

Principal Investigator: Last, first, middle Wagatsuma, Yukiko

ICDDR,B: Centre for Health & Population Research

RRC APPLICATION FORM

RESEARCH PROTOCOL

Protocol No. 2002-010

FOR OFFICE USE ONLY

RRC Approval: Yes/ No Date:

ERC Approval: Yes/No Date:

AEEC Approval: Yes/No Date:

Project Title:

Pilot study on epidemiological and socioeconomic factors related to malaria in endemic communities of Bangladesh

Theme: (Check all that apply)

- | | |
|--|---|
| ☐ Nutrition | ☒ Environmental Health |
| ☒ Emerging and Re-emerging Infectious Diseases | ☒ Health Services |
| ☐ Population Dynamics | ☐ Child Health |
| ☐ Reproductive Health | ☒ Clinical Case Management |
| ☐ Vaccine evaluation | ☒ Social and Behavioural Sciences |

Key words: malaria, epidemiology, disease burden, socioeconomic status, household expenditure, Bangladesh

Relevance of the protocol: Malaria is a major cause of morbidity in Chakaria and the cost of treating malaria from the perspective of household is unknown. There might be heavy economic burden on the individual and society due to household costs of malaria. Information on mosquito biting behaviors in the area is scarce. The proposed research aimed to find out the options for appropriate case-management as well as identify economic, social and behavioural barriers that malaria patients encounter during malaria episodes. Research findings on household costs of malaria will be useful in examining the ability of individuals and households in Chakaria to afford malaria preventive and curative care. Information on household cost of seeking malaria care will be useful to policy makers for planning and implementing effective malaria control programs and also to design interventions to reduce economic barriers during the episode of malaria. This study will directly contribute for designing the most appropriate service options through community self-help organizations that have been established in the study area.

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Co-Principal Investigator: Abbas Bhuiya, PHSD, ICDDR,B

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Robert Breiman, HSRD, ICDDR,B

Student Investigator/Intern:

Collaborating Institute(s):

National Malaria Control Programme, DGHS, MOHFW; Malaria Working Group, Chittagong Medical College; Department of Zoology, Chittagong University.

Population: Inclusion of special groups (Check all that apply):

- | | |
|---|---|
| Gender | ☐ Pregnant Women |
| ☒ Male | ☐ Fetuses |
| ☒ Females | ☐ Prisoners |
| Age | ☐ Destitutes |
| ☒ 0 - 5 years | ☐ Service providers |
| ☒ 5 - 9 years | ☐ Cognitively Impaired |
| ☒ 10 - 19 years | ☐ CSW |
| ☒ 20 + | ☐ Others (specify _____) |
| ☒ > 65 | ☐ Animal |

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Wagatsuma, Yukiko

Project / study Site (Check all that apply):

- ☐ Dhaka Hospital
- ☐ Matlab Hospital
- ☐ Matlab DSS area
- ☐ Matlab non-DSS area
- ☐ Mirzapur
- ☐ Dhaka Community
- ☒ Chakaria
- ☐ Abhoynagar

- ☐ Mirsarai
- ☐ Patya
- ☐ Other areas in Bangladesh _____
- ☐ Outside Bangladesh
name of country: _____
- ☐ Multi centre trial
(Name other countries involved)

Type of Study (Check all that apply):

- ☐ Case Control study
- ☐ Community based trial / intervention
- ☐ Program Project (Umbrella)
- ☐ Secondary Data Analysis
- ☐ Clinical Trial (Hospital/Clinic)
- ☐ Family follow-up study

- ☒ Cross sectional survey
- ☐ Longitudinal Study (cohort or follow-up)
- ☐ Record Review
- ☐ Prophylactic trial
- ☒ Surveillance / monitoring
- ☐ Others

Targeted Population (Check all that apply):

- ☒ No ethnic selection (Bangladeshi)
- ☐ Bangalee
- ☐ Tribal groups

- ☐ Expatriates
- ☐ Immigrants
- ☐ Refugee

Consent Process (Check all that apply):

- ☒ Written
- ☐ Oral
- ☐ None

- ☐ Bengali language
- ☐ English language

Proposed Sample size: Total sample size: _____ 10,000 _____ ☐

Sub-group _____ ☐ _____ ☐

Determination of Risk: Does the Research Involve (Check all that apply):

- ☐ Human exposure to radioactive agents?
- ☐ Fetal tissue or abortus?
- ☐ Investigational new device?
(specify _____)
- ☐ Existing data available from Co-investigator

- ☐ Human exposure to infectious agents?
- ☐ Investigational new drug
- ☒ Existing data available via public archives/source
- ☒ Pathological or diagnostic clinical specimen only
- ☐ Observation of public behaviour
- ☐ New treatment regime

Yes/No

- ☒ ☐ Is the information recorded in such a manner that subjects can be identified from information provided directly or through identifiers linked to the subjects?

- ☐ ☒ Does the research deal with sensitive aspects of the subject's behaviour; sexual behaviour, alcohol use or illegal conduct such as drug use?

Could the information recorded about the individual if it became known outside of the research:

- ☐ ☒ a. place the subject at risk of criminal or civil liability?
- ☐ ☒ b. damage the subject's financial standing, reputation or employability; social rejection, lead to stigma, divorce etc.

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Do you consider this research (Check one):

- ☐ greater than minimal risk
☐ no risk

- ☒ no more than minimal risk
☐ only part of the diagnostic test

Minimal Risk is "a risk where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical, psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as a part of routine physical examination".

Yes/No

☒ ☐ Is the proposal funded?

If yes, sponsor Name: _____ DFID _____

Yes/No

☐ ☒ Is the proposal being submitted for funding?

If yes, name of funding agency: (1) _____

(2) _____

Do any of the participating investigators and/or their immediate families have an equity relationship (e.g. stockholder) with the sponsor of the project or manufacturer and/or owner of the test product or device to be studied or serve as a consultant to any of the above?

IF YES, submit a written statement of disclosure to the Director.

Dates of Proposed Period of Support

(Day, Month, Year - DD/MM/YY)

Beginning date: 25/04/2002

End date: 31/08/2002

Cost Required for the Budget Period (\$)

a. 4 months study period: \$ 22,800

b. Direct Cost: \$22,800 Total Cost: \$ 28,500

Approval of the Project by the Division Director of the Applicant

The above-mentioned project has been discussed and reviewed at the Division level as well by the external reviewers. The protocol has been revised according to the reviewer's comments and is approved.

