Cover page

Official Title: Exploring the impact of scaling up mass testing, treatment and tracking on malaria prevalence among children in the Pakro sub district of Ghana

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PROJECT SUMMARY

Malaria poses a serious burden in sub-Sahara Africa. Efforts are ongoing to scale up interventions that work. These include the use of Long Lasting Insecticidal Nets (LLIN), Intermittent Preventive Treatment in children (IPTc), and test, treat and track (TTT). There is the need, however, for mass testing, treatment and tracking (MTTT) of the whole population to reduce the parasite load before implementing the aforementioned interventions. Though, Seasonal Malaria Chemoprophylaxis (SMC) is adopted for selected localities in Ghana, the impact of such interventions could be enhanced, if associated with MTTT in order to reduce the parasite load at baseline. MTTT of children in Ghana has demonstrated a parasite load reduction from 25% to 1%. However, unanswered questions include - could this be scaled up? What proportion of the community could be covered over a given time? What do the investigators need to accomplish large scale MTTT? In designing interventions that aim at reducing the burden of malaria in children under five, for example, MTTT has largely been left out. Adults who are not often targeted by such interventions remain reservoirs that fuel transmission. This study explores the scale-up of interventions that work using existing community volunteer teams to lower cost. These volunteers will play a surveillance role by conducting home-based management of malaria. To avoid challenges posed by stockouts, short message service (SMS) will be used to monitor the level of stocks for malaria medicine and Rapid Diagnostic Tests (RDTs). It is hypothesized that there are more asymptomatic malaria cases (those who carry the parasite but are not ill) than symptomatic cases reported by hospital records in the Pakro sub district and that, carrying out MTTT in combination with home-based management of malaria in specific communities could greatly reduce the burden. Through this study, the bottlenecks that hinder scaling-up of MTTT will be documented in order to facilitate the process.

GENERAL INFORMATION

Protocol Title: Exploring the impact of scaling up mass testing, treatment and tracking on malaria prevalence among children in the Pakro sub district of Ghana

PRIOR SCIENTIFIC REVIEW
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Principal Investigator:

Ndong Ignatius Cheng (PhD, Pharmaceutics)
Post-Doctoral Fellow
Epidemiology Department,
Noguchi Memorial Institute for Medical Research
University of Ghana
P. O. Box LG 581 Legon
Tel: +233 561817573
Email: NCheng@noguchi.ug.edu.gh

Co-PIs:

Collins Stephen Ahorlu, PhD
Head of Department
Department of Epidemiology
Noguchi Memorial Institute for Medical Research
T: +23321280162
E-mail: cahorlu@noguchi.ug.edu.gh

Prof. Kwado A. Koram, PhD
Department of Epidemiology
Noguchi Memorial Institute for Medical Research
University of Ghana
P. O. Box LG 581 Legon
T: +233 302 501180
C: +233 240 313130
Email: kkoram@noguchi.ug.edu.gh

Prof. Alexander Nyarko PhD
Dean School of Pharmacy
University of Ghana
P. O. Box LG 581 Legon
Tel: +233203465071
E-mail: ANyarko@noguchi.ug.edu.gh

Mentors

Prof. Corinne Merle Simone Collette
TDR
Telephone: (+41) 22 791 2235
E-mail:merlec@who.int

Dr. Alfred Amambua Ngwa
Medical Research Council
The Gambia
Tel: +2207817428
E-mail: angwa@mrc.gm

Stakeholders

Ghana Health Service, Noguchi Memorial Institute for Medical Research (NMIMR), the local communities and WHO.

Introduction/Rationale

The World Health Organization (WHO) in 2010 reported that malaria was endemic in 96 countries reflecting an improvement of the situation of 2005 where it was endemic in 106 countries (WHO, 2010). Malaria morbidity and mortality remain a serious problem in sub Saharan Africa especially in areas with holo-endemic transmission (Appawu, Baffoe-Wilmot et al. 1994). Over the last decade, the number of recorded malaria cases has steadily dropped from 247 million cases with 881,000 deaths reported in 2006 to 198 million with 584,000 deaths in 2013 (WHO, 2009, 2010, 2013). This has largely been due to the introduction of ACTs following the resistance witnessed against chloroquine as well as an increase in the number of control measures such as the use of insecticide treated nets, long lasting insecticidal nets (LLIN), vectors surveillance and intermittent preventive treatment in pregnancy (IPTp) and implementation of the WHO policy on test, treat and track (WHO, 2012). Despite the reported decrease, most of the endemic countries across sub Saharan Africa still bear the greatest burden of the disease where 90% of the deaths are reported with more than 75% of the mortalities in children under five (WHO, 2014).

Ghana National Malaria Control Programme (GNMCP) reports reveal that in 2006 malaria accounted for 37.5% of all out patient consultations, 36.0% of all hospital admissions, and about 33.4% of all mortality in children under age five years. Following the recommendation of the WHO, Ghana changed it malaria treatment guidelines adopting artesunate and amodiaquine as first line for the treatment of uncomplicated malaria to replace chloroquine (GNMCP, 2006). By 2012, hospital statistics across the country revealed that malaria was responsible for 38.93% of the

outpatient consultations and 38.80% of admissions. Of those admitted for malaria, 63% were children under 5 years of age while pregnant women constituted 16.8%. Furthermore, According to the Ghana Health Service (GHS) report of 2012, malaria accounted for 22.4% deaths in children less than five years of age and 3.4% deaths among pregnant women (GHS, 2012). Over the last decade, studies in Ghana have demonstrated that artesunate and amodiaquine combinations are not only efficacious in clearing the malaria parasites from patients (Koram et al. 2008) but if used for intermittent preventive treatment programmes for children under five could effectively clear more than 90% of the parasite in this age group (Ahorlu et al. 2009).

