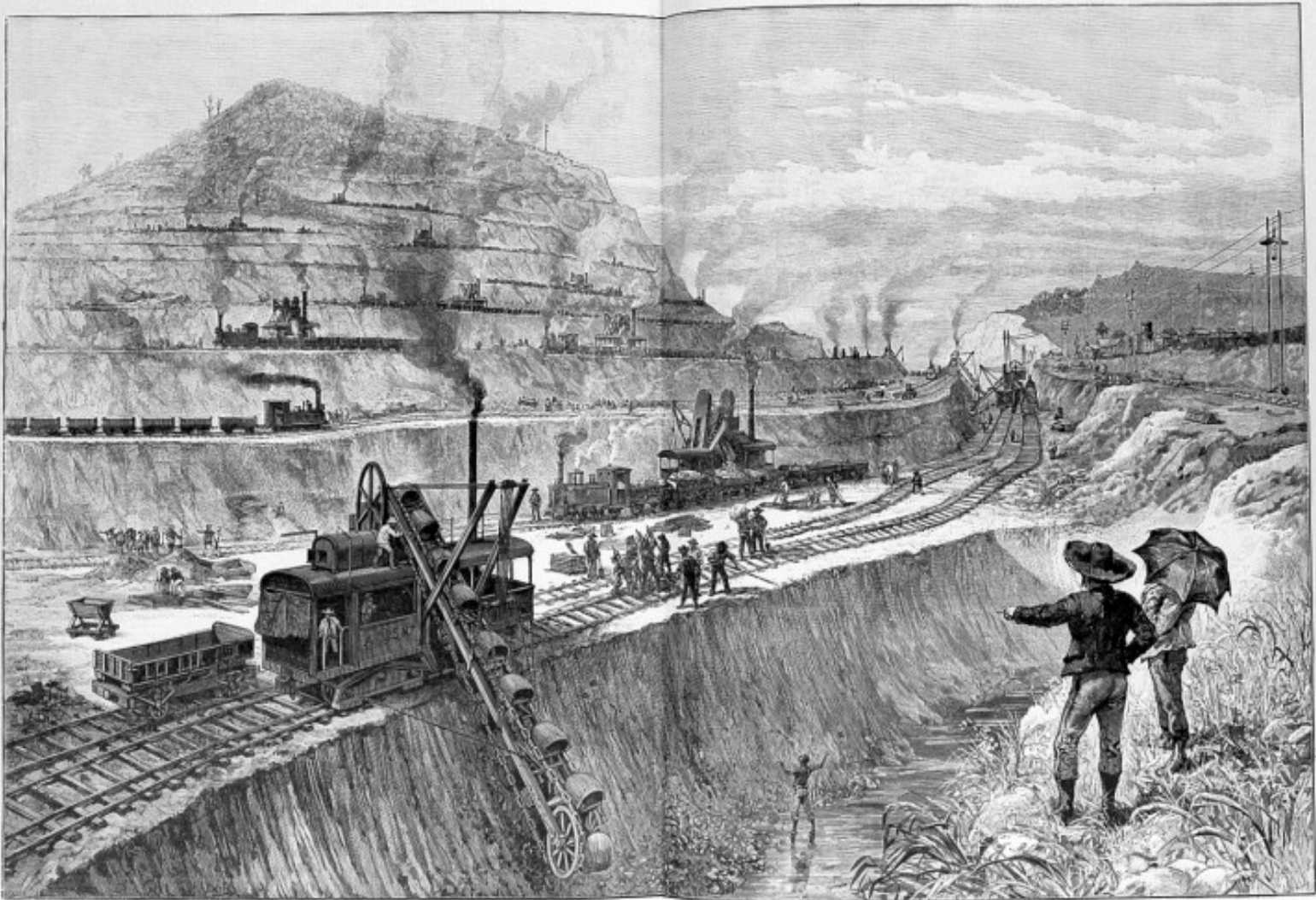


Administration of antimalarial drugs to all individuals in a community, whether infected or not, at specific points in time with the aim of reducing (interrupting) transmission



(Photo: Archivio Guido Casini)

600—THE ILLUSTRATED LONDON NEWS AND S. P. MAGAZINE
ACROSS TWO OCEANS, THE PANAMA RAIL CANAL.—DESIGNED BY OUR SPECIAL ARTIST, MR. MELTON PEROR.



CUTTING THROUGH THE CULEBRA MOUNTAINS—GENERAL VIEW, LOOKING WEST, TOWARDS PANAMA.

BUILDING THE PANAMA CANAL

(Wellcome Trust archives)

