HEART
HEALTH & EDUCATION ADVICE & RESOURCE TEAM

Helpdesk Report: Seasonal malaria chemoprevention (SMC) in Ghana

Date: 29 July 2013

Query: Produce a report focused the latest global evidence on the implementation and effectiveness of seasonal malaria chemoprevention (SMC) and make recommendations on how it could be most effectively implemented in Ghana.

Content

1. Overview

Malaria remains a leading cause of global ill health, causing an estimated 216 million cases of clinical malaria and 655 thousand deaths in 2010, of which more than 85% of malaria cases and 90% of malaria deaths occurred in sub-Saharan Africa (WHO, 2012). The treatment and prevention of malaria is a global priority.

Malaria treatment and prevention options exist for both endemic and non-endemic areas (van Vugt, et al., 2011). Key interventions currently recommended by WHO for the control of malaria are the use of insecticide treated nets (ITNs) and/or indoor residual spraying (IRS) for vector control, and prompt access to diagnostic testing of suspected malaria and treatment of confirmed cases. Additional interventions which are recommended in areas of high transmission for specific high risk groups include Intermittent Preventive Treatment in pregnancy (IPTp), and Intermittent Preventive Treatment in infancy (IPTi) (WHO, 2012).

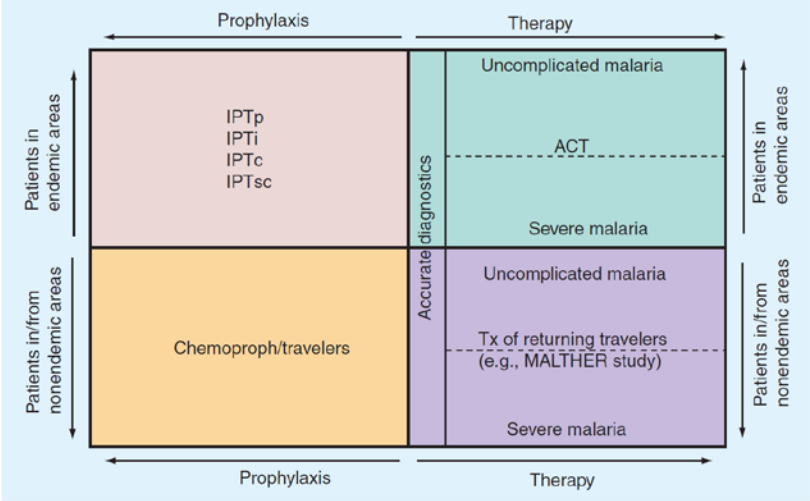

Figure 1. Malaria treatment and prophylaxis options in endemic and nonendemic countries.
ACT: Artemisinin combination treatment; IPT: Intermittent preventive treatment; IPTs: IPT in school children; IPTi: IPT in infants; IPTp: IPT in pregnant women.

van Vugt, et al., 2011 (http://www.futuremedicine.com/doi/pdf/10.2217/fmb.11.138 .

Across the Sahel sub-region of sub-Saharan Africa, most childhood malaria mortality and morbidity occurs during the rainy season, which is generally short (WHO, 2012). Giving effective malaria treatment at intervals during this period has been shown to prevent illness and death from malaria in children (WHO, 2012). With the recognition that the targeting of malaria control strategies to specific populations and/or locations can increase maximal effectiveness, WHO is now recommending a new intervention against Plasmodium falciparum malaria: Seasonal Malaria Chemoprevention. This intervention has been shown to be effective, cost-effective, safe, and feasible for the prevention of malaria among children less than 5 years of age in areas with highly seasonal malaria transmission (WHO, 2012).

The first trial of SMC took place in Senegal in 2002, where the intervention was known as Seasonal Intermittent Preventive Treatment in Children (IPTc) (Cisse et al., 2006, http://www.sciencedirect.com/science/article/pii/S0140673606682640). In 2012, IPTc became WHO Malaria Control Policy for areas with short malaria transmission seasons and was renamed 'Seasonal malaria chemoprevention'. As of 2013, SMC is starting to be implemented in West Africa (SMC review presentation, Professor Feiko O. Ter Kuile, LSTM).

Although the evidence indicates that SMC can be highly effective, concerns do exist regarding the potential role that mass implementation of SMC may play in the spread of drug resistance of the predominant malarial parasites, *P.falciparum*, to the most commonly used SMC treatment in West Africa, Sulphadoxine-pyrimethamine (SMC review presentation, Professor Feiko O. Ter Kuile, LSTM). There is some evidence for selection of resistant strains in IPT recipients, but no overall, population-wide impact on resistance has been identified (SMC review presentation, Professor Feiko O. Ter Kuile, LSTM).

Malaria in Ghana:

Malaria has been a major cause of poverty and low productivity accounting for about 32.5% percent of all outpatient attendances and 48.8% percent of under five years admissions in the country (NMCP annual report, 2009). Malaria is hyperendemic in all parts of the country, with all the 22.4 million population at risk. Transmission occurs all year round with slight seasonal variations during the rainy season from April to July. The seasonal variation is marked in the northern parts of Ghana where there is a prolonged dry season from September to April.

Ghana has been part of the Roll Back Malaria (RBM) initiative since 1999, and works within a strategic framework to guide its implementation. The government of Ghana supports the national malaria control programme using funding provided from the Global Fund. Financial and indirect support is also received from other partners such as WHO, UNICEF, USAID/PMI, DFID, etc. in the implementation of its activities.

2. Related terms

SMC – seasonal malaria chemoprevention

IPTc - intermittent preventive treatment in children

IPTp - intermittent preventive treatment in pregnancy

IPTi - intermittent preventive treatment in infancy

ITN – insecticide-treated net

LLIN - long-lasting insecticide-treated net

IRS – indoor residual spraying

ACTs - artemisinin-based combination therapies

SP- sulphadoxine-pyrimethamine

AQ- amodiaquine

VHWs - village health workers

RCH - reproductive and child health

3. Global evidence on SMC

i) Definition and current guidelines

WHO Policy Recommendation: Seasonal Malaria Chemoprevention (SMC) for Plasmodium falciparum malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa
WHO Global Malaria Programme. 2012.
http://www.who.int/malaria/publications/atoz/smc_policy_recommendation_en_032012.pdf

SMC, previously referred to as Intermittent preventive treatment in children, is defined as the intermittent administration of full treatment courses of an antimalarial medicine during the malaria season to prevent malarial illness with the objective of maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk.