Different studies have demonstrated very high level of asymptomatic malaria parasitaemia in both less than 5 years old and school age children. In 2009, Ahorlu et al, reported a parasite prevalence of 25% in less than five year old children in the Shime sub district in the coast of Ghana. In the same light, (Otupiri et al. 2012) reported a malaria parasitaemia prevalence of 58.6% among school children in the Ejusu Juaben District, while (Sarpong et al. 2015) reported a 41.5% prevalence of malaria parasitaemia in Ghanaian school children in the Ashainti and Upper West regions of the country. A related study in the Dodowa area demonstrated that children with high levels of asymptomatic parasitaemia have a higher risk of coming down with clinical malaria (Ofosu-Okyere et al. 2001).

The link between one parasite carrier or infected individual and the next relies on the mosquito picking up the parasite during a blood meal. This means that even if all patients with malaria are treated of the disease, those individuals who carry the parasite and are not ill could redistribute it to the healthy population with the help of the mosquito and therefore, the cycle simply continues. The high incidence of asymptomatic parasitaemia serves as a reservoir that fuels the malaria transmission cycle (Bousema et al. 2014 et al. 2016). If the parasite is cleared from the blood of asymptomatic individuals as well as the sick patients with the very efficacious Artemisinin-based Combination Therapy (ACT), then, even the most effective mosquito vector would have nothing to transmit following a blood meal (Ahorlu et al. 2011).

Continuous exposure to the malaria parasite has led to the development of immunity, especially in adults in endemic areas. This is often a slow process as it depends on repeated exposure to the parasites (Greenwood, 1987, Njama-meya et al., 2004).

This explains why children carry the greatest burden of the disease. As they grow beyond age 5 years, the prevalence of malaria or parasitaemia in this group begins to decrease following the development of immunity to the parasite (Bull et al. 1998). Age, therefore, has a great role to play when looking at the dynamics of the malaria burden. A study of trends in malaria admission in a Health Centre in Cameroon has demonstrated that the variation in the prevalence of malaria effectively reflected a variation in the prevalence in children age one to less than 15 years (Ndong et al. 2014). In endemic areas, children have been reported to harbour relatively high levels of the parasite without coming down with the disease (Snounou et al. 1997), and the population is continuously exposed to the infected mosquitoes. That is, the already parasitised individuals can be re-infected either with the same parasite, thus, increasing the parasite load or other parasite species leading to a co-infection in areas with more than one species of *Plasmodium*. On the other hand, the uninfected mosquito is initially harmless even if it bites. However, it becomes infective when infected by a parasitised individual who could either be febrile or asymptomatic. Therefore, while enormous effort is being made to prevent man-vector contact through the use of treated nets, the benefits from using these nets could be amplified if such programmes integrate mass parasite clearance as part of their agenda. That is mass testing, treatment and tracking should precedes the mass distribution of LLIN in a given area or intermittent preventive treatment in children.

There has been concerted effort in the past decade to evaluate the possible effects of massive parasite clearance using intermittent preventive treatment in less than five year old children in different part of Africa with interesting results. Most studies however, focused on the clinical incidence of the disease as outcome measure which has been observed to reduce with a range of between 20-80% depending on a number of factors (Dicko et al. 2008, Kweku et al. 2009). In a longitudinal study in a Coastal village in Ghana, Ahorlu et al, demonstrated that associating IPTc with home based management of malaria by community workers could clear more than 90% of the parasite pool in the community. This intervention reduced malaria parasitaemia prevalence from 25% at baseline to 1% at evaluation using artesunate and amodiaquine. This low level of parasitaemia in the study population was found to persisted over a period of two years (Ahorlu et al. 2011). Though, this intervention had targeted only under 5 years children, it revealed the potential role intermittent preventive treatment of the population could play in reducing malaria prevalence and

consequently paving the way for malaria elimination. Given that old members of the household are likely to have some immunity to the malaria parasite, they however, represent the reservoir that refuels the parasite pool whenever it is reduced by IPTc. Therefore, for sustainability of such implementation intervention, intermittent preventive treatment would be of greater benefit if all the members of each given household are targeted for mass testing, treatment and tracking at baseline and consequent prompt home-based treatment for suspected cases. Bearing in mind that huge resources are required for IPT of whole communities, it has been suggested that mass screening of whole communities be carried out once a year while IPTc be conducted regularly in combination with the home based management (Ahorlu et al. 2011). This could further enhance the efforts.

Implementation of rapid scale–up preventive interventions in the past decade has led to a reasonable decrease in the burden of the malaria (WHO 2011) especially given the introduction of the WHO policy of test, treat and track (T3) (WHO 2012). The challenges involved with translating research scenarios into implementation are enormous. It is important to understand the bottlenecks that hinder this process in order to undertake mass testing, treatment and tracking in a large scale using existing health systems, especially in an era when global funding for health services is slowing down (Rao et al. 2013).