MEDICATED SALT



Pinotti method

The Garki Project

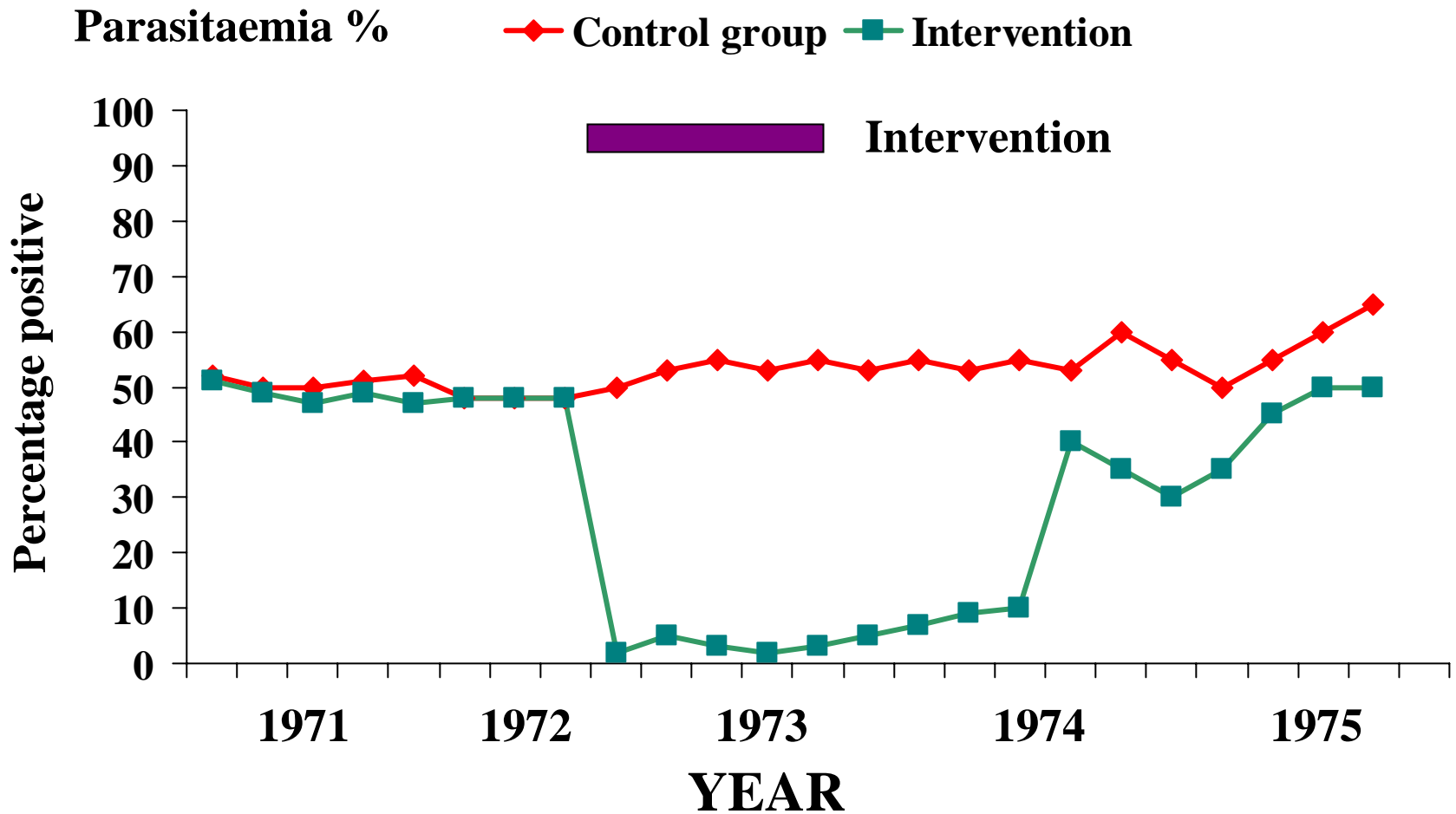
Research on the
Epidemiology and Control
of Malaria in the Sudan
Savanna of West Africa

L. Molineaux & G. Gramiccia



World Health Organization Geneva 1980

THE GARKI PROJECT



(Molyneux and Grammicia, The Garki Project 1980)

CHEMOPROPHYLAXIS



Administration of anti-malarial drugs to an at risk population, often in sub-therapeutic levels, so as to obtain sustained protective blood levels over the period at risk

MALARIA CHEMOPROPHYLAXIS IN YOUNG GAMBIAN CHILDREN

↑ weight gain

↑ haemoglobin

↓ splenomegaly

↓ gamma globulins



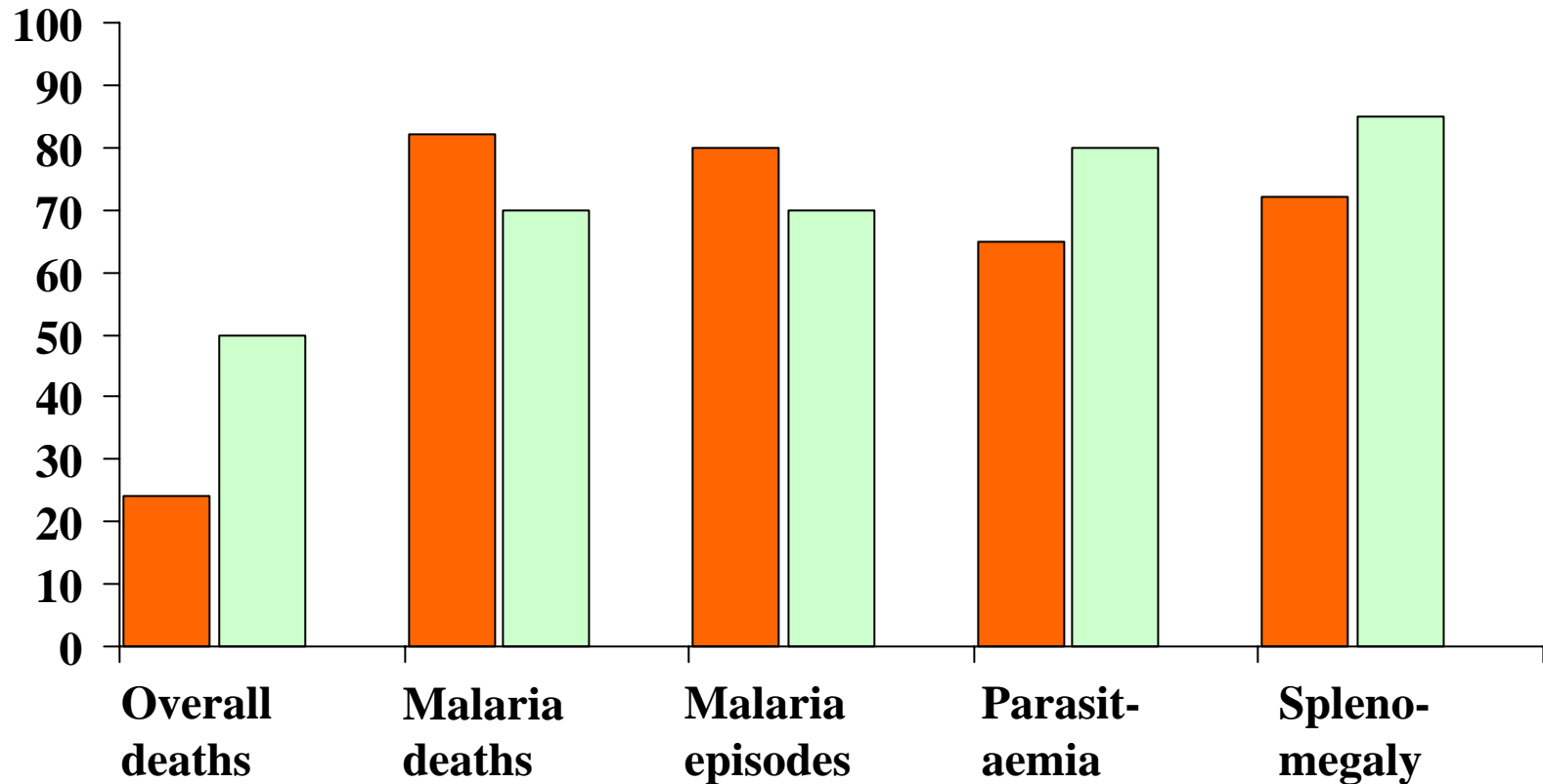
SUKUTA, THE GAMBIA
weekly chloroquine
0-36 months