Dr. Peter Kim Streatfield (Acting)

Name of the Division Director

Signature

P.K. Streatfield

Date of Approval

16/4/2002

Certification by the Principal Investigator

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

Signature of PI

Date:

Name of Contact Person (if applicable)

Y. Wagatsuma
16/4/2002

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☒

Check here if appendix is included

Principal Investigator: Last, first, middle Wagatsuma, Yukiko

PROJECT SUMMARY: Describe in concise terms, the hypothesis, objectives, and the relevant background of the project. Describe concisely the experimental design and research methods for achieving the objectives. This description will serve as a succinct and precise and accurate description of the proposed research is required. This summary must be understandable and interpretable when removed from the main application. (TYPE TEXT WITHIN THE SPACE PROVIDED).

Principal Investigator: Yukiko Wagatsuma

Project Name: Pilot study on epidemiological and socioeconomic factors related to malaria in endemic communities of Bangladesh

Total Budget: US\$ 28,500

Beginning Date: 25/04/2002

Ending Date: 31/08/2002

Malaria was nearly eradicated from most of Bangladesh by 1970's, but it re-emerged as one of the major public health problem in 1990's. Malaria is one of the most important health problems of Chakaria, Cox's Bazar District. There were approximately 1,500 confirmed cases with 70% falciparum malaria cases in 1999 in the Thana Health Complex. These figures has thought to be underestimated and suggested to be much more morbidity and mortality are occurring in endemic communities.

The ICDDR,B: Centre for Health and Population Research (The Centre) has a strong infrastructure with a facility in Chakaria. The Centre has been committed to continuously invest for Chakaria Research Centre by diversifying research and service activities. There will be; 1) commercial clinical pathology laboratory services; 2) community self-help organization cooperative system support; and 3) malaria healthcare service. Malaria healthcare service components will include diagnostic service (rapid dipstick and microscopic tests), Village Health Posts support and insecticide-treated material procurement and chemical re-dipping services. This proposed study is a small-scale pilot study with study duration of 3 months in a small geographical area (10,000 population) in Chakaria.

There are four components under this pilot study; 1) fever monitoring with diagnostic confirmation to describe malaria epidemiology in a peak season; 2) entomological study to describe malaria vector behaviour; 3) household malaria expenditure study and 4) qualitative analysis on perceptions among community members on curative and preventive measures.

Malaria is a major cause of morbidity in Chakaria and the cost of treating malaria from the perspective of household is unknown. There might be heavy economic burden on the individual and society due to household costs of malaria. The information on mosquito biting behaviors in the study area is scarce. The proposed research is aimed to find out the options for appropriate case-management as well as the economic barriers that malaria patients encounter during malaria episodes in Chakaria. Research findings on household costs of malaria will be useful in examining the ability of individuals and households in Chakaria to afford malaria preventive and curative care. Information on household cost of seeking malaria care will be useful to policy makers for planning and implementing effective malaria control programs and also to design interventions to reduce economic barriers during the episode of malaria. This study will directly contribute to design the most appropriate service through community self-help organizations that have been established in the study area.

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KEY PERSONNEL (List names of all investigators including PI and their respective specialties)

Name	Professional Discipline/ Specialty	Role in the Project
1. Yukiko Wagatsuma	Epidemiologist (Epidemic Control Preparedness Unit, PHSD)	Principle Investigator
2. Abbas U. Bhuiya	Social Scientist (Social and Behavioural Sciences Unit, PHSD)	Co-PI
3. Rashidul Haque	Parasitologist (Parasitology Unit, LSD)	Co-Investigator
4. Shakil Ahmed	Health economist (Health Economics Unit, PHSD)	Co-Investigator
5. Medical Anthropologist	TBA	Co-Investigator
6. Entomologist	TBA	Co-Investigator
7. A.K.M. Siddique	Epidemiologist (Epidemic Control Preparedness Unit, PHSD)	Co-Investigator
8. Robert Breiman	Epidemiologist (Associate Director, Heath Systems Research Division)	Co-Investigator

DESCRIPTION OF THE RESEARCH PROJECT

Hypothesis to be tested:

Concisely list in order, in the space provided, the hypothesis to be tested and the Specific Aims of the proposed study. Provide the scientific basis of the hypothesis, critically examining the observations leading to the formulation of the hypothesis.

There are identifiable individual, socioeconomic and environmental risk factors related to malaria morbidity.

Specific Aims:

Describe the specific aims of the proposed study. State the specific parameters, biological functions/ rates/ processes that will be assessed by specific methods (TYPE WITHIN LIMITS).

1. To describe epidemiological profile on malaria in a peak season in endemic communities.
2. To describe biting behaviors by *Anopheles* mosquito species related to the malaria risk.
3. To measure and value direct and indirect costs of malaria morbidity in endemic communities.
4. To describe community perceptions related to the use of specific preventive measures, especially mosquito nets.

Background of the Project including Preliminary Observations

Describe the relevant background of the proposed study. Discuss the previous related works on the subject by citing specific references. Describe logically how the present hypothesis is supported by the relevant background observations including any preliminary results that may be available. Critically analyze available knowledge in the field of the proposed study and discuss the questions and gaps in the knowledge that need to be fulfilled to achieve the proposed goals. Provide scientific validity of the hypothesis on the basis of background information. If there is no sufficient information on the subject, indicate the need to develop new knowledge. Also include the **significance and rationale** of the proposed work by specifically discussing how these accomplishments will bring benefit to human health in relation to biomedical, social, and environmental perspectives. (DO NOT EXCEED 5 PAGES, USE CONTINUATION SHEETS).

Background:

Malaria is one of the most important parasitic diseases giving enormous burden of disease in the endemic and epidemic areas in the world. Malaria has been prevalent in Bangladesh and its neighboring countries since many decades. It was nearly eradicated from Bangladesh from most of the country by 1970's, but never disappeared in eastern regions associated with tea gardens and forests having *Anopheles dirus*-transmitted falciparum malaria. Malaria has re-emerged as one of the major public health problems in 1990's with multidrug resistance (9-10, 15, 22, 25, 26, 28, 37). In the 1990s the upsurge of the disease has created an alarming situation with reports of focal *P. falciparum* outbreaks in northeastern border areas and increase of *P. falciparum* and *P. vivax* cases in the endemic areas. The total number of reported cases in the country as reflected through the regular surveillance mechanism has increased from 53,875 in 1990 to 165,102 and 152,729 confirmed cases in 1994 and 1995 respectively. A total of 100,864 confirmed cases were reported in 1996. Subsequently cases decline during 1997, 1998 and 1999 (68,541 in 1997, 60,023 in 1998 and 63,738 in 1999) (14, 16).