Any effective control strategy that interrupts the link between man, the parasite and the vector could seriously reduce the transmission of malaria. In this light, interventions focused on clearing of the parasites in asymptomatic individuals in combination with intensive use of other control measures could pave the way for pre-elimination of the parasite in endemic communities (Bousema et al. 2014). This study aims at reducing the asymptomatic parasitaemia in the Pakro sub district of the Eastern Region of Ghana by conducting MTTT for malaria parasitaemia among household members of age 6 months and older and carrying out targeted treatment of all cases with confirmed asymptomatic parasitaemia or clinical malaria. These interventions intend to follow up enrolled participants over a period of two years. Hospital records will also be studied to document trends in malaria admissions and occurrence of other diseases in the area before and after the interventions.

Rationale

Malaria continues to poses a serious burden to the local populations in sub-Sahara Africa. Several efforts have been made to scale up interventions that work such as preventing man-vector contact, intermittent preventive therapy, seasonal malaria chemoprophylaxis as well as TTT for febrile patients (WHO, 2012). However, much still has to be done to target the mass testing, treatment and tracking of whole populations in order to reduce the parasite load before implementing the above mentioned interventions. Though SMC is adopted for selected localities in Ghana, MTTT could be used to drastically bring down the parasite load in a given population before the implementation of interventions such as SMC. Elsewhere, it has been demonstrated that incorporating the antimalarials in vaccination programmes could delay the first malaria episode in children under five (Dicko et al., 2008). Furthermore, MTTT of children in a community in Ghana has been reported to reduce the parasite load in a given community from 25% to 1% (Ahorlu et al., 2011). The questions that remain are - could this be scaled up? What proportion of the community could be covered over a given time? What will it take to accomplish MTTT in large scale? In designing interventions that aim at reducing the burden of malaria in children under five, for example, MTTT could be used to clear parasites from the general population before the interventions are implemented. This is because the adults who are not often included in the interventions that target children under 5 years old tend to act as reservoirs that fuel the transmission. To solve the problem of personnel who are limited at the level of the health service and coverage, this study will be making use of the existing network of community nurses/volunteer teams that are used during vaccination programmes. These volunteers, who recite in the communities, will carry out the interventions in the given communities and conduct the home-based management of malaria between interventions thereby increasing surveillance and reducing cost. Furthermore, to solve the problem of stock-outs and quality of the RDTs and antimalarials, the investigators will make use of SMS through mobile phones and a team will conduct monthly monitoring and evaluation of the field activities of the volunteers as well as refill the medicine and RDTs. The volunteers will be trained based on the 2014 guidelines for managing uncomplicated malaria.

The investigators hypothesize that in the Pakro sub district, there are more asymptomatic malaria cases than the symptomatic cases reported by hospital records and that if the investigators carry out MTTT in combination with home-based

management of malaria in specific communities over two years, a large proportion of the parasite reservoir will be cleared and consequently open up possibilities for pre-elimination of malaria in the area. It is also intended that the bottlenecks involved in scaling up mass testing, treatment and tracking will be documented in order to facilitate the process.

Main objective

The main objective of this study is to explore the impact of scaling up mass testing, treatment and tracking on malaria prevalence among children under fifteen years of age in the Pakro sub district of Ghana.

Specific Objectives

1. To evaluate the effect of scaling up targeted MTTT/home-based treatment on malaria parasitaemia and hospital consultations and admissions.
2. To determine the prevalence of asymptomatic parasitaemia among afebrile participants.
3. To reduce the burden of malaria in the participating communities.
4. To document challenges which hinder the scale up of mass testing, treatment and tracking of malaria in Ghana.
5. To conduct a cost benefit analysis of the intervention in the area.

Study Design:

This is an Implementation Research (IR) with a longitudinal cohort design to be undertaken within a two year frame work. The interventions are designed to compare the baseline to evaluation findings following the modified protocol of (Ahorlu et al., 2011). **There are two components to this implementation study a). The longitudinal (cohort) study: This is basically the prevalence surveys to be conducted with the selected cohort of children 6 months to 15 years – at baseline and before each of the subsequent MTTT rounds. b). The Survey involves using structured questionnaire to interview caretakers of children under five to solicit their views on the implementation process perceived benefits and challenges etc.** Though the target group is children from 6 months to 15 years of age, all parasitised adults will be cleared of the parasite during the interventions as well to reduce the parasite reservoirs. **Prevalence of malaria**

trends in cohort group over the study period will reveal the effect of MTTT scale-up on the children 6month to 15 years. Between interventions, the teams will conduct homes-based management of malaria for all febrile cases confirmed to be positive for malaria parasites. The challenges faced by the implementation team will be documented at every stage and discussed with all the stakeholders at every stage of the implementation.