(McGregor et al., BMJ 1956; ii:686-692)

CHEMOPROPHYLAXIS IN GAMBIAN CHILDREN

Percentage reduction

■ 1-2 years ■ 3-4 years



(Greenwood et al., Lancet 1988; i:1121)

POTENTIAL PROBLEMS FOR CHEMOPROPHYLAXIS

- Cost
- Safety
- Compliance
- Drug resistance and choice of drug
- Impairment of immunity and rebound in morbidity and/or mortality

INTERMITTENT PREVENTIVE TREATMENT



Administration of a full dose of antimalarial treatment at irregular intervals separated by periods without drug exposure

CHEMOPROPHYLAXIS AND INTERMITTENT TREATMENT IN PREGNANT MALAWIAN WOMEN

PREVALENCE OF PLACENTAL MALARIA

**Chloroquine +
weekly chloroquine
prophylaxis** **32%**

**Fansidar +
weekly chloroquine
prophylaxis** **26%**

Fansidar x 2 **9%**

**RECOMMENDATION FOR THE PREVENTION
OF MALARIA IN PREGNANCY, 2003**

***‘ADMINISTER ANTIMALARIAL AT THE FIRST
ANTENATAL CLINIC VISIT AFTER QUICKENING
AND AT EACH SUBSEQUENT VISIT WITH A MINIMUM
ADMINISTRATION OF TWO DOSES’***