The current WHO guidelines for SMC are:

- SMC is recommended in areas of highly seasonal malaria transmission across the Sahel sub-region. A complete treatment course of amodiaquine plus sulfadoxine-pyrimethamine (AQ+SP) should be given to children aged between 3 and 59 months at monthly intervals, beginning at the start of the transmission season, to a maximum of four doses during the malaria transmission season (provided both drugs retain sufficient antimalarial efficacy).
- The age-based recommended dosing schedule is:
    - Infants < 12 months old: AQ –half (½) of a 153mg tablet given once daily for three days and a single dose of SP -half of a 500/25mg tablet.
    - Children 12 –59 months: AQ –a full tablet of 153 mg given once daily for three days and a single dose of SP -a full tablet of 500/25mg.
    - The single dose of SP is given only on the first day together with the 1st dose of AQ.
- Target areas for implementation are areas where:
    - Malaria transmission and the majority of clinical malaria cases occur during a short period of about four months.
    - The clinical attack rate of malaria is greater than 0.1 attack per transmission season in the target age group.
    - AQ+SP remains efficacious (>90% efficacy).
- SMC Contraindications: SMC should not be given to –
    - A child with severe acute illness or unable to take oral medication.
    - An HIV-positive child receiving co-trimoxazole.
    - A child who has received a dose of either AQ or SP drug during the past month.
    - A child who is allergic to either drug (AQ or SP).

While there are several potential approaches to implementing SMC, there is presently insufficient evidence to recommend a standard deployment strategy and individual approaches best suited to local conditions should be used. However, if possible, its delivery should be integrated into existing programmes, such as Community Case Management and other Community Health Workers schemes.

ii) Coverage

There is no national level programmatic experience with SMC at this point. Following the recommendations in 2012, several countries in West Africa are considering the implementation of SMC. An identification of appropriate geographical areas for SMC in sub-Saharan Africa was conducted by Cairns and colleagues:

Estimating the potential public health impact of seasonal malaria chemoprevention in African children
Cairns, M., Roca-Feltrer, A., Garske, T., Wilson, A.L., Diallo, D., Milligan, P.J., Ghani, A.J., Greenwood, B.M. 2012. Nature Communications. DoI: 10.1038/ncomms187
http://www.nature.com/ncomms/journal/v3/n6/pdf/ncomms1879.pdf

This paper uses rainfall to define a predictor of malaria seasonality. The authors use spatial rainfall, malaria endemicity and population data to identify areas likely to have highly seasonal malaria incidence, and estimate the population at risk and malaria burden in areas where seasonal malaria chemoprevention would be appropriate. The authors estimate that in areas suitable for seasonal malaria chemoprevention, there are 39 million children under 5

years of age, who experience 33.7 million malaria episodes and 152,000 childhood deaths from malaria each year. The majority of this burden occurs in the sahelian or sub-sahelian regions of Africa. The data suggest that seasonal malaria chemoprevention has the potential to avert several million malaria cases and tens of thousands of childhood deaths each year if successfully delivered to the populations at risk.

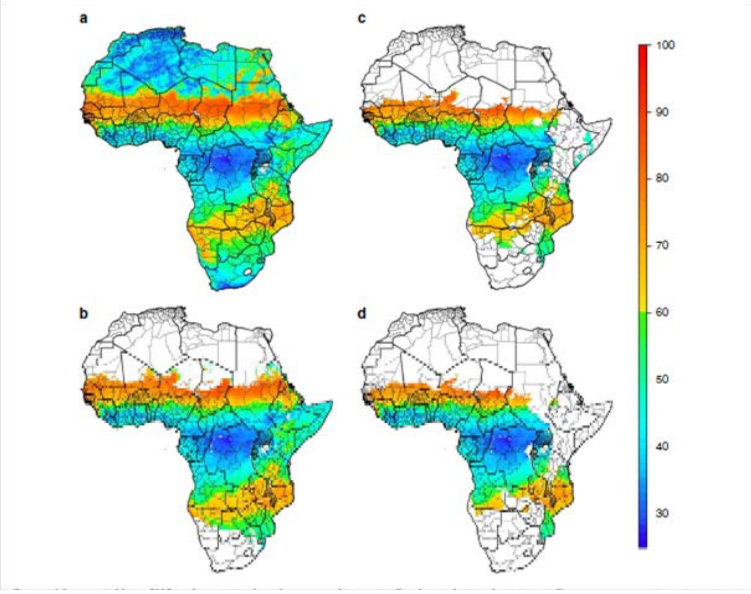

Figure 2. Areas suitable for SMC implementation based on seasonality in rainfall and on malaria endemicity. a) The maximum proportion of annual rainfall occurring within three consecutive months. Orange-red areas are those indentified as suitable for SMC based on >60% of annual rainfall in 3 months. Green-blue areas indicate areas with less than 60% of annual rainfall within 3 months. First administrative areas are superimposed on the map. b) The maximum proportion of annual rainfall restricted to areas with stable endemic P.falciparum, as estimated by the malaria atlas project. c) and d) indicate rainfall seasonality in areas with prevalence above 8.8 and 17.3%, as estimated by the malaria atlas project, corresponding to incidence above 0.1 and 0.2 cases per child per year, respectively.

iii) Strategies

Ghana currently utilises a variety of distribution strategies in its malaria control programmes. National Free Mass Campaigns (FMCN), Routine Free Distribution through the public sector (RFD), and Subsidised Private Sector Distribution have all been used at various times (van Eijk et al., 2011). Although none of these strategies is currently used to deliver SMC in Ghana, other West African countries have compared various methods of SMC delivery. This section is focused on potential delivery strategies for SMC in children rather than IPTp in pregnant women, as they require very different delivery strategies to children 3-59 months.