Methodology

Study Area

Pakro is one of five sub-districts in the Akwapim south district health directorate (DHD) in the Eastern region of Ghana (DHD, 2014). The Akwapim south district lies within the semi-equatorial climatic region, and experiences two rainfall seasons in a year, with an average rainfall of 125cm to 200cm. The first rainy season begins from May to June with the heaviest rainfall in June, whilst the second rainy season begins from September to October. According to the Ghana Statistical Service (GSS), the average household size in the Akwapim South district is estimated to be 4.0 whilst the average number of households per house or compound is estimated to be 1.6 (GSS, 2010). The Pakro sub-district has an estimated population of 7,889, and is bounded to the east by Akwapim North district; to the north by Ayensuano district; and to the west by Nsawam Adoagyiri Municipality. The sub-district is made up of 22 communities, and has 3 health care facilities (1 Health Centre and 2 Community-Based Health Planning Service (CHPS) compounds) (DHD, 2014).Due to limited resources, only seven communities will be selected for this study. This include Abeasi Newsite, Fante Town, Zongo (Adjenase/Kweitey), Piem/odumsisi, Adesa Latebibio, Sacchi/Tabankro and Odum Tokuro. These are communities with a relatively high population density. The Pakro Health Centre is one of thirty sentinel sites monitoring malaria prevalence in the country coordinated by the Noguchi Memorial Institute for Medical Research (NMIMR). Malaria parasite positivity rate was estimated to be 45.7% in 2014 (DHD, 2014). In the same year anaemia among pregnant women at 36 weeks of gestation was 21% (DHD, 2014).

Study participants

Community entry activities to sensitise the chiefs and the general population will be conducted at the beginning of the study through meetings and durbars (Ansah et al., 2015; Ahorlu, et al., 2009). Once the community leaders and the population have accepted the project, the household will be numbered and participants per household will be registered during a household census. All households will be given a unique identification code. Each individual within the household will be assigned a code that links them to a particular household and community. After obtaining consent from the household heads, the children will be enrolled but individual assent and consent will be obtained from the other adolescents and adults in the household. **A cohort of 460 children age 6 months to 15 years will be selected and enrolled into the longitudinal study which will consist of prevalence surveys undertaken before each MTTT. Caregivers of the children in the cohort will be enrolled for the community surveys using questionnaires. In this implementation research the entire population of the seven selected communities will be tested, treated and tracked. This is intended to clear the parasite pool in the community.**

Intermittent preventive treatment for the household members

The research team **together with Community assistants/volunteers** will conduct **house-to-house** testing (using RDTs) of all children (from 6 months old) and adults residing in 7 selected communities for the presence of malaria parasites. **For this study,** the investigators **will use the *Ag P.f RDT* which detects histidinie-rich proteins II antigens (HRP-2 Ag) specific to *P.falciparum* in human blood. The RDTs will be supplied by the Ghana Health service through the National malaria control programme which uses the services of WHO-FIND Lot Testing Programme for quality assurance. Thus,** the investigators **are using the same RDT that has been procured by the NMCP and are being used routinely in Ghana.** To enable follow up studies in a case where treatment failure is reported, 200ul (two drops) of blood will be collected on filter paper. This will be used to determine immunological parameters such as antibody levels to specific antigens using Polymerase Chain Reaction (PCR) and Enzyme Linked Immunosorbent Assay (ELISA). **RDT confirmed cases who are treated but presents persistent malaria related symptoms such as fever on day 7 will be tested using microscopy and to determine clinical failure. This study is not designed to test for parasite**

resistance to drug (drug efficacy) and the Project clinicians will advise on the next line of action. This could be taken up by a masters' student**. However, the student will need to submit a different protocol to the ERC for approval**). All participants confirmed **(using RDTs)** to be carrying the malaria parasite will be treated using ACTs following the Ghana National Malaria Treatment Guidelines and followed up **on days 1, 2, 3 during treatment as DOTs (Directly observed therapy) and on day 7 post treatment. The research team together with Community volunteers will be provided the treatment guidelines which specify the dosage for each treatment regimen.** Participants who receive the treatment will be observed for five minutes to ensure that they retain the drug. Those who vomit within this period will have the treatment repeated.

Follow-Up

All treated cases will be followed up on days 1, 2, **3 during treatment and day 7** post-treatment to ensure that the participants take the drugs on time as well as document and report all adverse effects.

Questionnaire/Focus group Discussion

The questionnaire will include questions about malaria treatment, prevention and control measures practiced by the household members. Occupants of the household will provide a blood sample for testing. **Focus group discussions will be organized with community members and health care workers to increase the scope of information obtained.**

Timely treatment of suspected febrile malaria case in the community

In other to render operational the home-based management component of the project, two volunteers will be selected from each community and trained on home-based management of malaria and be provided with the protocol, RDTs and ACTs. **The interventions will be carried out quarterly (see the timetable).** Between one MTTT intervention and the next trained community members will provide prompt home-based treatment for children and adults reporting signs and symptoms of malaria and confirmed to be carrying the parasite using RDTs. This will be done using national malaria management protocol. There will be monthly visits by the research team to supervise the community volunteers involved in home-based

management to ensure that the protocol is being respected as well as replenish their stocks. There is a need to visit the health facilities that service the community to enable tracking and linking of medical records with study participants (a master student is required for this component). The investigators hypothesize that a reduction in parasite load in the community will consequently lead to a reduction in the number of hospital malaria related consultations and admissions paving the way for pre-elimination. This will be realised by comparing baseline hospital malaria admission data to evaluation data. **MTTT has already been adopted by the NMCP as one of the control and elimination activities and** the investigators **are anticipating its being scaled-up in the country, and therefore documenting its implementation challenges will inform the decision in the future.**