**[WHO STRATEGIC FRAMEWORK FOR MALARIA CONTROL
DURING PREGNANCY IN THE AFRICAN REGION]**

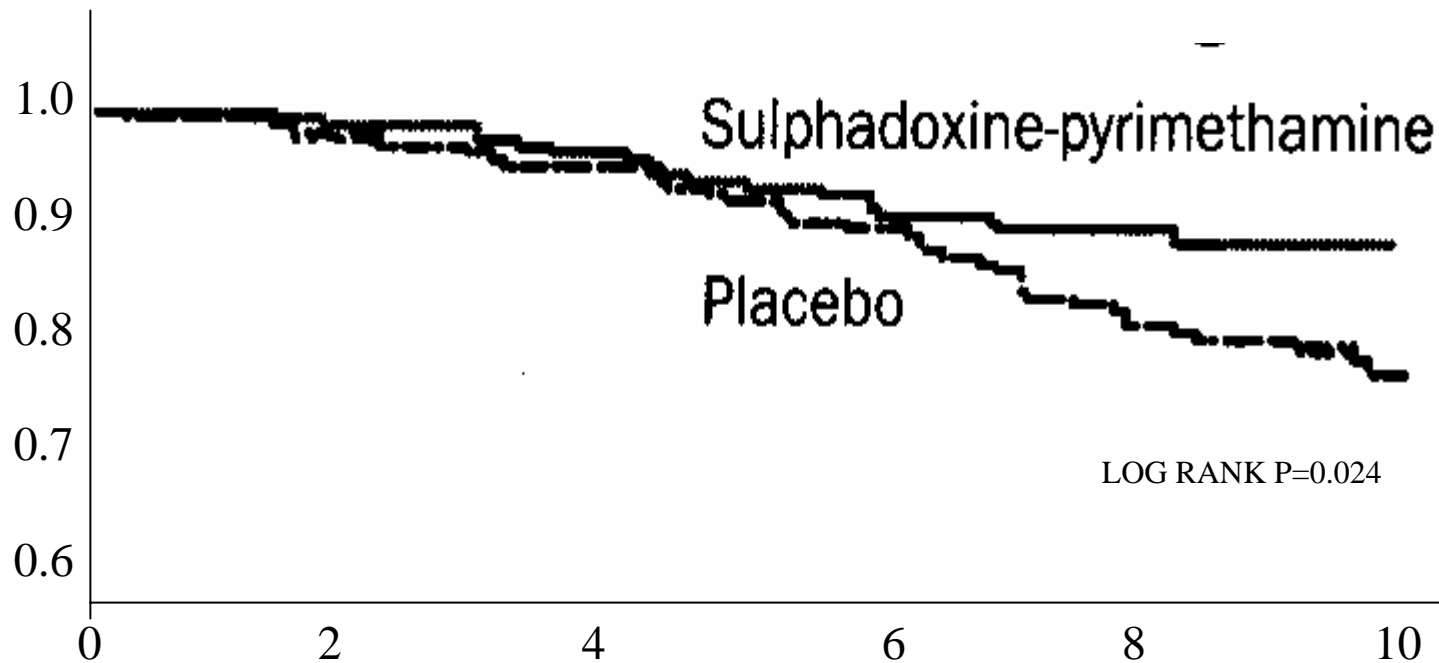
IPT IN CHILDREN



IPT IN INFANTS IN TANZANIA GIVEN AT THE TIME OF VACCINATION

From first dose until 12 months of age

Proportion free of severe anaemia

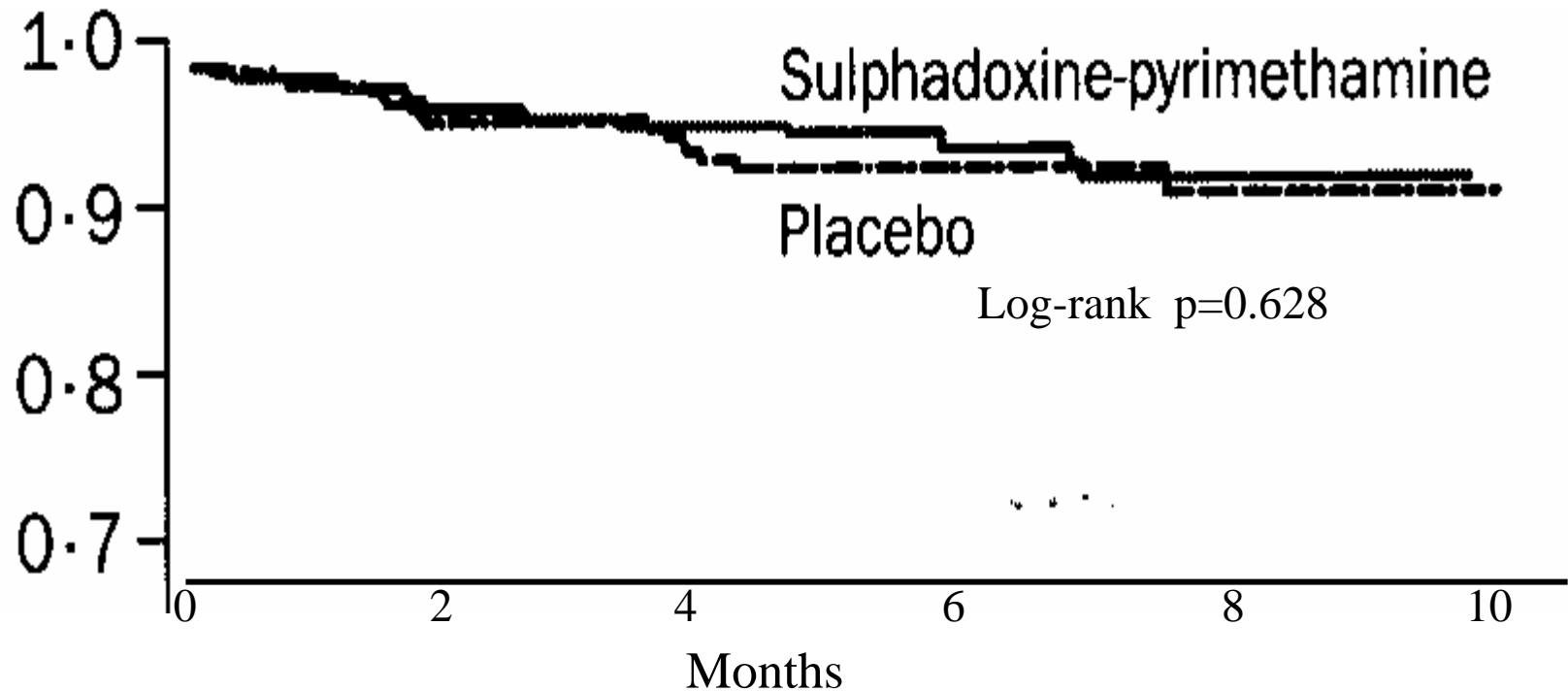


(D.Schellenberg et al, Lancet 2001; 357:1471)

IPT IN INFANTS IN TANZANIA – LACK OF REBOUND

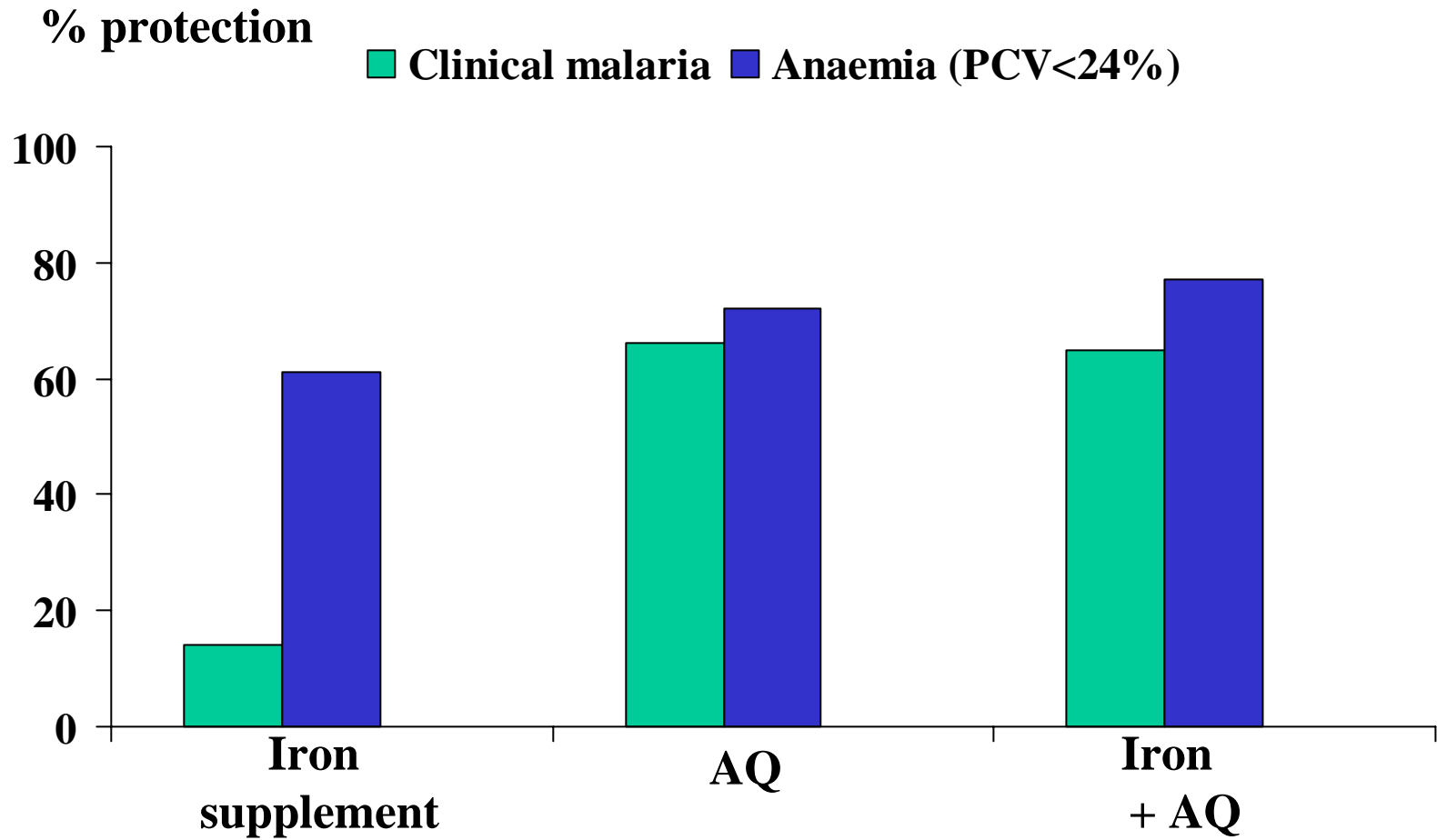
From 30 days after dose 3 until end of follow-up

Proportion free of severe anaemia



(D. Schellenberg et al., Lancet 2001; 357: 1475)