Falciparum malaria is a geographically focal problem of Bangladesh and about two-third of the total cases are reported from four out of the total 64 districts of the country (15). The forest and forest fringe areas particularly in the northeastern and southeastern border report 96% of total positive cases and 99% of total *P. falciparum* cases in the country (16). Malaria population at risk has been estimated as 15 million in Bangladesh, which signifies as one of the major public health problems. Malaria problem has not been given adequate attention because the disease never affects the most economically high impact cities and districts. The country, however, has initiated and plans to adopt the Poverty Reduction Strategy Paper in the very near future. Investing for malaria healthcare for socioeconomically less advantaged sub-population might assist re-focusing poverty and equity issues.

Malaria is one of the most important health problems of Chakaria upazilla in Cox's Bazar District. There were approximately 1,500 confirmed cases with 70% falciparum malaria in 1999 according to the Thana Health Complex statistics. These figures have thought to be underestimated and much more morbidity and mortality might occur in endemic communities. Recent studies conducted in a neighboring upazilla (Khagrachari (MSH, personal communication)) have shown much more cases and deaths occurring in the study areas than respective hospital statistics. A recently published study conducted in Chakaria on correlates of perceived malarial episodes and treatment seeking behavior showed that education level and socioeconomic status were correlated with recommended treatment compliance (11). This might imply a vicious circle for the poor to continuously suffer from disease burden, especially due to the disease such as malaria, life-threatening illness with minimum access to appropriate, available and affordable prevention and curative services.

In response to political and economic demands, health sector reforms are underway, with the overall aim of improving efficiency in the management and the use of health resources. Such reforms are not expected to impair the quality of service delivery and coverage, but instead, by engaging in partnerships with other sectors, private healthcare providers and communities, they should finally lead to important improvements in the quality of care. The costs of extending public health services to the community level have accelerated the process of involvement by communities and the private sector as partners in malaria control. This can be expected to be a slow but continuous process. So far, information is becoming available, largely from Africa, on the cost-effectiveness of three types of interventions undertaken at the community level: the provision of widely available curative treatment, usually by village volunteers; chemoprophylaxis for pregnant women; and the use of insecticide-treated materials. Information is needed from different epidemiological settings on the simultaneous use of such interventions (34).

Insecticide-treated nets (ITNs) are effective in reducing malaria mortality and overall child mortality, this efficacy has been established through several large-scale randomized trials in Africa and confirmed by many other studies in a range of different epidemiological settings. Key issues in taking ITNs to scale are the capacity and efficiency of delivery systems – health impact versus cost recovery. An experience in Malawi shows that while everybody wants to own a net, 90% of people surveyed stated “lack of money” as a reason for non-ownership (36). Demand for nets and the rate of increase in net coverage is therefore price sensitive, and effective promotion will increase demand only if nets are available at an economically reasonable price. This is further demonstrated by the positive correlation between net and radio ownership with socioeconomic status in rural Malawi, ownership increasing with increasing socioeconomic status. The main challenge to scaling-up ITNs is presented by the fact that malaria risk is inversely proportional to socioeconomic status. Specific challenges are: 1) Maximum coverage for minimum donor investment; and 2) coverage needed to achieve maximum health impact. ITNs have been conceived, tested and developed mostly by scientists. Much attention has been given to their efficacy, not enough to their acceptability. A mosquito net is primarily a household item and is usually not perceived as a medical tool. As such, its acceptability will be mostly based on criteria such as color, pattern, or shape. ITN design will vary from one area to the other and will be a key element in acceptability and marketing strategies. Consumer surveys will have to be carried out more systematically and socio-anthropologists should be more involved in efforts to further improve acceptability of ITNs. In Bangladesh, ITNs are rarely distributed by institutional buyers in the private sector (MOHFW, personal communication).

The ICDDR,B: Centre for Health and Population Research (The Centre) has a strong infrastructure with a facility in Chakaria. The Centre has been committed to continuously invest for Chakaria Centre through diversified research and service activities. There has been decided to initiate 1) commercial clinical pathology laboratory services at Chakaria Centre; 2) community self-help organization cooperative system support; and 3) malaria healthcare services. Malaria healthcare service components will include diagnostic service (rapid dipstick and microscopic tests) through self-help organizations and 2) insecticide-treated material procurement and chemical re-dipping services for the communities. This protocol describes a small-scale pilot study on epidemiological and socioeconomic factors that are critical to be preceded before this commercial service components on malaria healthcare service starts (5, 7-8, 19-20, 23).

There are four components under this umbrella protocol; 1) fever monitoring with diagnostic confirmation to describe malaria epidemiology in a peak season; 2) entomological study on vector behaviours in endemic communities; 3) household malaria expenditure study; and 4) qualitative

analysis on perceptions among community members on preventive measures, especially for mosquito nets.

Significance and Rationale:

Malaria is a major cause of morbidity in Chakaria and the cost of treating malaria from the perspective of household is unknown. There might be heavy economic burden on the individual and society due to household costs of malaria. Information on mosquito biting behaviors and parasite load in the area is scarce. The proposed research aimed to find out the options for appropriate case-management as well as to identify economic, social and behavioral barriers that patients encounter during malaria episodes. Research findings on household costs of malaria will be useful in examining the ability of individuals and households in Chakaria to afford malaria preventive and curative care. Information on household cost of seeking malaria care will be useful to policy makers for planning and implementing effective malaria control programmes and also to design interventions to reduce economic barriers during the episode of malaria. This study will directly contribute for designing the most appropriate malaria healthcare service options through community self-help organizations that has been established in the study area.

Research Design and Methods

Describe in detail the methods and procedures that will be used to accomplish the objectives and specific aims of the project. Discuss the alternative methods that are available and justify the use of the method proposed in the study. Justify the scientific validity of the methodological approach (biomedical, social, or environmental) as an investigation tool to achieve the specific aims. Discuss the limitations and difficulties of the proposed procedures and sufficiently justify the use of them. Discuss the ethical issues related to biomedical and social research for employing special procedures, such as invasive procedures in sick children, use of isotopes or any other hazardous materials, or social questionnaires relating to individual privacy. Point out safety procedures to be observed for protection of individuals during any situations or materials that may be injurious to human health. The methodology section should be sufficiently descriptive to allow the reviewers to make valid and unambiguous assessment of the project. (DO NOT EXCEED TEN PAGES, USE CONTINUATION SHEETS).