Two Strategies for the Delivery of IPTc in an Area of Seasonal Malaria Transmission in The Gambia: A Randomised Controlled Trial
Bojang, K.A., Akor, F., Conteh, L., Webb, E., Bittaye, O., Conway, D.J., Jasseh, M., Wiseman, V., Milligan, P.J., Greenwood, B. 2011. PLoS Medicine Volume 8(2): e1000409.
http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000409

This paper compared two approaches to the delivery of IPT to Gambian children: distribution by village health workers (VHWs) or through reproductive and child health (RCH) trekking teams, which provide most of the health care to children under the age of 5 years and antenatal care for pregnant women in rural areas.

During the 2006 malaria transmission season, the catchment populations of 26 RCH trekking clinics in The Gambia, each with 400–500 children 6 years of age and under, were randomly allocated to receive IPT from an RCH trekking team or from a VHW. Treatment with a single dose of sulfadoxine pyrimethamine (SP) plus three doses of amodiaquine (AQ) were given at monthly intervals during the malaria transmission season. Financial and economic costs associated with the two delivery strategies were collected and incremental cost and effects were compared. A nested case-control study was used to estimate efficacy of IPT treatment courses.

The authors found that the malaria treatment was safe and well tolerated. There were 49 cases of malaria in the areas where IPT was delivered through RCH clinics and 21 cases in the areas where IPT was delivered by VHWs. Delivery through VHWs achieved a substantially higher coverage level of three courses of IPT than delivery by RCH trekking teams. The efficacy of IPTc against malaria during the month after each treatment course was 87%.

For both methods of delivery, coverage was unrelated to indices of wealth, with similar coverage being achieved in the poorest and wealthiest groups. Delivery of IPTc by VHWs was less costly in both economic and financial terms than delivery through RCH trekking teams, resulting in incremental savings of US$872 and US$1,244 respectively. The annual economic cost of delivering at least the first dose of each course of IPTc was US$3.47 and US$1.63 per child using trekking team and VHWs respectively.

In this setting in The Gambia, delivery of IPTc to children 6 years of age and under by VHWs is more effective and less costly than delivery through RCH trekking clinics.

iv) Potential Impact

a. Public health impact of SMC

Intermittent preventive treatment for malaria in children living in areas with seasonal transmission
Meremikwu MM, Donegan S, Sinclair D, Esu E, Oringanje C. 2012. Cochrane database of systematic reviews. Volume 2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003756.pub4/pdf

This review evaluated the effects of IPTc in preventing malaria in preschool children living in endemic areas with seasonal malaria transmission. Studies that used individually randomised or cluster-randomized controlled trials of full therapeutic dose of antimalarial or antimalarial drug combinations given at regular intervals and had been compared with placebo or no preventive treatment in children aged six years or less living in an area with seasonal malaria transmission were selected for review.

Seven trials (12,589 participants) met the inclusion criteria. All were conducted in West Africa, and six of seven trials were restricted to children aged less than 5 years. IPTc prevents approximately three quarters of all clinical malaria episodes (rate ratio 0.26; 95% CI 0.17 to 0.38; 9321 participants, six trials, high quality evidence), and a similar proportion of severe malaria episodes (rate ratio 0.27, 95% CI 0.10 to 0.76; 5964 participants, two trials, high quality evidence). These effects remain present even where insecticide treated net (ITN) usage is high (two trials, 5964 participants, high quality evidence). IPTc probably produces a

small reduction in all-cause mortality consistent with the effect on severe malaria, but the trials were underpowered to reach statistical significance (risk ratio 0.66,95% CI 0.31 to 1.39,moderate quality evidence).The effect on anaemia varied between studies, but the risk of moderately severe anaemia is probably lower with IPTc (risk ratio 0.71,95% CI 0.52 to 0.98; 8805 participants, five trials, moderate quality evidence).

Serious drug-related adverse events, if they occur, are probably rare, with none reported in the six trials (9533 participants, six trials, moderate quality evidence). Amodiaquine plus sulphadoxine-pyrimethamine is the most studied drug combination for seasonal chemoprevention. Although effective, it causes increased vomiting in this age-group (risk ratio 2.78, 95% CI 2.31 to 3.35; two trials, 3544 participants, high quality evidence).When antimalarial IPTc was stopped, no rebound increase in malaria was observed in the three trials which continued follow-up for one season after IPTc

The authors conclude that in areas with seasonal malaria transmission, giving antimalarial drugs to preschool children (age < 6 years) as IPTc during the malaria transmission season markedly reduces episodes of clinical malaria, including severe malaria. This benefit occurs even in areas where insecticide treated net usage is high.

A Systematic Review and Meta-Analysis of the Efficacy and Safety of Intermittent Preventive Treatment of Malaria in Children (IPTc)
Wilson AL, on behalf of the IPTc Taskforce. 2011. PLoS ONE 6(2): e16976.
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0016976

This systematic review was conducted to assess the protective efficacy of IPTc to control the burden of seasonal malaria in the Sahel and sub-Sahelian areas of Africa. Twelve IPTc studies were identified: seven controlled and five non-controlled trials. The controlled studies demonstrated protective efficacies against clinical malaria of between 31% and 93% and meta-analysis of these showed an overall protective efficacy of monthly administered IPTc of 82% during the malaria transmission season. Pooling results from twelve studies demonstrated a protective effect of IPTc against all-cause mortality of 57% during the malaria transmission season.

Safety aspects of IPTc were reviewed. No serious adverse events attributable to the drugs used for IPTc were observed in any of the studies. Data from three studies that followed children during the malaria transmission season in the year following IPTc administration showed evidence of a slight increase in the incidence of clinical malaria compared to children who had not received IPTc.

The author concludes that IPTc is a safe method of malaria control that has the potential to avert a significant proportion of clinical malaria episodes in areas with markedly seasonal malaria transmission and also appears to have a substantial protective effect against all-cause mortality. These findings indicate that IPTc is a potentially valuable tool that can contribute to the control of malaria in areas with markedly seasonal transmission.

b. Additional impact of SMC in regions already experiencing some form of malaria control

Intermittent Preventive Treatment of Malaria Provides Substantial Protection against Malaria in Children Already Protected by an Insecticide-Treated Bednet in Mali: A Randomised, Double-Blind, Placebo-Controlled Trial
Dicko A, Diallo AI, Tembine I, Dicko Y, Dara N, et al. 2011. PLoS Medicine 8(2): e1000407.
http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000407

This article investigates the additional impact of IPTc in areas where children sleep under insecticide-treated nets (ITNs). A randomised, double-blind, placebo-controlled trial of IPTc with sulphadoxine pyrimethamine (SP) plus amodiaquine (AQ) in three localities in Kati, Mali was conducted. After initial screening, eligible children aged 3–59 months were given a long-lasting insecticide-treated net (LLIN) and randomised to receive three rounds of active drugs or placebos. Treatments were administered under observation at monthly intervals during the high malaria transmission season in August, September, and October 2008.