IPT WITH AMODIAQUINE IN TANZANIAN INFANTS GIVEN AT THE TIME OF HEALTH CENTRE VISITS



(Massaga et al., Lancet 2003; 361:1853-60)

IPTi STUDIES APPROACHING COMPLETION

GHANA
Navrongo
Kumasi
Tamale



KENYA
Eldoret

All employing S/P monotherapy

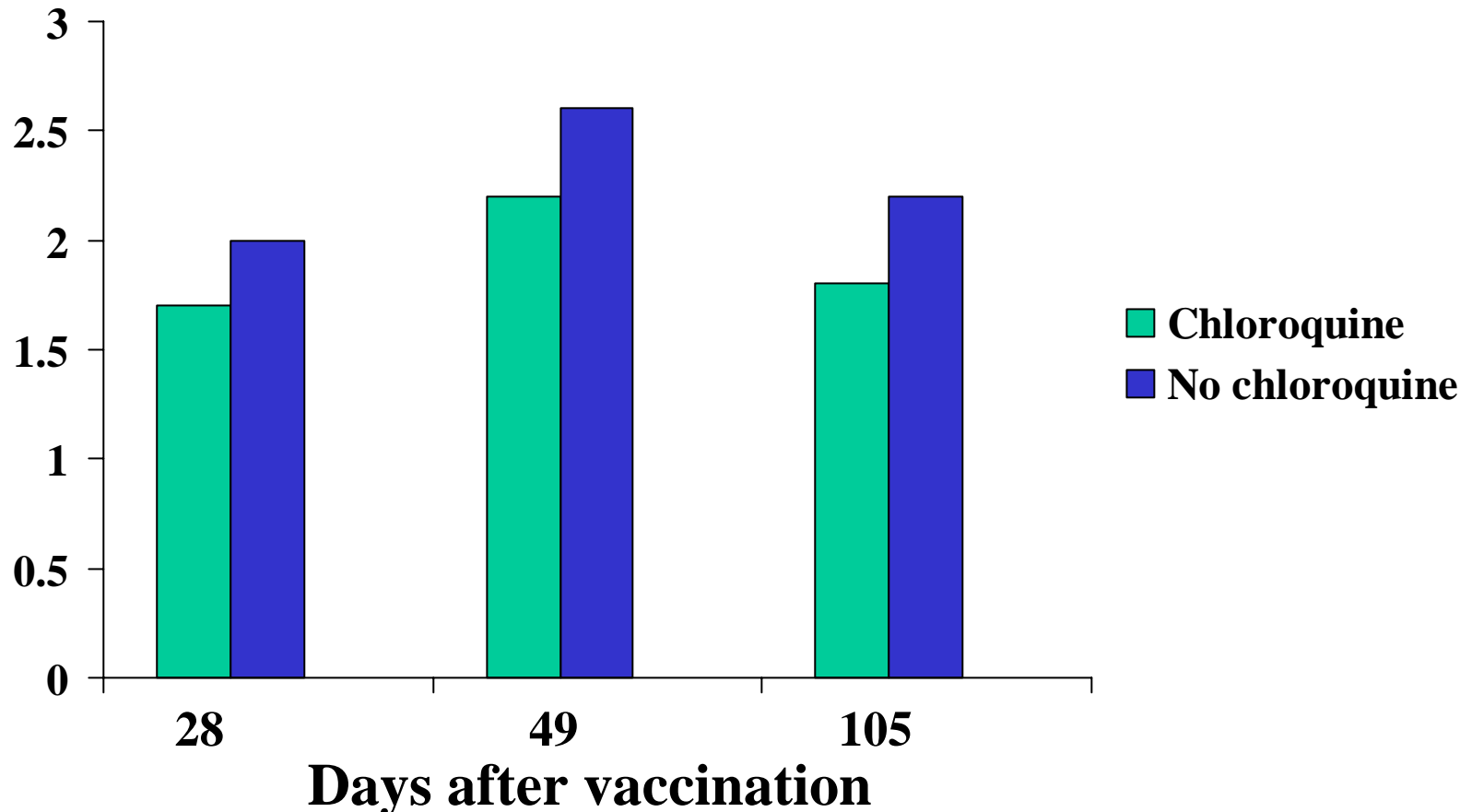
QUESTIONS ABOUT IPTi

- **How does it work ? Does it require a long-acting drug ?**
- **Will anti-malarials interfere with the immune response to vaccination?**
- **What drugs can be used to replace S/P for IPTi in areas of SP resistance ?**
- **Will it select for drug resistant parasites ?**
- **Will IPTi reduce infant mortality?**
- **Will IPTi be acceptable and cost effective ?**
- **How best can IPTi be introduced into the routine health service?**










MALARIA, ANTI-MALARIALS AND THE IMMUNE RESPONSE TO VACCINATION

Suppressive effect of anti-malarials

Log rabies antibody titre

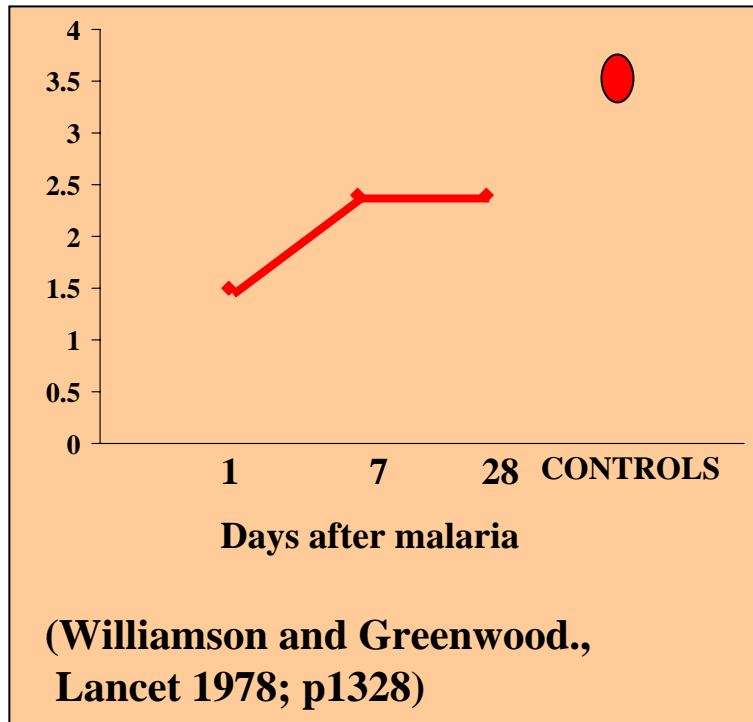


Suppressive effect of antimalarials

<u>DRUGS</u>	<u>VACCINES</u>	<u>IMPACT</u>
Chloroquine	Pneumococcal polysaccharide	
	Yellow fever	
	DTP	
	Oral cholera	
Proguanil	DPT	
	Oral typhoid	
Mefloquine	Oral cholera	
Atovaquone	Oral cholera	
	Oral typhoid	