Study Area and Study Population

This project will be based in Chakaria Thana, Cox's Bazar District where ICDDR,B is currently having the "Chakaria Community Health Project (1994-)." Chakaria is the largest upazilla among the all upazillas in Cox's Bazar District, with the population of 550,000 (Recently the Government has decided to divide into two upazillas). The major objectives of the Chakaria Community Health Project include: formulating strategies to ensure community participation in health activities; identification and establishment of a threshold-level external input, just enough to give impetus to community initiatives, without making them dependent on external agencies; improvement of public health by raising awareness about health and health problems; promoting appropriate preventive and curative measures; disseminating information on available health-related resources in the locality; and studying the impact of project activities on community health.

The location of Chakaria has made it very vulnerable to cyclone and tidal bore in addition to regular monsoon flooding. Despite its vulnerability to natural calamities, the development efforts in the area have been quite limited. Traditionally, the main economic activities in the area have been agriculture, forestry and fishing. Cox's Bazar is one of the four most affected districts for malaria.

Although Bandarban and Rangamati have shown higher incidence during the past few years, these areas are sparsely populated and logistic needs suggests Cox's Bazar as a preferred study district. There are approximately 10,000 confirmed cases with 7,000 falciparum cases in the district in 1999. There has been observed a peak of epidemics in 1995 with 25,000 confirmed cases (16,000 falciparum cases; 16).

Health service statistics available in the upazilla health complex suggest that diarrhea diseases, acute respiratory infection, and malaria are the most important health problems (3). There were approximately 1,500 confirmed cases with 70% falciparum cases in 1999 in the Thana Health Complex (not included cases from a mission hospital in the area).

The highway from Chittagong to Cox's Bazar passes through Chakaria. The east side of Chakaria is hilly, while the west side is low toward the Bay of Bengal. The hilly areas of Chakaria contain a part of the National Reserve Forest. One union (Kakara; 4,600 households; 23,000 population) will be involved in this study. This union was chosen because 1) it showed the highest incidence of falciparum malaria in 1999 according to the Upazilla Health Complex report; and 2) it has been active intervention area to promote health through community self-help organizations. We will stratify the study union and identify the high-risk zone (e.g., within 2-3 km distance from the edge of the hill-tract forest area; *P.falciparum* transmission is highest in forest zone because of specific vector bleeding (15-16)). We estimated the population in this high-risk area is 10,000 (2,000 households). There are two main referral hospitals in the catchment area - 1) Thana Health Complex Hospital and 2) Christian Memorial Hospital. There is a small private hospital (Zam Zam Hospital) in Chakaria town.

Study Design

All people living in the high-risk zone (see description above) will be assigned unique identification numbers and each family will be given the malaria family card for fever episode monitoring. All communities in the high-risk zone will be allocating the dipstick posts within 1 km radius (20 minutes walk distance for ill patients) and trained malaria community health workers assigned by the Self-help Organization will assist the examination and referral to the Village Health Post operated by the same organization. In Kakara, the ICDDR,B has been operating community health intervention for the past 5 years. There has been observed difference on health-related awareness.

The patients who meet with clinical malaria criteria (described below) will receive the case-management with dipstick diagnosis for *P. falciparum*. All positive cases will receive currently recommended one of the 2nd line drugs (quinine+sulfadoxin/primethamine; Q3+SP). Patients will pay the service costs currently assigned by the Self-help Organization for treatment cost and malaria microscopic examination cost (about Tk50; \$0.85) for dipstick test.

Community Malaria Healthcare Service (to be piloted)

Selected communities in high-risk zone will be involved to provide diagnostics and treatment services (2 months study period with intensive technical support from ICDDR,B, later continue by community Self-help Organization by themselves. The service spots will be chosen to ensure availability within a 20 minutes walk distance. In this way, one dipstick post may cover about 1000

population. Since we have approximately 10,000 population under study area with about 5 administrative sub-areas with average of 2,000 population, we will set up 2 dipstick posts per sub-area (2 posts/sub-area x 5 sub-areas = 10 posts). Two or three malaria community volunteers (MCVs) per service spot will be required to ensure 24 hrs service, 7 days per week. MCVs involved in the study will be selected from all MCV pools in the community (e.g., select specifically higher secondary school graduates or above). The selected MCVs will participate in a two-day training session that covers malaria epidemiology, biology, clinical aspects, indications for diagnostic tests and procedures for treatment and referral. It has been reported that only two hours would be needed to adequately train personnel specifically on the use and interpretation of dipsticks (5, 20, 33). The study employed and trained CHWs together with Chakaria Community Health Project Research Officers will supervise and evaluate the Dipstick Posts activities. Procedures for the Paracheck® rapid dipstick diagnostic test will follow the manufacture's instruction. We will instruct providers to:

1. Refer all subjects with severe symptoms (including vomiting) to hospitals regardless of malaria status (suspected or diagnosed).
2. Perform dipstick diagnosis on those presenting with at least one of the following: fever, headache, backache or generalized myalgia, or with the history of these symptoms within the past day. We discouraged, but permitted, dipsticks on anyone not fulfilling the symptom criteria - as long as patients' symptoms are recorded.
3. If symptom persists, repeat the dipstick tests for those initially negative within 12-24 hours. If the second result is still negative, they will refer to hospitals for persistent or worsening symptoms.
4. Record the number who presented but did not meet criteria for dipstick use. For those getting a dipstick, record the patient name, age, sex, house number, presenting symptoms, test result, and treatment/referral. Keep all used dipsticks for collection by supervisory staff.
5. Prescribe chloroquine treatment for dipstick negative patients (possible *P. vivax* infection). For dipstick positive patients, observe the first dose treatment with quinine and instruct for three days' regimen and educate patients with the importance of the completion of the three-day course. Ask patients to return compliance sheets after completing the treatment. The compliance sheet contains the simple illustrations of tablets' type and marking boxes by patients. This also includes the information on history of vomiting after taking tablets. If the sheets are not returned, MCVs will collect them from houses.
6. Educate those in their respective village areas about malaria healthcare services available through community self-help organization. Periodical assessment will be conducted by the study investigators for these community education activities.

Dipstick Diagnosis

There are different types of the Rapid Diagnostic Tests (RDTs) currently available for malaria diagnosis. ParaSight-F® (Becton-Dickenson, USA) was the most established and documented test, but stopped producing (1-2, 4, 6, 13, 21, 27, 29). Paracheck® test (Orchid Biomedical Systems, India) uses the same antigen and was assisted for the development by the PATH (Program for Appropriate Technology in Health, USA & Canada). The aim of this production was to produce

effective but affordable malaria RDT for developing countries. Since this India company has started producing Paracheck® recently, many cross quality checkings have been done for this product (15; personal communications with quality certificates from various authorities). Since WHO is currently coordinating a multi-country study for the efficacy/effectiveness of RDTs, it might be possible for the Government of Bangladesh to acquire less expensive but effective one in the near future including this Paracheck® test. The WHO is also coordinating dipstick development so that all products meet a minimum level of validity. We may also develop the lot checking system for the quality assurance for the product.