3,017 children (1,508 in the control and 1,509 in the intervention arm) were enrolled in the study. 1,485 children (98.5%) in the control arm and 1,481 (98.1%) in the intervention arm completed follow-up. During the intervention period, the proportion of children reported to have slept under an ITN was 99.7% in the control and 99.3% in intervention arm ($p = 0.45$). A total of 672 episodes of clinical malaria were observed in the control arm versus 126 (incidence rate of 0.34; 95% CI 0.29–0.41 episodes per person year) in the intervention arm, indicating a protective effect of 82% (95% CI 78%–85%; $p<0.001$) of IPTc on clinical malaria incidence.

IPTc reduced the prevalence of malaria infection by 85% (95% CI 73%–92%) ($p<0.001$) during the intervention period and by 46% (95% CI 31%–68%) ($p<0.001$) at the end of the intervention period. The frequencies of adverse events were similar between the two arms. There was no drug-related serious adverse event.

The authors conclude that IPTc given during the malaria transmission season provided substantial protection against clinical episodes of malaria, malaria infection, and anaemia in children using an LLIN. The treatment was safe and well tolerated. These findings indicate that IPTc could make a valuable contribution to malaria control in areas of seasonal malaria transmission alongside other interventions.

c. Impact of SMC on effectiveness of malaria treatments and on subsequent susceptibility to malaria infection

Prevalence of molecular markers of drug resistance in an area of seasonal malaria chemoprevention in children in Senegal
Lo, A., Faye, B., Ba, E., Cisse, B.A., Tine, R., Abiola, A., Ndiaye, M., Ndiaye, J.L, Ndiaye, D., Sokhna, C., Gomis, J.F., Dieng, Y., Faye, O., Ndir, O., Milligan, P., Cairns, M., Hallet, R., Sutherland, C., Gaye, O. 2013. Malaria Journal. Volume 12: 137
http://www.malariajournal.com/content/12/1/137

The authors studied the safety, feasibility and cost effectiveness of SMC in Senegal between 2008 and 2010 using a combined malaria treatment of sulphadoxine-pyrimethamine (SP) plus amodiaquine (AQ).The study also measured the impact of SMC on generation of drug resistance to malaria treatments. Three health districts in Senegal with 54 health posts were studied, with a gradual introduction of SMC. Three administrations of the combination AQ + SP were made during the months of September, October and November of each year in children aged less than 10 years living in the area. The authors found that there was lower malaria incidence in the areas that received SMC than in the control areas. The presence of genetic markers indicating drug resistance to the malaria treatment was also lower in the SMC regions. The sensitivity of P. Falciparum to SMC drugs should be regularly monitored in areas deploying this intervention.

Malaria Morbidity in Children in the Year after They Had Received Intermittent Preventive Treatment of Malaria in Mali: A Randomized Control Trial

Dicko A., Amadou Barry, A., Dicko, M., Diallo, M.D., Tembine, I., Dicko, Y., Dara, N., Sidibe, Y., Santara, G., Conaré, T., Chandramohan, D., Cousens, S., Milligan, P.J., Diallo, DA., Doumbo, OK., Greenwood, B. 2011. PLoS ONE Volume 6 (8): e23390.
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0023390

The authors report the results from a follow-up study of IPTc which was undertaken to establish whether children who had received IPTc would be at increased risk of malaria during the subsequent malaria transmission season.Morbidity from malaria and the prevalence of malaria parasitaemia and anaemia were measured in children who had previously received IPTc with SP and AQ.

1396 of 1508 children (93%) who had previously received IPTc and 1406 of 1508 children (93%) who had previously received placebos were followed up during the high malaria transmission season of the year following the intervention. Incidence rates of clinical malaria during the post-intervention transmission season (July –November 2009) were 1.87 (95% CI 1.76 –1.99) and 1.73 (95% CI; 1.62–1.85) episodes per child year in the previous intervention and placebo groups respectively; incidence rate ratio (IRR) 1.09 (95% CI 0.99 –1.21) (P = 0.08). The prevalence of malaria infection was similar in the two groups, 7.4% versus 7.5%, prevalence ratio (PR) of 0.99 (95% CI 0.73–1.33) (P = 0.95). At the end of post-intervention malaria transmission season, the prevalence of anaemia, defined as a haemoglobin concentration<11g/dL, was similar in the two groups (56.2% versus 55.6%; PR = 1.01 [95% CI 0.91 – 1.12]) (P = 0.84).

The authors conclude that IPTc with SP+AQ was not associated with an increase in incidence of malaria episodes, prevalence of malaria infection or anaemia in the subsequent malaria transmission season.

Immunological consequences of intermittent preventive treatment against malaria in Senegalese preschool children
Boulanger, D., Sarr, J.B., Fillol, F., Sokhna, C, Cisse, B., Schacht, A.M, Trape, J.F., Riveau, G., Simondon, F., Greenwood, B., Remoué, F. 2010. Malaria Journal. Volume 9:363
http://www.malariajournal.com/content/9/1/363

This article investigates whether SMC renders children more susceptible to subsequent malaria infection by preventing naturally-acquired immunity. Immune responses to P. Falciparum were measured in Senegalese children (6 months to 5 years old) who had received three rounds of IPTc with artesunate +sulphadoxine-pyrimethamine (or placebo) at monthly intervals eight months earlier.

The results showed that children who had received IPTc had lower anti-Plasmodium immunity than the non-treated controls. When epidemiological parameters were incorporated into the analysis, gender, nutritional status and haemoglobin concentration did not have any significant influence. In contrast, parasitaemia, past malaria morbidity and increasing age were strongly associated with a higher anti-Plasmodium immunity.