(Straeten et al., NEJM 1986; 315:712. Barry et al., AJTMH 1991; 44:79
Gyhrs et al., AJTMH 1991; 45:613. Kollaritsch et al., JID 1997; 175:871)

The suppressive effect of malaria



Meningococcal antibody
1/12 post vaccination

	<u>Group A</u>	<u>Group C</u>
Chloroquine	2.7	3.0
Control	1.9	2.4

Greenwood et al., Ann Trop Med
Parasitol 1981; 75:261)

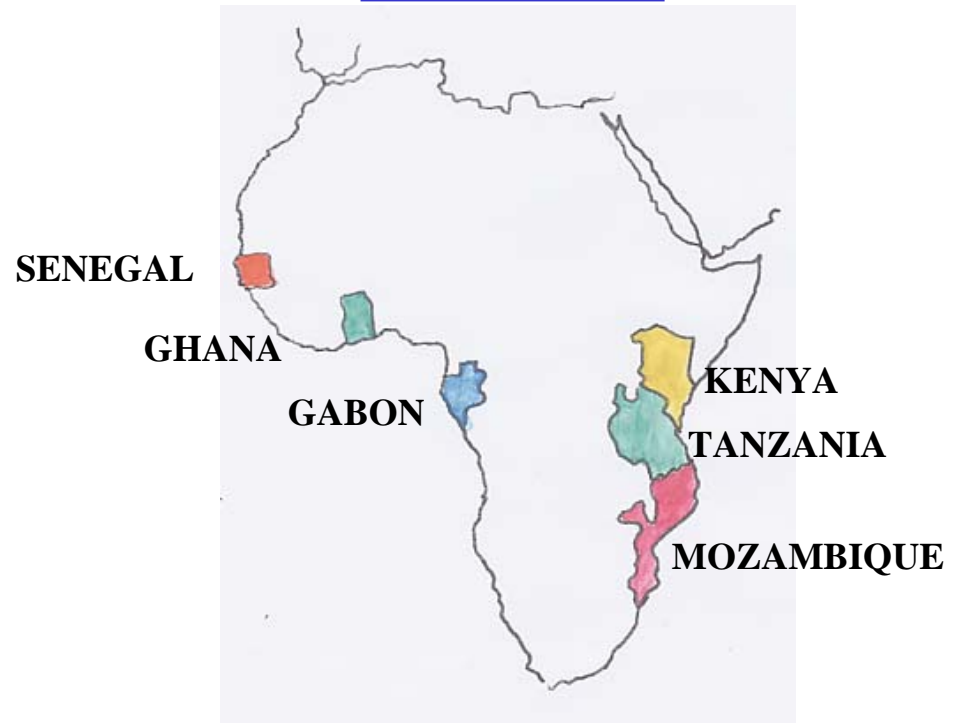
Review – Rosen & Bremen Lancet 2004; 363:1386)

IPTi CONSORTIUM

EUROPE



AFRICA



USA - CDC, Atlanta



MANHICA
MOZAMBIQUE

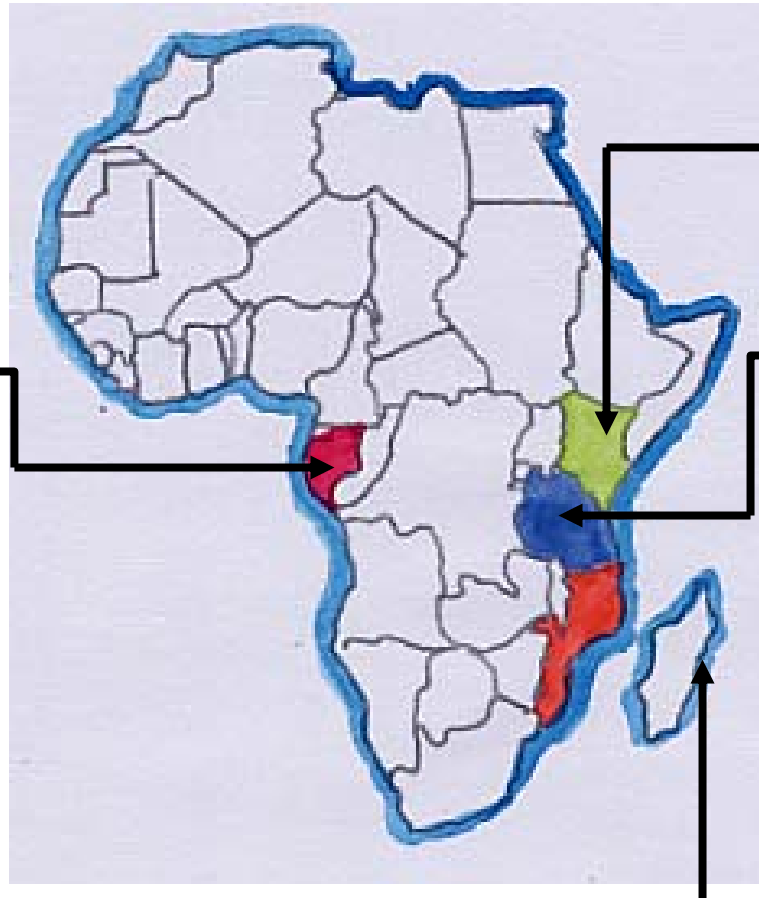
**Bill Gates announces
\$168 million in grants
for malaria research**

**International Herald Tribune
Monday, September 22nd
2003**

STUDIES APPROVED FOR FUNDING THROUGH THE IPTi CONSORTIUM

GABON

Trial of S/P
emphasis
on safety
and nutrition



KENYA

Trial of SP/amodiaquine/
Lapdap

TANZANIA

Trial of SP/Lapdap/
mefloquine in high and low
transmission areas

-Implementation studies

MOZAMBIQUE

Trial of S/P;
immunology
anthropology

STUDIES UNDER REVIEW

- **A study of the impact of IPTi with SP on mortality in the first two years of life**
- **Study of the impact of the various anti-malarials being considered for IPTi on the immune response to EPI vaccines**
- **Formulation of a liquid mixture of anti-malarial suitable for giving at EPI clinics**

IPTi AND THE RESPONSE TO EPI VACCINES

Ifakara study

	% <u>Seroconversion to measles vaccine</u>	
	<u>SP</u>	<u>PLACEBO</u>
Measles 1 st assays	82	91
Measles 2 nd assays	90	92
Combined	86	92

(Schellenberg et al.)