MCVs will be trained for the procedure for the dipstick diagnosis. All patients who meet the clinical malaria criteria will be examined by dipsticks. The standard procedure by the manufacture (Paracheck® test, Orchid Biomedical Systems) will be used (17). It involves blood collection by finger prick onto an immunochromatographic paper strip. This strip is processed by adding a series of reagents directly to the strip and read by eye for color change within several minutes. The test requires no special storage conditions nor is electricity required. Non-laboratory personnel can be taught to perform finger prick and tests within two hours of training. The test detects *P. falciparum* antigen.

Antimalarial Drug Treatment Methods

All dipstick result positive cases will immediately referred to the Village Health Posts to receive currently recommended 2nd line drugs (quinine+sulfadoxin/primethamine; Q3+SP). Chloroquine will be used for dipstick negatives.

Dosage and administration (Dosage and administration followed by WHO guideline (30))

Chloroquine

(Available as tablets as 100,150, and 300 mg base (as phosphate or sulfate); as syrup 50mg base in 5ml)

Adults including pregnant women:

Total dose: 1500 mg (or approximately 25-30mg/kg) given over 3 days.

Day 1: 900 mg (600 mg as first dose, 300mg 608 hours later)

Day 2 and 3: 300 mg in a single dose.

Children:

Total dose: 25 mg/kg given over 3 days (as tablet or syrup).

Day 1: first dose 10mg/kg; 6-8 hours later 5 mg/kg

Day 2 and 3: 5mg/kg

Quinine

Available as tablet 300mg base (as bisulfate or sulfate)

It is administered orally to less seriously ill patients with infections likely to be resistant to chloroquine, sometimes in combination with pyrimethamine/sulfadoxine or a tetracycline. The study will administer in combination with primethamine/sulfadoxin. Quinine should be used, whenever possible, to treat chloroquine-resistant malaria during pregnancy (quinine 3-7 days).

Pyrimethamine/sulfadoxine

Available as tablet 25 mg of pyrimethamine + 500 mg of sulfadoxine

Quinine + Pyrimethamine/sulfadoxine (Q3+SP) administration

Adults: quinine 600 mg every 8 hours (3x) for 3 days. A single dose of pyrimethamine 75 mg plus sulfadoxine 1.5g (3 tablets) at Day 4.

Children: quinine 10 mg /kg every 8 hours for 3 days. A single dose of pyrimethamine/sulfadoxine as per their body weights:

31-45 kg: 2 tablets

20-30 kg: 1.5 tablets

11-20 kg: 1 tablet

5-10 kg: 0.5 tablet

In case of pregnancy

Quinine should not be withheld during pregnancy, despite its alleged abortifacient properties at high dosage, since it safeguards the life of the mother (30). At the village health post level, whenever practical, quinine should be given orally. If part or all of a dose is vomited within 1 hour, the same amount must be readministered immediately.

Adults: quinine 600 mg every 8 hours (3x) for 3-7 days

Children: quinine 10 mg /kg every 8 hours for 3-7 days.

Case-management at Village Health Post (VHP)

VHP will handle only uncomplicated malaria cases (see definitions above). Severe and complicated malaria cases (including suspected cases) are to be immediately referred to the hospital in Chakaria. VHP staff will assist for writing referral card for the patients. For uncomplicated malaria cases, the VHP will conduct diagnosis (dipstick and blood smear) and treatment services. If treatment failure malaria were detected without the sign of severe malaria, VHP will provide other 2nd-line drug regimen, i.e., quinine 7 days. If infection persists, the VHP should refer to the hospital in Chakaria (study will establish well referral contact with local hospitals). Some services will be offered at VHPs (e.g., temperature, respiration rate, blood pressure, haematocrit, etc.) and others will be requested to commercial pathology laboratory at Chakaria (ICDDR,B plan to establish clinical pathology laboratory commercial service in near future at Chakaria Research Centre). The doctors and paramedics serving at VHP will participate a training session of clinical diagnosis of malaria during the study period. Case-management at community level will follow the WHO guideline (34).

Working definitions used in this protocol

Uncomplicated malaria

Signs and symptoms of uncomplicated malaria include; chills, rigor, high temperature. There may also be headache, nausea, joint pains and sweating. An enlarged spleen is observed especially in children (and in adults not immune to malaria).

Diagnosis of uncomplicated malaria follows a fever protocol and diagnostic chart (Fig.1). Take a full history and ask about; the above symptoms, travel to malarious areas within 1-3 weeks or usual residence in malaria area; pregnancy (pregnant women are more prone to malaria and its complications); previous treatment. Diagnosis of uncomplicated malaria when there is a fever or a history of fever within the previous few days and either; travel /residence status in malarious area; rigors; an enlarged spleen in the non- or semi-immune; absence of another obvious cause of fever. If this history or one of these signs is not present consider other causes of

a fever before starting treatment. Be sure to check that there are no signs and symptoms of severe and complicated malaria.

Severe and complicated malaria

Signs and symptoms of severe and complicated malaria are seen in Fig. 1. If Health Post health workers suspect malaria and any one of these symptoms is present then a diagnosis of severe and complicated malaria must be made. Warning signs in children under 5 years conclude; unable to drink or breast feed (prostration); unable to sit or stand (in a child previously able to do); vomiting everything; recent history of convulsions; lethargic or unconscious.

Severe and complicated malaria must be treated as an emergency. Therapy must be initiated without delay for a greater chance of recovery without complications. Initiation of parental treatment before referral is essential. Quinine is the drug of choice for patients diagnosed with severe and complicated malaria and to improve the chance of recovery the first dose can be given at a health post before referral. The quinine should be administered parenterally by intramuscular injection (in a dose of 10mg/kg; not exceeding 600 mg) and immediately refer to the hospital with a referral letter.