The authors conclude that the intensity of contact with *P. Falciparum* seems to represent the main factor influencing anti-Plasmodium immunity. Previous IPTc does not seem to interfere with this parasite-dependent acquired immunity eight months after the last drug administration.

Spatiotemporal mathematical modelling of mutations of the dhps gene in African Plasmodium falciparum
Flegg**,** J.A., Patil**,** A.P., Venkatesan, M**.,** Roper**,** C**.,** Naidoo, I., Hay**,** S.I., Hopkins Sibley, C., Guerin, P.J. 2013**.** Malaria Journal. Volume 12**:** 249.
http://www.malariajournal.com/content/pdf/1475-2875-12-249.pdf

Plasmodium falciparum has repeatedly evolved resistance to first-line anti-malarial drugs, thwarting efforts to control and eliminate the disease; in some periods of time this has contributed largely to an increase in mortality. The authors developed a mathematical model to map the spatiotemporal trends in the distribution of genetic mutations in the P. falciparum dihydropteroate synthetase (dhps) gene that confer resistance to the anti-malarial treatment sulphadoxine. These variations are a useful marker for the combination of genetic alleles that is highly correlated with resistance to sulphadoxine-pyrimethamine (SP). The aim of this study was to present a proof of concept for spatiotemporal modelling of trends in anti-malarial drug resistance that can be applied to monitor trends in resistance to components of artemisinin combination therapy (ACT), or other anti-malarials, as they emerge or spread.

Prevalence measurements of single nucleotide polymorphisms in three codon positions of the dihydropteroate synthetase (dhps) gene from published studies of dhps mutations across Africa were used. The maps presented visualise the changing prevalence of the drug resistant mutations in sub-Saharan Africa. These allow prediction of space-time trends in malaria parasite resistance to SP, and provide probability distributions of resistance prevalence in places where no data are available as well as insight on the spread of resistance in a way that the data alone do not allow.

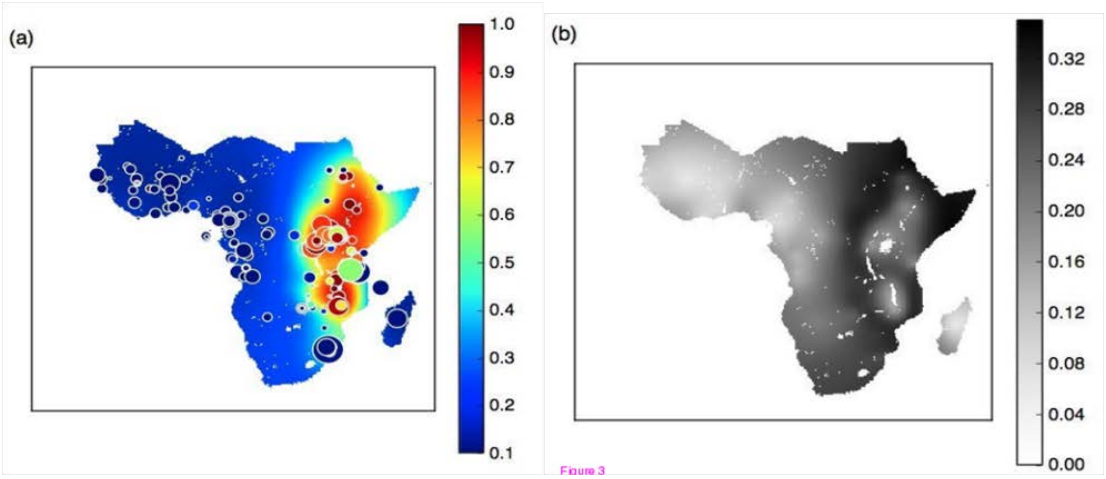

Figure 3. Spatial maps in 2010. The spatial distribution of median dhps540E prevalence from the model output in 2010 (a) and the associated model uncertainty (b). Studies that were conducted before or during the year of 2010 are represented on the median surface maps. All of the available data, from all years, were used to inform the 2010 map in the spatiotemporal model.

4. Epidemiology of malaria in Ghana

Strategic plan for malaria control in Ghana 2008-2015
http://www.ghanahealthservice.org/includes/upload/publications/STRATEGIC%20PLAN.pdf

Ghana is about 92,000 square miles (238,500 square kilometers) in area. In the north, a prolonged dry season occurs from September-November to March-April, with a rainy season that peaks in August; mean annual rainfall is 45 to 50 inches. The southern part of the country has rainfall ranging 50 to 86 inches. There are two rainy seasons (April-June and September-November) and two relatively dry periods that occur during the harmattan season (December-February) and in August. The Accra Plains are unusually dry for the coast, with a climate resembling that of the north.

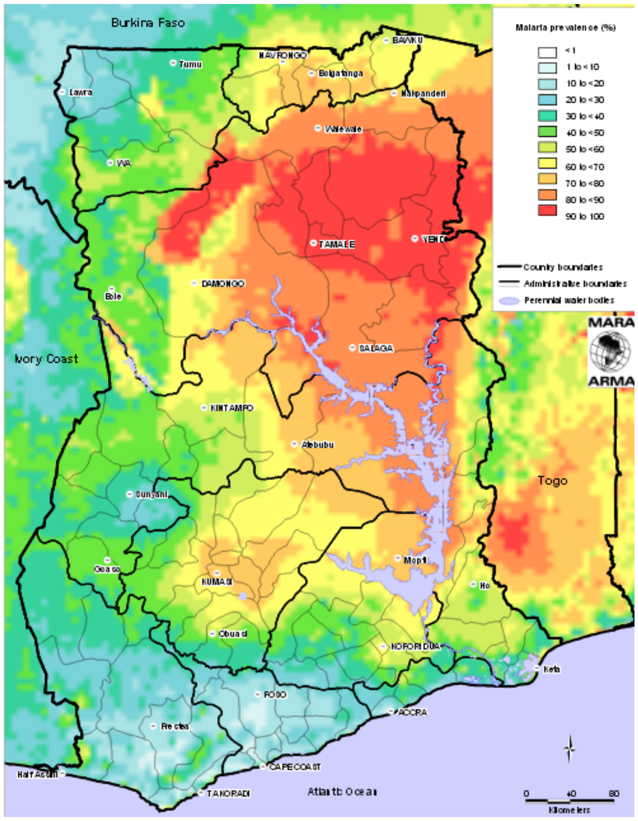

Figure 1. Malaria prevalence model for Ghana.