Sample size

This is an implementation study aimed at enrolling an entire population estimated at 4500 participants from the 7 selected communities in Pakro sub district. This population was obtained following data from a head count in preparation for the mass distribution of LLIN in 2016 - Abase newsite = 800, Fante town = 1450, Adjenase/Kwettey = 1102, Piem/Odumsisi = 323, Adesa/Nsuablaso = 480, Sacchi/Tabnkro = 201, Odumtokro = 129 (Pakro Health Centre records). However, since the target effect of this intervention is focused at the children age 6 months to 15 years, a community survey with a sample of 368 children will be needed to determine the malaria prevalence projected at 50% in the study population. This has been determined using the formula of Yamane where $n = N/[1+N(e)^2]$ (Israel 1992) considering a 95% confident level (CI) and ±5% precision. Assuming a loss to follow up of 10% and a non-response rate of 10%, the sample size is readjusted to 460 children calculated from (38/1-0.2) for the community survey. At evaluation the available sample size will be determined. This is the group for which questionnaires will be administered. Following a census of the households, children under 6 months to 15 years old will be **randomly selected for the longitudinal cohort study, they will then be** divided into the various age groups 6 months to 11 months, 1-4 years, 5 -10 years and 11-15 years. For each age group the investigators will randomly select 116 children.

Inclusion criteria

To be included in the longitudinal cohort study, participant must be between the age range six months to 15 years and be resident in the study area for the period of the study. Willingness to participate will be proven by a completed and signed consent form from the parent or guardian of each child. All other community members will be engaged in the survey studies.

Exclusion criteria

If an individual intents to stay less than one year in the study site or would be absent at some time because he/she is schooling in a boarding school or has a life threatening illness (excluding malaria). However, all individuals including those with clinical malaria signs who are present during surveys will be tested and if confirmed to carry the parasite will be treated.

Data collection

Following consent, blood will be drawn from a finger prick. All participants will be tested for the presence of malaria parasites using RDTs. Additionally, blood will be collected on filter paper to enable molecular characterization in case treatment failure is observed in a given patients as explained above. All samples will be stored at NMIMR. To test for anaemia (for children in the cohort study only), a portable automated Hemocue photometer will be used to determine the concentration of Haemoglobin. Anaemia in this study is defined as Hb levels less than 10g/dl. Children with severe anaemia (Hb less than 7g/dl) will be referred to the Pakro Health Centre for follow up. **At evaluation, family members will be asked questions on how much they used to spend on malaria before the intervention and how much they have spent after. Malaria case management records before and after the intervention will be consulted, firstly to determine the change in prevalence and also for cost benefit analysis purposes.**

Data Management and Analysis

Data Management will be conducted with the support of the Data management unit in the Department of Epidemiology of NMIMR. A database will be created to manage the data. Data will be entered into Epi-info and analysed using SPSS. The unit of enrolment will be the household. Malaria prevalence will be reported as, proportion of subjects identified during the study period with RDT confirmed clinical malaria with

temperature ≥37.5 or asymptomatic parasitaemia and stratified by subject characteristics, including age, sex and community. A Chi square statistic will be used to compare prevalence across age and gender categories as well as communities. **To determine whether interventions had an effect on the prevalence of malaria in the area, the baseline prevalence data will be compared with the evaluation data. Also a cost benefit analysis will be conducted by comparing what the NMCP put in in previous years to treat malaria to what it would spend if MTTT is implemented.**

Problems Anticipated

It is anticipated that ACTs and RDTs supplies could delay. In order to avoid this, the investigators have approached the national malaria control programme to arrange for drugs and RDTs supply through the Eastern Regional Store. The investigators anticipate the number allocated to houses in the communities could be wiped and so the investigators have each house data linked to the name of the house. This could enable us to trace the participants easily. In the field the investigators will use forms that already carry the names of the families following the census. Names of new people could be added.

Project Management

The PI will carry out day to day implementation and supervise of all aspect of the project. Co-PIs are part of the implementation team and will participate in the decision making at all stages of the project. The Research assistant will help in facilitating project logistics. The Regional/District Health Directorates through the health facility in Pakro will facilitate the work. The volunteers are community members that assist in data collection while the driver facilitates movements.

Quality Assurance

In order to ensure the quality of data collected, 20 volunteers will be trained and 14 will be selected for the project. The questionnaires will be pretested and corrections effected. All data collected will be cross checked by two persons in the fields. To avoid loss of data, all data from the field will be recorded in the data transfer sheet before being transferred to the data management unit. All ACTs and RDTs will be

procured from the National Malaria Programme through the Eastern Region medical store. The expiry dates for all procurements made will be verified.

Ethical Consideration

The ethical clearance for this study will be sought from the GHS-ERC

Consent Procedure

The investigators will obtain consent at different levels. Administrative authorization will be obtained from the Ghana Health Service. There will be community consent given by the chiefs, households consent given by the head or parents/caretakers for children below 18 years, individual assent for 12-17 years old and consent for adults in each household. People from 18 years old are considered as Adults.

Privacy and confidentiality

All information/samples obtained from participants and their results will be kept confidential and not be released to a third party.

Data storage and Usage

This information will be stored in a secure location at the Epidemiology Department of NMIMR. Some staff of Epidemiology Department of NMIMR may access the data for research purposes only, such as malaria prevalence studies in asymptomatic individuals. Findings will be published with no reference to any personal identifiers. The data collected will be stored for a period of five years at NMIMR.