IPTi AND THE RESPONSE TO EPI VACCINES

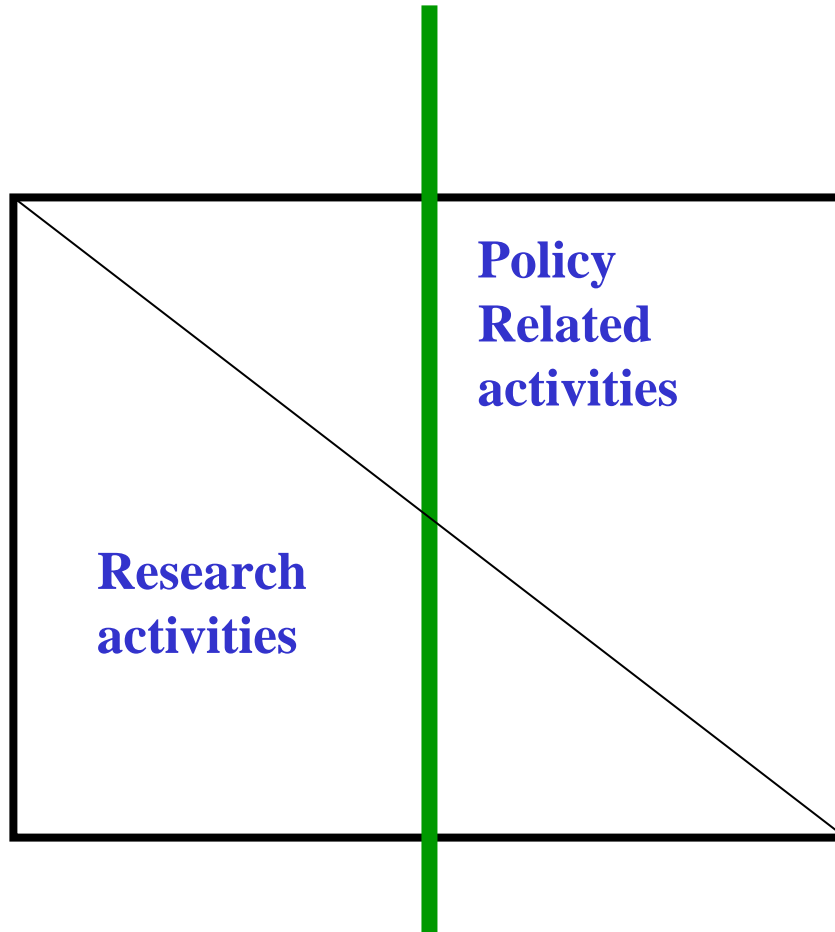
Expanded Serology Study

- Evaluation of responses to all EPI vaccines including Hib
- Evaluation of the effects of amodiaquine, mefloquine and Lapdap as well as SP

Powered to detect a 5% reduction in protective antibody concentrations for measles and 10% for other vaccines

[1000 and 500 infants required]