Malaria is hyperendemic in all parts of the country, with all the 22.4 million population at risk. Transmission occurs all year round with slight seasonal variations during the rainy season from April to July. The seasonal variation is marked in the northern parts of Ghana where there is a prolonged dry season from September to April.

Over the past five years, between 3.1 and 3.5 million cases of clinical malaria are reported in public health facilities each year, of which over 900,000 cases occur in children under five years. Presumptively diagnosed outpatient malaria cases accounted for 37.5% of all outpatient illnesses, 36% of all admissions and 33.4% of all deaths in children under-five years in 2006. In that same year, amongst pregnant women it accounted for 13.8% of all OPD attendances, 10.6% of admissions and 9.4% deaths.

The main parasite species causing malaria in Ghana are P. falciparum (80-90%), P. malariae (20-36%), and P. ovale (0.15%). Mixed infections of P. falciparum and P. malariae are not uncommon.

The principal mosquito vectors are the Anopheles gambiae complex and Anopheles funestus. These species are highly anthropophilic, biting mostly late in the night, and are commonly found in the rural and peri-urban areas where socio-economic activities lead to the creation of conducive breeding sites.

The groups affected most by malaria are children under-five years and pregnant women who constitute 20% and 4% respectively of the general population.

MAP: the malaria atlas project
http://www.map.ox.ac.uk/

The Malaria Atlas Project aims to disseminate free, accurate and up-to-date information on malaria and associated topics, organised on a geographical basis

Populations at risk of Plasmodium falciparum malaria in 2010 table for Ghana

		Stable transmission[2]				
Age group	**Unstable risk[1]**	***Pf PfPR*$_{2-10}$[3]≤5%**	**5%>*PfPR*$_{2-10}$[3]≤40%**	***PfPR*$_{2-10}$[3]>40%**	**Total stable**	**Total PAR[4]**
All	1.03	15.98	131.26	95.11	242.36	243.39
15+	0.63	9.82	80.61	58.41	148.84	149.47
5-14	0.25	3.85	31.64	22.92	58.41	58.66
0-4	0.15	2.31	19.01	13.78	35.10	35.25

1. Population in 100,000s living in areas of unstable *P. falciparum* risk (*Pf*API <0.1 per 1,000 people p.a.)
2. Population in 100,000s living in areas of stable *P. falciparum* risk (*Pf*API ≥0.1 per 1,000 people p.a.)
3. *Pf*PR2-10 is the *P. falciparum* parasite rate in two to ten years olds
4. The total population at risk (PAR) in 100,000s living in areas of *P. falciparum* malaria transmission

These population at risk estimates were generated using estimates of population and estimates of malaria risk (endemicity). The population grid was overlaid with the categorised endemicity map and the total and age-specific population located within each endemicity class was computed. An equivalent calculation was made of the land area associated with each endemicity class, by replacing the population grid with one quantifying the surface area of each pixel, taking into account the equi-rectangular map projection used.

Spatio-temporal malaria transmission patterns in Navrongo demographic surveillance site, northern Ghana
Kasasa, S., Asoala, V., Gosoniu, L., Anto, F., Adjuik. M, Tindana, C., Smith, T., Owusu-Agyei, S., Vounatsou, P.2013. Malaria Journal, Volume 12:63.
http://www.malariajournal.com/content/pdf/1475-2875-12-63.pdf

This paper investigates the relationship between entomological measures of malaria transmission intensity and mortality. Currently, the relationship is uncertain, partly because transmission is heterogeneous even within small geographical areas. This study analysed data from Kassena-Nankanadistricts in northern Ghana to obtain small area estimates of malaria transmission rates allowing for this uncertainty.

Mosquitoes were trapped from 2,803 unique locations for three years. Anopheles gambiae mosquitoes constituted 52%, the rest were Anopheles funestus mosquitoes. The mean biting rates for An. Funestus and An. gambiae were 32 and 33 respectively. Most bites occurred in September, the wettest month. The number of mosquitoes with infective immature parasites present in their salivary glands was higher in the dry periods of the last two years compared with the wet period. The annual entomological inoculation rate (EIR) varied from 1,132 to 157 infective bites, and the monthly EIR varied between zero and 388 infective bites.

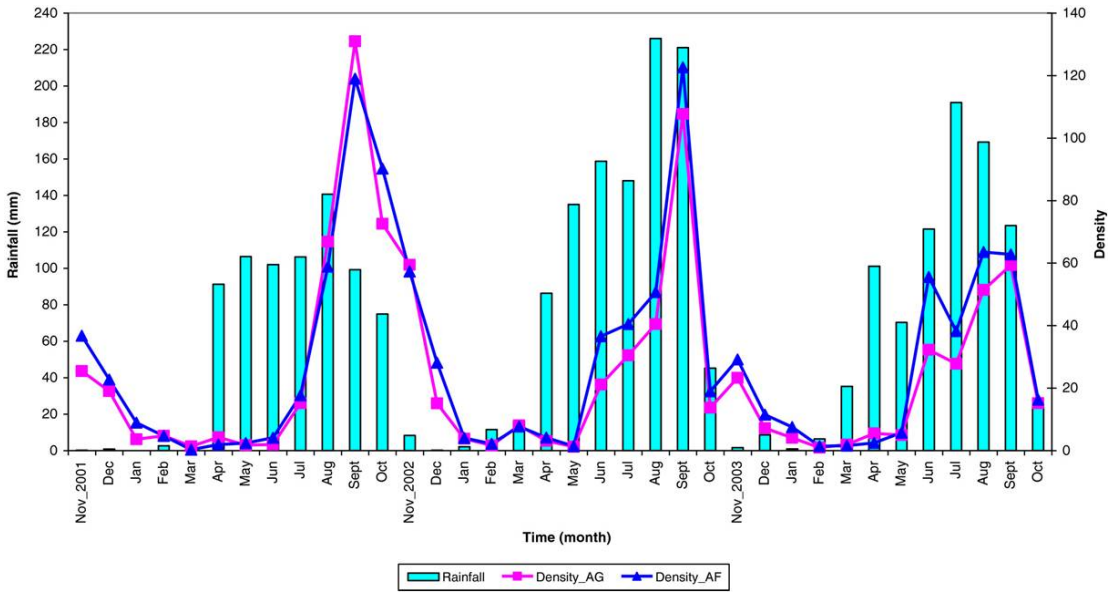

Figure 1. Monthly rainfall and observed mosquito density.