Data ownership

Data resulting from this study is own by the NMIMR.

Risk

There is no health threatening risk. Some participants may vomit within five minutes after taking the ACTs. It is assumed that if a patient vomits within five minutes he/she has not absorbed an acceptable quantity of the medicine. In this case the treatment will be repeated (Ahorlu et al., 2009). Some other patients may show adverse

reactions after taking the drugs such as stomach upset, dizziness, nausea, body weakness, etc (Sinclair et al., 2009). In other to cross check for some of these adverse events, the team will monitor volunteers for four days following treatment.

Conflict of Interest

The PI and co-PIs declare no conflict of interest in the execution of this project.

Benefits

All confirmed malaria parasitaemia cases will be treated for free. Continuous monitoring and treatment of confirmed cases will improve the health of residents. The study will reduce household spending on malaria thereby free some funds to be spent on other household items. This project could reduce the malaria related burden in the implementing communities.

Expected Outcome/Results

1. The effect of scaling up targeted MTTT/home-based management on hospital admissions will be understood.
2. The prevalence of asymptomatic malaria parasitaemia among afebrile children aged 6 months to 15 years and adults in the Pakro sub district will be known.
3. Reduced burden of malaria in the participating communities
4. Document challenges that hinder the scale up of mass testing, treatment and tracking of malaria in Ghana.
5. The cost benefit analysis of the scaling up MTTT intervention in the area will be known.

Dissemination

The findings of this study will be discussed at every stage with stakeholders and published.

Work Plan

Outcome	**Measure**	**Time frame**	**Mile stone**
Proposal development	Draft proposal is available	Aug –Oct 2016	Submitted to the STC/IRB

Ethical Clearance	Ethical clearance is obtained	Nov - Jan 2016	clearance is available
Administrative/ Ethical clearance from Ghana Health Service	Administrative and GHS-ERC clearance are obtained	**Feb – April 2016**	Clearance is available
Communities/durbar	Meeting/durbars held	Nov 2016	Project is accepted by the community
Mapping of households /census of participants	All households are numbered and individual identified	Nov 2016	Each households has a number
Planning for data collection	Consumables are prepared, RDTs are bought	Dec - Jan 2016	All necessary equipment and consumable are available in the field
Primary	The prevalence of asymptomatic malaria parasitaemia among afebrile children aged 6 months to 15 years and adults will be known in the Pakro sub district.	**Two years** 1st survey **Apr - Jul** 2017 2nd survey **Aug - Oct** 2017 3rd survey **Nov - Jan** 2017 4th survey **Feb - May** 2018 5th survey **Jun - Sep** 2018 6th survey **Nov 2018 - Feb 2019**	Reports, Publications, Presentations at conferences and workshop demonstrating the effect of the intervention on malaria prevalence in Pakro sub district in the Eastern Region of Ghana
Secondary	Reduce the burden of malaria in the participating communities.		
	Challenges that hinder the scale up of mass testing, treatment and tracking of malaria in Ghana are documented.		
	The cost benefit analysis of the scaling up MTTT intervention in the communities will be known.		
	Options for policy are proposed.		
Evaluation	What is the effect of the intervention? What is the prevalence? What are the lessons learned for scaling up.	**Jan - July 2019**	Report publication

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Budget & Budget Justification

Budget

Item	specification	Cost ($)
RDTs	Ag P.f/Pan test is a rapid, qualitative and differential test for the detection of histidine-rich protein II (HRP-II) antigen of *Plasmodium falciparum* in human whole blood.	19,958.4
Treatment	Artemether lumefantrin (AL) for both adults and children. The number of treated cases will be decreasing over time.	6,690
Hemocue photometer	Hb levels will be assessed to determined anaemic status.	2,582
Consumables/ materials	Gloves, tissue, zip-lock bags, safety boxes and silica gel, filter paper and PCT reagents	2,024
Incentives for Under five children	Biscuits	2,025
Data analysis	Statistician will enter the data and conduct analysis	**3,000**
Community entry	Meetings and durbars with chiefs	70.0
Longitudinal Cohort study	Questionnaires will be administer to parents of enrolled children or guardians	3,895.5
Training	Aquent the volunteers with the intervention instruments and pretest.	832.32
Study of hospital admission records	To study admission trends	2,500
Communication	Communication credit enable the team liaise with the volunteers on home-based management.	1,149.12
Bags for the volunteers	These are require for transport of materials	510
Home-based management of malaria	14 community volunteer (2 from each community) conduct home-based management of malaria following the protocol.	2,112.6
Personnel	Census and mapping the study site, 6 surveys visits and the monitoring visits. The team includes 1 driver, 1 Research Assistant, 14 community volunteers and one PI.	15,232.09
Rechargeable lamp	In case there is no light (2)	123.48
Transport	Car hiring, fuel for censor, surveys and monitoring	10,567
Conference / workshops and training		10,000
Publication		6,000
Total	**93,508.78 + 5% contingency**	**98,184.209**

Explanation of Budget

Intervention team members

The project team will be composed of one Principal Investigator (PI), 1 research assistant, and 14 community workers and a driver. We will require two cars for each survey which will last 16 days. Surveys will take place quarterly, making a total of 6 interventions over two years.