Treatment failure

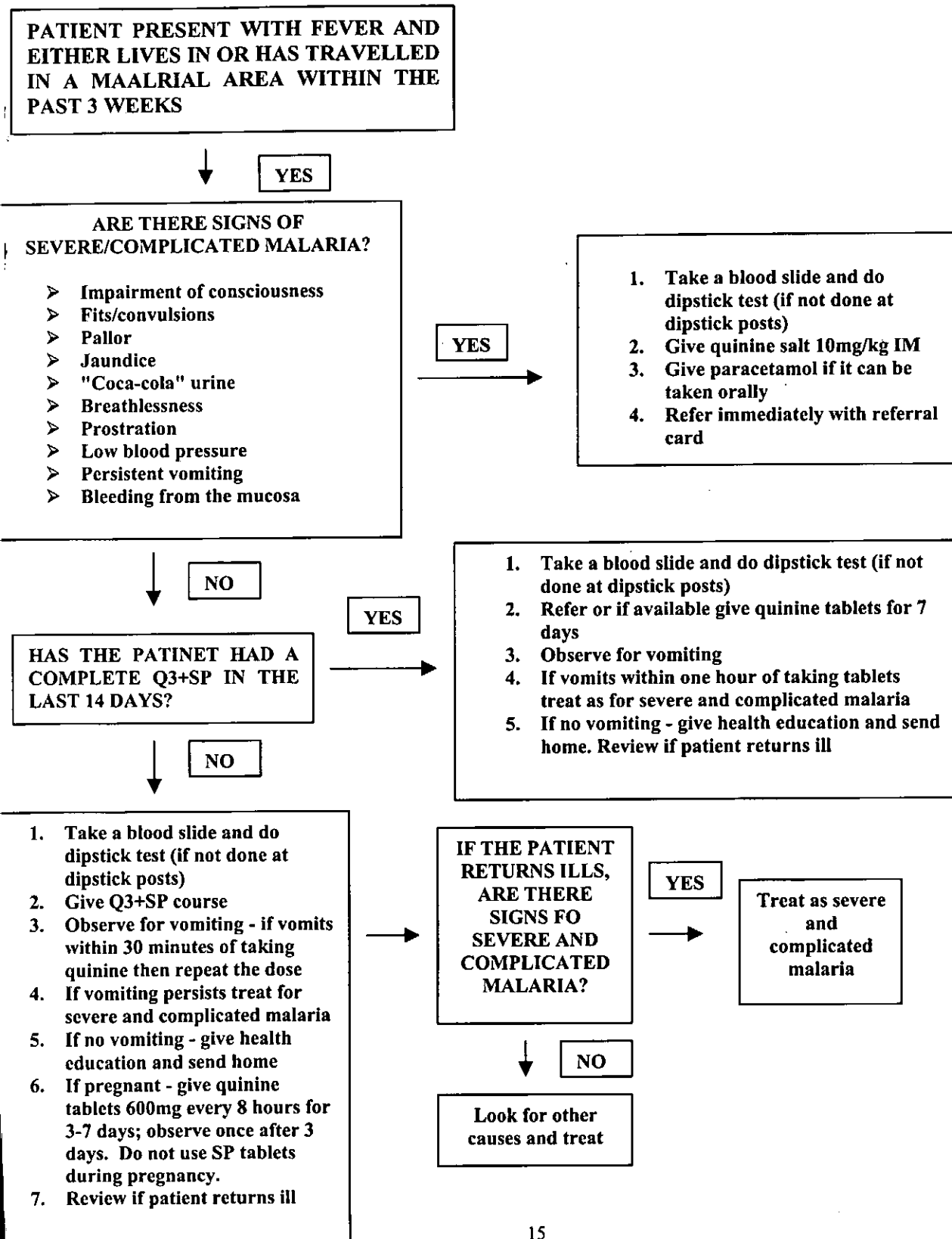
Clinical and parasitological criteria are used to classify the response to treatment as adequate clinical response, early treatment failure (from 1 to 3 days) and late treatment failure (from day 4 to 14). The basic protocol has been adopted through the WHO workshops in 1997, which included modifications enrolment of all age groups, treatment based on reappearance of parasitaemia and follow-up of patients up to day 28 (32). Monitoring of therapeutic efficacy is complex and requires specific technical expertise, given the present requirements of the test, general health service staff with minimal supervision is unable to carry it out. However, the WHO protocol can be used to train staff of the national malaria control program in operational research methods. This proposed pilot study does not aim to monitor therapeutic efficacy, but used for routine case-management improvement.

Antimalarial drug resistance

The definition of resistance requires demonstration of malaria parasitaemia in a patient who has received an observed treatment dose of an antimalarial drug and simultaneous demonstration of adequate blood drug and metabolite concentrations using established laboratory methods. In vivo studies of drugs for which true resistance is well known infrequently include confirmation of drug absorption and metabolism; demonstration of persistence of parasites in a patient receiving directly observed therapy is usually considered sufficient (35).

Figure 1: Malaria Management Protocol for Kakara Village Health Post

The following flowchart will assist health workers with the diagnosis and appropriate treatment of uncomplicated and severe/complicated cases of malaria and also those cases of treatment failure.



Clinical Malaria Episode and Treatment Monitoring

All families in the study area will have the Family Fever Monitoring Cards. Any episodes of fevers will be recorded in these cards either by themselves or with the assistance of MCVs. Community Health Workers (CHWs; study employed staff) will visit houses every two weeks to review the information on the card and transfer the information on the Record Keeping Book kept by CHWs. The Record Keeping Book contains the information on all public and private sector consultation and treatment as well as self-medication for suspected cases for malaria (using the defined clinical malaria criteria described above). They also record the information on name, age, sex, household number, consultation type and date, treatment type and date, compliance (duration of treatment) and cost involved (including transportation, wage lost, etc.). By doing this the utilization of the dipstick post (coverage) will be calculated. Clinical malaria episodes reported to the dipstick posts will be crosschecked by comparing the family fever monitoring cards with dipstick post records.

For treatment monitoring, a special drug picture/demonstration card will be prepared without indicating the name of the drugs and mixed with all commonly prescribed drugs in the communities. CHWs will use this card to assist their interview to fill their Record Keeping Book (e.g., what drug and how many days did they take, etc.).

At the Upazilla Health Complex and the Christian Memorial Hospital (these two are the only referral hospitals in the study area), malaria outpatient and inpatient data (malaria statistics) will be routinely collected. For inpatients (i.e., severe malaria cases), information to be collected will include patients' demographic data, residence, microscopic diagnosis, treatment administered and admission and discharge dates. Questionnaire for household expenditure includes for their reasons of the types of healthcare seeking. At the hospitals, admission criteria and routine recording procedures are not to be affected by the study.

MCVs will report to CHWs monthly by submitting the service record with examined dipsticks, and replenish dipsticks. The study will also communicate weekly with the local government offices (HAs and THFWO) to report the case and treatment numbers in the communities.