Epidemiology of malaria in the forest-savanna transitional zone of Ghana
Owusu-Agyei, S., Asante, K.P., Adjuik, M., Adjei, G., Awin, E., Adams, M., Newton, S., Dosoo, D., Dery, D., Agyeman-Budu, A., Gyapong, J., Greenwood, B., Chandramohan, D. 2009. Malaria Journal. Volume 8:220.
http://www.biomedcentral.com/content/pdf/1475-2875-8-220.pdf

The authors investigated the epidemiology of malaria in a rural site in central Ghana using surveillance of clinical malaria cases. Active surveillance of clinical malaria was carried out in 335 children below five years of age and the prevalence of malaria was estimated 1,484 subjects of all ages over a 12-month period. Participants were sampled from clusters drawn around sixteen index houses randomly selected from a total of about 22,000 houses within the study area.

The average parasite prevalence in the all age cohort was 58% (95% CI: 56.9,59.4). In children below five years of age, the average prevalence was 64% (95% CI: 61.9, 66.0). More than 50% of all children less than 10 years of age were anaemic. Children less than 5 years of age had as many as seven malaria attacks per child per year. The main vectors were Anopheles funestus and Anopheles gambiae. The authors conclude that the transmission of malaria in the forest-savanna region of central Ghana is high and perennial.

5. Malaria control strategy in Ghana

i) National control programme

Roll back malaria: National malaria control programme
http://www.ghanahealthservice.org/malaria_control.php

Ghana has been part of the Roll Back Malaria (RBM) initiative since 1999, and works within a strategic framework to guide its implementation. The Ghana RBM programme emphasizes the strengthening of health services through multi and inter-sectoral partnerships and making treatment and prevention strategies more widely available.

The original goal of the RBM was to reduce malaria specific morbidity and mortality by 50% by the year 2010, using the following strategies:

- Promote multiple prevention which includes promotion of treated bed nets usage; chemoprophylaxis in pregnancy and environmental management.
- Improve malaria case management at all levels(from household to health facility);
- Encourage evidence-based research to come up with effective interventions and
- Improve partnership with all partners at all levels.

The current iteration of the malaria control programme aims at reducing death and illness due to the malaria disease by 75% by the year 2015 in line with the attainment of the Millennium Development Goals (MDGs). This goal is to be achieved through overall health sector development, improved strategic investments in malaria control, and increased coverage towards universal access to malaria treatment and prevention interventions.

The specific objectives the current malaria control programme are:

- 100% of households will own at least one ITN
- 80% of the general population will sleep under ITNs
- Increase the number of children under-five and pregnant women sleeping under treated net from current levels to 85%
- 100% pregnant women shall be on appropriate Intermittent Preventive Treatment (Receive at least two or more doses of sulphadoxine-pyrimethamine under Directly Observed Therapy (DOT))
- 90% of all structures in targeted districts will be covered through indoor residual spraying
- All health facilities will provide prompt and effective treatment using Artemisinin Combination Therapies (ACTs)
- 90% of all patients with uncomplicated malaria will be correctly managed at public and private health facilities using ACTs
- All communities will have access to community-based treatment for uncomplicated malaria
- 90% of caretakers and parents will be able to recognise early symptoms and signs of malaria
- 90% of children under five years of age with fever will receive an appropriate ACT within 24 hours of onset.

Strategies to achieve these objectives include:

- Equipping all health facilities with malaria diagnostic facilities (microscopes or RDTs) and provide effective antimalarial drugs.
- Strengthening human resource through in-service training of laboratory technicians and clinicians.
- Scaling-up community based treatment of malaria in all districts through the home base care of malaria targeting children under five years living in rural areas and areas with limited access.
- Insecticide Treated materials (ITM) scale-up access to Long Lasting Insecticide Nets to achieve universal coverage -:Access to Insecticide treated nets.
- Indoor Residual Spraying (IRS) will be scaled up rapidly, building on the models of IRS campaigns in Obuasi and the Northern Region.

- Strengthening the routine data collection system to capture reliable information, and undertake regular operational researches to provide evidence for decision making.
- Forge functional partnerships and mechanisms between departments, programmes within and outside the health sector.

The expected outcomes following implementation of these strategies are improved malaria prevention, improved access to prompt and effective treatment, strengthened monitoring and evaluation and operational research, strengthened health systems at all levels, and partnerships for malaria control created and maintained.

The government of Ghana supports the national malaria control programme using funding provided from the Global Fund. Financial and indirect support is also received from other partners such as WHO, UNICEF, USAID/PMI, DFID, etc. in the implementation of its activities.

ii) Interventions by GFATM

Renewal scorecard Ghana – malaria
The global fund to fight AIDS, TB and malaria. March 14, 2013.
www.theglobalfund.org/GrantDocuments/GHN-M-13_GSC_0_en/

GFATM is the major supporter of the Ghana National Strategic Plan for Malaria Control. A series of interventions take place across a spectrum of activities, including prevention, diagnosis and ensuring effective treatment.

The interventions detailed in the Country Coordinating Mechanism (CCM) request for funding are evidence based, with the potential to achieve high impact in the Ghanaian epidemiological context. Several are focused directly on most at risk groups or concentrated on geographical areas of greatest need. The interventions include:

- Affordable/low cost artemisinin-based combination therapy (ACTs) in public and private sectors and expanding services to remote/community zones;
- Preventive intermittent preventive treatment of malaria during pregnancy (IPTp) treatment and chemotherapy;
- Increasing rapid diagnostic test (RDT) and microscope testing;
- LLIN distribution (universal coverage was reached by the end of 2012);
- Indoor residual spraying (IRS) in 40 of the highest burden districts in Ghana.