RDTs

Survey

A pack contains 40 RDTs. Given that the target population of the targeted communities is 4,500 people, it is important to buy 5000 RDTs for each intervention (i.e. 125 packs). This is because some of the RDTs could give inconclusive results which will require that the process be repeated. Each RDT pack of 40 cost *$25.15*. Each RDT cost $0.63. The total cost for RDTs for the 6 surveys is given by *($0.63*5000*6)* of ***$18,900*****.** Pakro Health Centre is a sentinel site for monitoring malaria prevention which is being let by the Epidemiology Department of Noguchi. In this light, the RDTs and Antimalarials will be obtained from the National Malaria Control Programme, so the estimated cost which was based on RDT and drugs has been dropped.

Home-base testing

We estimate that the volunteers will test 10 suspected case of malaria each month. Given that there are 7 communities, we have *(7*10*24) = 1680 RDTs*. Total cost for home based testing is given by *$0.63*1680* = ***$1,058.4.***

Total cost of RDTs ***1,058.4 + 18,900 = 19,958.4***

Anaemia

Anaemia is estimated to be 27% in under five children. It is estimated that 30% (1350) of the population of Pakro is made up of children under five years, giving 1350*0.27 = 365 anaemic cases. Assuming a 5% reduction after the first intervention, in the second intervention we will target 22% aiming at reducing it to 17 % while in the third intervention we aim to reduce it to 12%. For cost purposes we

will maintain it at 12% after the third intervention. Hemocue photometer = *$1000*, total number of micro cuvettes = 365 + 297 + 4(230) = 1,582. One cuvette cost $1, giving *($1*1,582) = $1,582.*
Total cost for anaemia is ***$2,582***

Treatment

Survey
The population of the targeted communities is estimated at 4500 people. We estimate 50% prevalence in the first intervention. Assuming a 15% reduction after the first intervention, the second intervention will target 35% prevalence which is expected to drop to 25%. After the third intervention we expect the prevalence to drop to 15% further to 10% after the fourth intervention. The 10% will be use as the prevalence over the next one year. As prevalence decreases the number of cases treated also decrease and consequently the cost. In the course of the different intervention we estimate that we will treat the following number of cases – first intervention *(0.5*4500) = 2,250*, second intervention *(0.35*4500) = 1,575*, third intervention *(0.15*4500) = 675* people. Beginning from the forth intervention we estimate a prevalence of 10% for remaining interventions giving *(0.1*4500) = 450* cases. Given that after the fourth intervention we have two more interventions, this give us *(450*2) = 900* cases. The total number of cases to be treated over two years is obtained by adding *(2250+1575+675+450+900) cases = 5,850* cases. The course of treating one case is estimated at *$1* giving a total of ***$5,850.***

Home-based management of malaria
We estimate that an average of 5 cases are additionally identified and treated in each community by the volunteers each month over the two years. This gives 7*5*24 = 840 cases. This will give an additional of 840*$1 = ***$840.***
Total cost of treatment = (*$5,850+ $840)* = **$6,690**

Consumable
Cost of consumable required such as gloves, safety boxes, silica gel, filter paper and PCT reagents will cost ***$2,024***. PCR will only be considered in case of treatment failure.

Incentive to children enrolled in the study

It is estimated that children under five years make up 30% of the population of Pakro sub district. This gives (0.3*4500) 1350 children. We will be giving a token of a biscuit pack worth $0.25 to each under five child tested. The adults will not be included in this package as the free treatment is already a good incentive for the community. Cost of incentives for children $0.25* 1350 = $337.5 per survey. The 6 surveys will cost $337.5*6 = **$2,025**

Communication Cost

This is to enable constant communication with the field team. The PI will work closely with the team in the field for update on home-base management and follow up of treated cases. This is to ensure that adverse effects are captured on time. Stockouts will be communicated through SMS. Each volunteer will be given a monthly communication credit of *$1.26* over two years ($*1.26*14*24* = $*423.36*) while the PI will require *$30.24*24 = $725.76*. This gives a total communication cost over the two years of ***$1,149.12***.

Field bags

Each team member will be given a bag to carry study material. We have 17 team members. Each bag will cost *$30*. Therefore we have *17*$30 = $510*.

Community Entry

We will need to introduce the study to the local authorities. This will be done through meetings and durbars with the chiefs. This is to facilitate community understanding and ownership of the project. Each of the chiefs will be provided a gift worth *$10*. There are 7 community heads giving (*7*$10)* = ***$70***.

Home–based management of malaria

Following each intervention, volunteer workers are required to implement the home-base management of malaria between surveys. This is to clear residual as well as missed cases of parasitaemia in the community. Two volunteers from each of the communities (14 in total) who are already involved in IPT in children will carry out

this task. Each volunteer will receive an allowance of $25.15 every three months. For a total of 6 interventions we have *14*$25.15*6* = ***$2,112.6***

Longitudinal Cohort study

The PI and research assistant will spend one week in the community before each intervention administering the questionnaire to children enrolled in the cohort study. This will give a total of (6*7=42days) per person. The cost is as follows (Drivers ($25.15*42) =*$1,056.3*, 1 Research Assistant = ($30.18*42) = *$1,267.56,* PI ($37.73*42) = *$1,571.56 giving a total of* ***$3,895.5***

Personnel

Personnel cost will be broken into censors, surveys and monitoring cost. During each of these activities in the field, the personnel will be paid a daily allowance.