Identification of *P. vivax* infection/ parasitological density by blood smear

All suspected malaria cases with criteria described above are also taken a blood smear by CHWs or MCVs simultaneously with a dipstick test to identify *P. vivax* infection (dipstick can only diagnose for *P. falciparum* infection). Then, if they are positive, they are treated according to the protocol. The blood films collected will be sent to the study microscopist in Chakaria and the result will be given next day (i.e., average commercial lab in Chakaria return the laboratory results 1-2 days later). Since all indicator subjects are under continuous monitoring, we will be able to calculate the incidence (passive detection; patients have to be motivated to come to the health post by themselves) by monitoring negative subjects who become positive using man-months in the denominator. Re-infection rates will be also calculated by monitoring once cure persons who become positives (2 months study period might be too short to calculate this).

Measurement of Treatment Failure and Compliance

When the patients are continuously having or started to have malaria symptoms after completing treatment doses, they are encouraged to report to village posts for continuous monitoring by

examining blood slides for parasite existence (e.g., can be repeated at least up to 28 days). When they identified falciparum malaria, these patients will be also encouraged to come back to report 28 days later to MCVs to collect second blood films for testing the parasitological cure. We will calculate treatment failure rates by using the WHO formula to subtract the possible effect due to reinfection (from incidence estimates as described above) within 28 days after treatment. Compliance will be monitored by routine fever and treatment-monitoring system as described in "Clinical Malaria Episode and Treatment Monitoring" section of the protocol. The "Compliance Sheet" will be requested for patients to submit after completion of treatment. If on 5th day, the sheet is not submitted, CHWs will collect from their homes and cross check with the Record Keeping Book.

Entomological study of malaria vectors

The study will use man-biting mosquito collection technique for an index of vector population size when they are carried out at regular intervals. Collection technique from resting shelter is a valuable indicator of the effectiveness of control measures. The study will detect the parasite rates in vectors either by standard circumsporozoite (CS) or rapid dipstick test (24) to calculate the Entomological Inoculation Rate (EIR). EIR has been proven the best indicator for estimating the transmission force for a specific population.

Ten percent (10%; n=200) of high-risk zone study area houses (n=2,000) will be selected for mosquito collection in indoor and outdoor man-biting conditions from 4:00pm to 8:00 am. Outdoors collection should be made up in 2 conditions, one in human landing and the other animal landing (e.g., cows). Collecting mosquitoes in the act of biting is a convenient method of sampling adult populations. Mosquito collectors (trained CHWs) quietly stay at collection sites for 15 minutes, and collect mosquitoes that land on the exposed skin (usually on hands and legs). The mosquitoes will be collected with manual and mechanical aspirators. The study will also collect Anopheline mosquitoes in resting condition. They usually rest in dark, cool and humid places. The mosquito collectors or their assistants will record for collected mosquitoes with time of collection, type of aspirator used, collected numbers (see attached "Mosquito Collection Recording Sheet"). The collected mosquitoes will be transported to the Chakaria Centre for species identification under a microscope (see attached "Mosquito Identification Recording Sheet").

The mosquito collectors will be provided for malaria prophylaxis (e.g., mefloquine, 250 mg weekly) and in case of suspected malaria, diagnosis, treatment and transportation cost will be provided by the study. Since mosquito collectors are from nearby malaria endemic communities, they expose to malaria risk at normal life condition. No more than minimal risk involved to be a mosquito collector. This man-landing collection technique is a popular and established technique applied in many studies and we follow the WHO training module for collection and handling of mosquitoes (31).

Questionnaire on health-seeking behavior and household expenditure

A cross-sectional study on health-seeking behavior and household expenditures will be carried out in 2,000 randomly chosen households (or practically every 2nd household in the census household list; systematic sampling) from all households listed in the census book in Kakara Union (4,600 households; 23,000 population). This whole union area includes both forest (higher risk zone) and forest fringe (lower risk zone) areas. The working definition of malaria episodes for questionnaire survey will be:

Malaria Episodes: All episodes in the past one month that patients or household members thought that observed symptom(s) was due to malaria and sought for some sorts of malaria care and spend some money and/or lost productivity. The episodes with only resting at home or self-medication or seek advice from village doctors without any medications are also included. The study estimates approximately half (50%) of households have at least one malaria episode.

During the household survey each respondent will be asked about the length of time spent since the onset of last malaria illness and the extent to which their daily activities had been affected. They will be also asked about their last source of treatment and costs of receiving treatment related to last source. In addition to those household cost on 'self-treatment' and malaria prevention will be collected (questionnaire attached).

Direct patient costs will be assessed on the basis of expenditure for drugs, hospital and provider fees and transportation. Information on other direct cost like complementary cost of treatment will be collected. Complementary costs of treatment include cost of special drinks and foods.

Indirect patients costs will be determined as income reductions resulting from partial or complete inability to work during illness. These costs will be assessed both for the patient as well as for other household members who will assist patient care and will be accordingly unable to continue their regular work. The overall total indirect costs however, will be estimated based on the time that economically active patient were absent from their normal productive activities as a result of the malaria attack. The total number of days lost to production by both patients and their caretakers will be valued according to their age, gender and occupation. The age-gender-occupation specific daily wage rates in Chakaria will be multiplied by their corresponding total days lost to productive activities by the patients.

Information on financing methods those patient households will use, including out-of-pocket payments, loans, the sale of household assets, and transfer payments from private sources other than patients' household members will be collected.

Key Informant Interviews / Focus Group Discussions

Key informant interviews (12-15 interviews) and focus group discussions (6-8 discussions) will also be conducted for selected communities to assess communities' perceptions and attitudes (key informant interview schedule and focus group discussion guide are attached). A study investigator (medical anthropologist) will work with two anthropology/social science master graduates for conducting key interviews and focus group discussions. A small number of participants (e.g., 6-10) will be participating for each group session. The sessions will be cassette tape recorded and transcribed.

Geographical Information System

All households in the study area will be plotted by GPS (geographical positioning system). The study will develop a study area map for overlaying the attributable variables (e.g, malaria cases, EIR, etc.).

Sample Size Calculation

With the assumption of 5 episodes per person-year for all clinical malaria cases (E.Yunus, personal communication); among them, only one-third is confirmed malaria (9, 18); 70% of confirmed cases are *P.fulciparum* cases (16), the study has an estimate of 0.10 episodes per person-month. To have a precision of 0.10 ± 0.01 episodes per person-month, the study require approximately 3,500 person-months (12). We estimated our study population living in the high-risk zone (within 2-3 km from the forest edge) would be approximately 10,000, and observe for two months period (20,000 person months; taking into account of non-participation, migration and mortality rates, the study would expect 16,000 person-months). For the stratification by age group, socioeconomic status, etc, we keep this rather large population for the study. Ultimate goal would be incidence estimates per person-year with appropriate precision (e.g., 1.17 ± 0.12 episodes per person-year (all ages)).