IPTi POLICY PLATFORM



Advocacy

**Endorsement by
WHO EPI/GAVI**

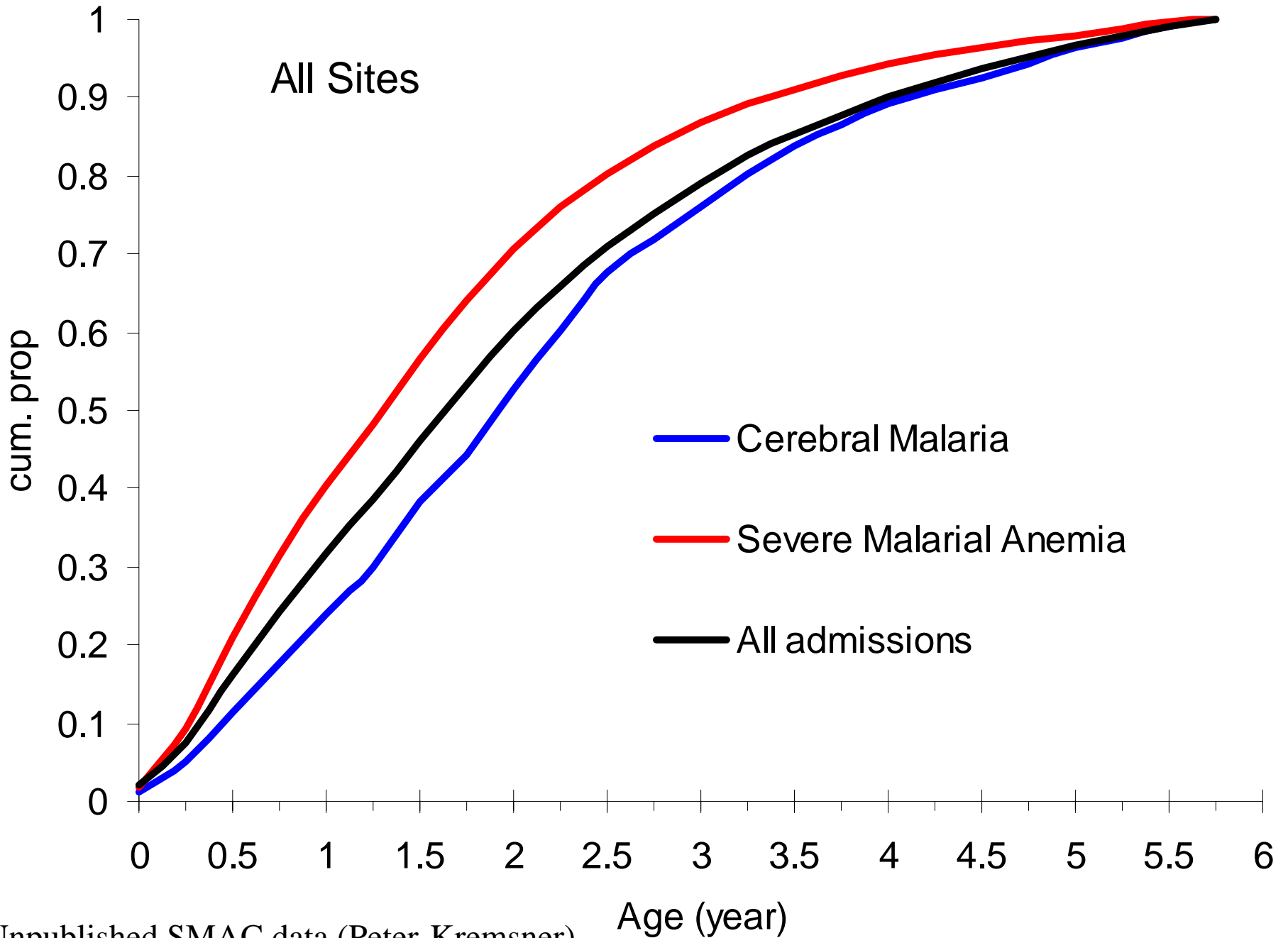
**Obtaining local
acceptance**

Costs

**Implementation
issues**

EXTENSION OF THE IPT PRINCIPLE TO OTHER GROUPS OF CHILDREN

- Children in areas where the main burden of malaria is later than the first year of life and/or is highly seasonal
- Children in high risk groups



All Sites

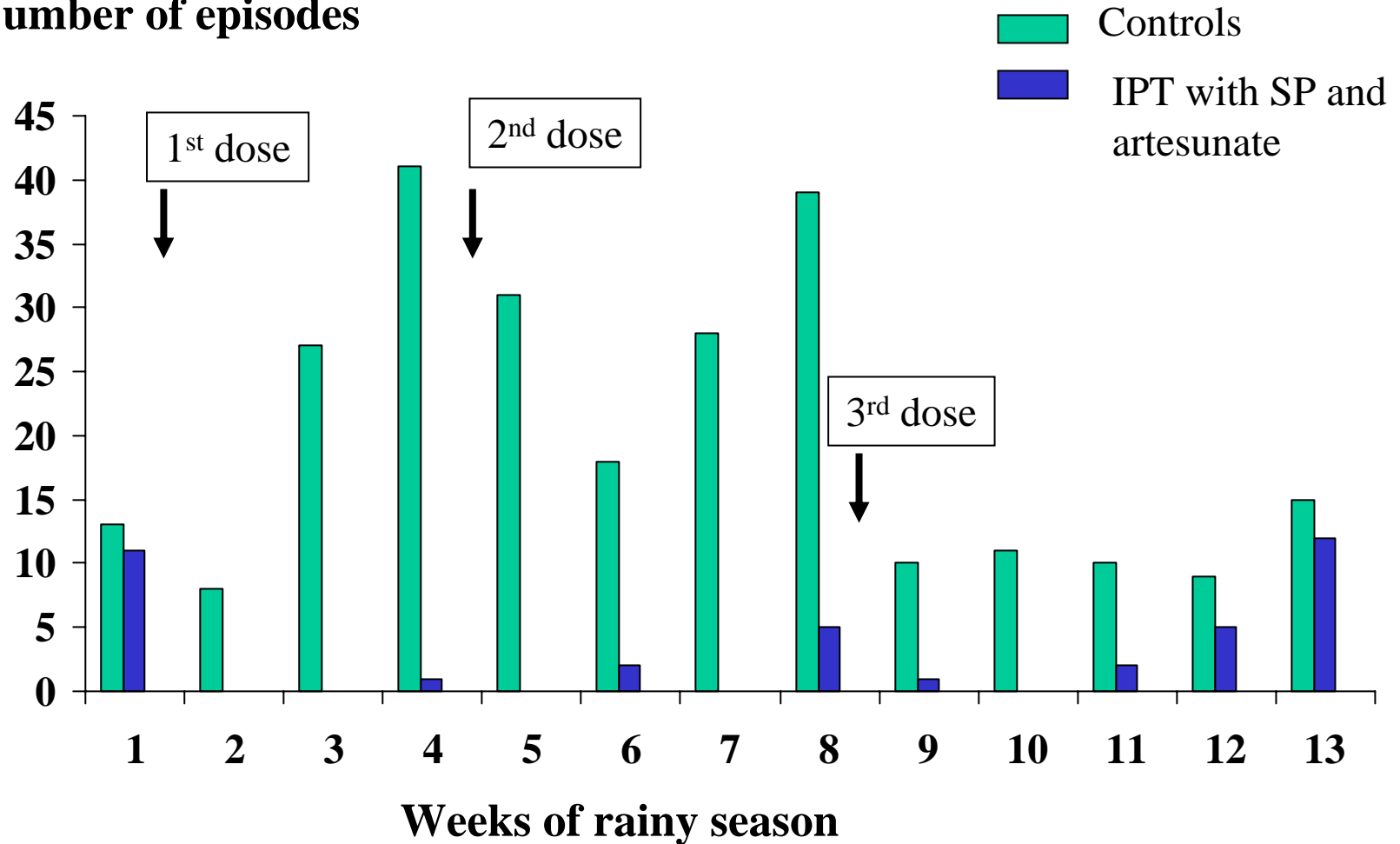
- Cerebral Malaria
- Severe Malarial Anemia
- All admissions

CROIX-ROUGE GÉNÉRAL A.S.E.
**CASE DE SANTE
DE KALOM**
CROIX-ROUGE FRANÇAISE



CLINICAL ATTACKS OF MALARIA IN SENEGALESE CHILDREN <5 YEARS OLD

Number of episodes

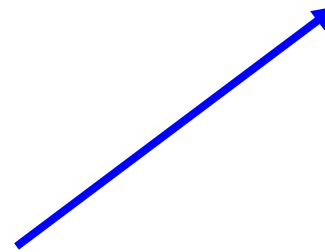


(Cisse, unpublished)

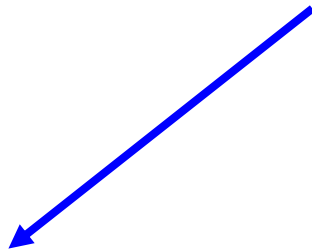
HOW COULD IPT_c BE DELIVERED ?

Could it be linked to catch up
vaccination campaigns ?

MDA



**IPT - THE OPTIMUM
BALANCE ?**



CHEMOPROPHYLLAXIS

ACKNOWLEDGMENTS