Household Census

This will be undertaken by 17 personnel in 7 days (14 community volunteers, PI, 1 research Assistant and 1 driver). The PI, the research assistant and the driver will spend an extra one day to plan the census. During the census we will be supervising. We estimate that each volunteer will register an average of 46 people each day. Each of the team members will receive a daily allowance calculated as follows - volunteers (*$5.04*14*7days) = $493.92,* the driver (*$25.15*8) =$201.2*, Research assistant *($30.18*8) =$241.44* and the PI (*$37.73*8) = $301.84* giving a total of ***$1,238.4***

Intervention

A total of 17 personnel will be involved in the interventions which will be conducted every four months giving a total of 3 interventions per year and 6 over a two year period. The interventions will last 12 days. Each volunteer will spend a total of 72 intervention days (6*12) over the two years in the field. The PI, research assistant will spend 6 extra days planning each intervention in the field. The cost is as follows – volunteers *($5.04*72*14) = $5,060.16,* Drivers ($25.15*78) =*$1,961.7*, 1 Research Assistant = ($30.18*78) = *$2,354.04,* PI ($37.73*78) = *$2,942.94* giving a total of ***$12,318.61****.*

Training

A three days training will be organized for the volunteers before the interventions begins. To take part in the training will be 17 volunteers, two resource persons from the district health service will provide the training, the PI, a research assistant and the driver. This cost will include Transport for participants (*$*2.5*20*3 =***$150)**, Food (*$*3*20*3 = ***$180)**, resource persons = (*$37.73*2*3 = $**224.22**),* PI (*$37.73*3 = **112.11),*** research assistant (*$30.18*3 = $**90.54**),* driver (*$25.15*18 =**75.45**).*

*The total cost for the training is **$832.32***

Monthly Monitoring visits

We will undertake field visits to the study area every month to monitor progress, each lasting 2 days. This is to verify that the volunteers are doing the right thing, discuss challenges faced as well as replenish their stocks of RDT and ACTs. Each visit will last two days. Three persons will be involved, the PI, one research assistant and a driver. Since 6 of the 24 months will be involved in the surveys, the monitoring will take place over the 18 remaining months. The cost is calculated as follows - driver (*$25.15*18) = $452.7*, 1 Research Assistants (*$30.18*18) = $543.24*, and the PI (*$37.73*18) = $679.14* giving a total of ***$1675.08***

The total personnel cost is ***$15,232.09***

Data mining from the hospital records

The registers of the Health Centre will be consulted and data will be extracted to study the trends of malaria admissions in this area over the last 10 years at baseline. Then after one year and at evaluation, another study of record will be conducted. This will require research assistants or a master student. This is estimated at ***$2500**.*

Transportation

Transport will involve hiring of the vehicle and fuel cost. From Accra to Pakro is 44.8Km (i.e. 89.6km in and out). There will be an initial trip to censor the area, 6 intervention trips of 12 days each, 16 monitoring trips of two days each over a two year period.

Mapping of the households and identification of people

This will involve one trip of 7 days. As it involves going to all the households we estimate 20Km per day. This gives us *89.6Km + (7*20Km)* = ***226.6Km***

Surveys

We estimate to cover 10Km each day within the Pakro sub district during the surveys *(12days*10Km+ 89.6Km interventions = 249.6Km for each intervention)*. We will be conducting 6 interventions which gives us 249.6Km*6* = ***1,497.6Km***

Monitoring visits

Six of the project months will involve the intervention and therefore monitoring will occur over18 months within the study period. This will involve the PI going to the field and meeting with the volunteer and replenishing their stocks workers. We estimate to cover 15Km in addition to the 89.6Km (in and out) for each trip giving a distance of *104.6Km*. Total distance during monitory is *104.6Km*18* ***= 1,882.8Km***

Total distance to be covered = (226.6 + 1,497.6 + 1,882.8) km **= 3,607Km**

Car Hiring Cost

Currently, the cost for the use of NMIMR vehicle stands at $0.76 per Kilometer. The total cost for hiring NMIMR cars is *3,607 * $1* = ***$3,607.***

Fuel Cost

We estimate to use $300 worth of fuel for each trip undertaken. Given that we are going to undertake 6 interventions, 18 monitoring and 1 censor visit, which gives (6+18+1)*$300 = **$7500**

Total transport cost ***= $3,607 + $7,500 = $10,567***

Rechargeable lamps

Since these are rural communities and people are involved in different daily activities, work would have to start very early in the morning and extend into the night in order to reach out to a greater portion of the community as most of them will go out very early and come back late. Seven rechargeable lamps are therefore required at *$17.64* each giving a total of ***$123.48*.**

Statistical analysis

The statistician at NMIMR will enter the household data into software and conduct analysis for 20 working days at *$150* a day, giving a total of ***$3000.***

Conference and publications

The findings from this study will be disseminated through conferences, workshops and meetings with stakeholders. The PI is also expected to undertake some hands-on training on economic evaluation and cost benefit analysis.

Consent Form (Attached)

Assent Form and Parental Consent Form (Attached)

Data Collection Instruments (Attached)