The most recent available data shows that the National Malaria Control Program (NMCP) has been recording steady improvements in the key impact/outcome indicators since the program started scaling up interventions with the support from The Global Fund and other development partners.

A national model for malaria control in Ghana
ANGLOGOLD ASHANTI Sustainability Review 2009
http://www.anglogold.com/subwebs/informationforinvestors/reports09/obuasi-malaria.htm

AngloGold Ashanti, a mining company based in Johannesburg, was one of the recipients of a grant of up to $133m to Ghana from the Global fund. AngloGold received this money to roll out a model developed at Obuasi to 40 districts in Ghana. The aim of the Obuasi pilot was to reduce the incidence of malaria by 50% in two years.

Results from Obuasi indicate that the programme reduced the burden of malaria in the community and increased school attendance. Since 2005, there has been a 75% decrease in

cases seen by the mine hospital. Medication costs have been reduced to $9,800 per month. Lost days due to malaria have been reduced from 6,983 per month in 2005 to only 282 in 2009.

The programme is a partnership with the Ghana Health Service, the National Malaria Control Programme (NMCP) and the local Obuasi Municipal Assembly, acting with the approval of the Ministry of Health. This was the first time that a private sector company has been appointed as the principal recipient of a GFATM grant in Africa and only the second globally.

iii) Interventions by PMI

President's malaria initiative, Ghana.
Malaria Operational Plan Financial Year 2013
http://pmi.gov/countries/mops/fy13/ghana_mop_fy13.pdf

The Global Health Initiative (GHI) is a U.S. government-funded programme aimed at reducing the burden of disease around the world. The President's Malaria Initiative (PMI) is a core component of the GHI. PMI was launched in June 2005 as a 5-year, $1.2 billion initiative to rapidly scale up malaria prevention and treatment interventions and reduce malaria-related mortality by 50% in 15 high-burden countries in sub-Saharan Africa. Funding for PMI has now been extended through Financial Year 2014 and, the goal of PMI has been adjusted to reduce malaria-related mortality by 70% in the original 15 countries by the end of 2015.

This will be achieved by continuing to scale up coverage of the most vulnerable groups — children under five years of age and pregnant women — with proven preventive and therapeutic interventions, including artemisinin-based combination therapies (ACTs), insecticide-treated nets (ITNs), intermittent preventive treatment of pregnant women (IPTp), and indoor residual spraying (IRS).

Ghana became a PMI country in December 2007. The PMI/Ghana strategy for 2013 is to continue to support all four prevention and treatment interventions and prioritise procurement of RDTs and pediatric formulations of ACTs; support for large scale prevention activities in regions with relatively high population and high parasite prevalence; and targeting major interventions based on epidemiological information and data. The FY 2013 planned budget is $27 million.

The planned support for each of the four interventions is as follows:

Artemisinin-based combination therapies: PMI will procure approximately 4.75 million Rapid Diagnostic Tests and 4.5 million treatments of pediatric ACTs. PMI will support healthcare workers who have received malaria case management training in the past and expand malaria case management capacity to community based health planning and services and peripheral healthcare facilities. The PMI strategy includes a private sector approach to increase pharmacy and licensed chemical seller compliance with Ghana Health Services (GHS) malaria case management guidelines.

Insecticide-treated Nets: PMI will procure 1.1 million Long-Lasting Insecticide-treated Nets (LLIN) and support the Government of Ghana to implement and strengthen the routine LLIN distribution system and implement LLIN promotion activities. PMI will also support an evaluation of the routine LLIN distribution system to develop evidence to improve the system in Ghana and in other malaria endemic countries.

Intermittent Preventative Treatment of pregnant women: The PMI strategy for IPTp will be to solidify the knowledge, skills, and practices of healthcare workers at antenatal clinics (ANC) and expand IPTp capacity at peripheral healthcare facilities and services. PMI will

support activities to promote ANC and IPTp services among women of reproductive age. PMI will emphasise support for IPTp in regions where the IPTp rate is lagging.

Indoor Residual Spraying: Evidence indicates that PMI's well-implemented IRS activity in the Northern Region is not having the intended effect on parasite prevalence and malaria morbidity is building. Therefore, PMI is considering scaling back IRS activities in the north following the LLIN universal coverage campaign, continuing intensive epidemiologic and entomologic monitoring in the Northern Region, and scoping a new location for the PMI IRS activities in the middle forest or coastal zone.

The Financial Year 2013 PMI plans also include capacity building among Ghanaian partners and support for monitoring and evaluation (M&E).The technical interventions supported by PMI are designed to build the capacity of Ghana Health Service and other Government of Ghana routine systems to sustain gains

iv) Interventions by other partners

Renewal scorecard Ghana – malaria
The global fund to fight AIDS, TB and malaria. March 14, 2013.
www.theglobalfund.org/GrantDocuments/GHN-M-13_GSC_0_en/

Although the Global Fund is likely to remain the single largest donor for malaria activities over the period of 2013-2015, a number of other partners are likely to provide important funding and assistance to malaria control efforts in Ghana over the period.

DFID: Along with UNICEF, PMI and the Global Fund, DFID was one of the major supporters of the "Hang up" campaign of mass bed net distribution in 2011-2012. The DFID malaria strategy is currently in development, but in coming years DFID is likely to focus on:

- Improving diagnosis.
- Malaria Prevention.
- Increasing/Improving data relating to malaria.

Provided current DFID proposals are approved, the budget for these activities will be approximately 10 million GBP (US$15m) over the period 2013-2015 (with the possibility of up to 20 million GBP over 4 years).

UNICEF: A key implementer in the mass LLIN distribution, UNICEF undertake LLIN distribution in five regions and support supervision and monitoring in five northern districts.

WHO: The WHO provides technical assistance to the NMCP and will play a leading role in the upcoming Malaria Prevalence Survey (due to commence in 2013) in line with the Global Fund grants' efforts to improve availability of data. Current work in partnership with USAID on resistance to insecticides may also prove useful in ensuring the ongoing effectiveness of the IRS program managed by Anglo Gold Ashanti.

6. Additional information

Author
This query response was prepared by **Geraldine Foster, Catherine Holley and Stephen Thomson**

Contributors
Anja Terlouw, Research Fellow, LSTM

Professor Feiko ter Kuile, LSTM

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