Limitations of the Study

Since our study site for the community-based study is only in one upazilla in one district, it may have a limitation to generalize the conclusion for all falciparum malaria endemic areas in the country. Validity of incidence, compliance and treatment failure rates are totally depend on reported coverage of cases at health posts. Some of these indicators may fail to be calculated from this small-scale pilot study. Incidence estimates from two months data may be too low to conduct stratified analysis for all household or individual factors. Because of acquired immunity effect, more malaria episodes are not necessary related to high risk environment – interaction with immuno-profile.

Entomological assessment cannot cover all households to match confirmed malaria cases with vector information. Extrapolated indicator values on vector density and biting behavior from this study might be different if we conduct a much larger study. Certain people attract mosquitoes than others. Using different mosquito collectors may influence mosquito biting rate estimates. The study will rotates collectors and repeat measurements for a particular location.

Measurements of drug compliance will depends on correct self-reporting to CHWs (it is not directly observed therapy). This method may have a limitation of validity on compliance rate (over-reporting or under-reporting). We will cross check the compliance indirectly by measuring the parasitological cure rate 28 days after treatment.

Facilities Available

Describe the availability of physical facilities at the place where the study will be carried out. For clinical and laboratory-based studies, indicate the provision of hospital and other types of patient's care facilities and adequate laboratory support. Point out the laboratory facilities and major equipments that will be required for the study. For field studies, describe the field area including its size, population, and means of communications. (TYPE WITHIN THE PROVIDED SPACE).

The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) has large multi-disciplinary international and national scientific research staff. The study will be conducted at rural Charakia Thana in Cox's Bazar District. Chakaria Community Health Project has acquired a new ICDDR, B Research Centre at Chakaria in 2000. This facility will accommodate the base station for project coordination and implementation with a laboratory facility. The communication means in the Chakaria Research Centre has been well organized. There are mobile phone connections and daily courier services between Dhaka main office and Chakaria field office.

Currently ongoing Chakaria Community Health Project can continuously offer effective monitoring system for the health- and demographic indicators that will be the most advantage for our project design. The established linkage between the study staff of the ICDDR,B and the community will be the most important existing advantage to choose this site for the assurance of high coverage of monitoring information. The valuable inputs of human resources as well as physical research and laboratory space in the rural setting of an malaria endemic area can be assured by maximally utilizing existing knowledge of community-based health researches in Chakaria.

The government Upazilla Health Complex at Chakaria and the Christian Memorial Hospital will also provide their statistics related to the referral malaria cases. Both hospitals have the capacity to adequately examine malaria in their laboratory (blood films) and treat patients according to the current national guideline. The study area is one union in Chakaria bordering with the forest area. All the communities within 3 km from the forest border will be involved in the study. A total study population of 10,000 will be involved in the study.

Data Analysis

Describe plans for data analysis. Indicate whether data will be analyzed by the investigators themselves or by other professionals. Specify what statistical softwares packages will be used and if the study is blinded, when the code will be opened. For clinical trials, indicate if interim data analysis will be required to monitor further progress of the study. (TYPE WITHIN THE PROVIDED SPACE).

The investigators and supervisors will review all data forms for accuracy and completeness. Whenever necessary, additional visits will be made to clarify inconsistencies and missing data. After editing, data will be entered in to the databases (FoxPro). Data consistencies will be systematically cross-checked by data management staff. Monitor who will review the information flow for data quality assurance. Once the data are completed for editing, all identifier to identify individuals will completely deleted and only use the case codes for data analysis. The original recording sheets will be kept at the locked cabinets in the ICDDR,B.

Data analysis will be done using software packages EpiInfo, SPSS and STATA. Identifiable household level factors include housing characteristics, socioeconomic status, domestic animals, etc. Identifiable individual level factors include sleeping location, mosquito net use, treatment-seeking, etc. Mean values and rates will be calculated using data from samples drawn periodically from the population using the appropriate units with the confidence intervals. Initially, univariate analysis will be performed to provide a description of the study subjects (age, sex, community, education, socioeconomic status, etc.) . Values and rates will be compared between different age, sex and socioeconomic status using appropriate tests. Prevalence of drug resistance malaria will be calculated from the 28-days follow up data (it might not be valid; not aimed for this study). The incidence rates of malaria will be calculated using the subsample of originally negative patients or cured patients. We will examine the variables associated with the malaria cases by using logistic regression analysis or other appropriate multivariate analyses. Epidemiological and entomological data will be plotted for GIS analysis on clustering cases.

Key informant interview data will be translated into English with a proportion back-translated into Bangla. We will examine the notes for emerging themes and sorting data. Data will be entered into software packages (e.g., EZ-Text) for further analysis and to inform the development of health education efforts.

Ethical Assurance for Protection of Human Rights

Describe in the space provided the justifications for conducting this research in human subjects. If the study needs observations on sick individuals, provide sufficient reasons for using them. Indicate how subject's rights are protected and if there is any benefit or risk to each subject of the study.

Chakaria is an endemic area for malaria. All subjects in the endemic areas are at the greatest risk for malaria. The Community Health Workers will explain the aim of the study to all study participants. Information from the results of rapid dipstick diagnosis, microscopic examination for vivax malaria, treatment failure will provide direct benefit by identifying efficacious treatment. Documentation of the epidemiological profiles of different species of malaria will provide indirect benefit to patients by facilitating specific therapy for malaria species identified. No invasive procedure will be carried out for the patients in this study.

There is no major potential risks - finger prick blood will be collected from the subjects having clinical diagnosis of malaria. Severe cases of malaria will be referred to hospitals. Confidentiality will be strictly maintained by coding each subject.

Signed informed consents will be obtained from adult subjects and for children from the parents or legal guardian of the children. There will also be research activities (fever monitoring, questionnaires, interviews, group discussions and mosquito collections). No information will be withheld from the subjects. There is no potential risk to the subjects or privacy of individual is involved. Study participants will followed for malaria case management as per the study protocol.

Subjects who will participate will benefit from this study will provide dipstick diagnosis and secondline effective treatment for confirmed cases with minimum affordable cost at Village Health Post (less expensive than they are provided by commercial sector).

Use of Animals

Describe in the space provided the type and species of animal that will be used in the study. Justify with reasons the use of particular animal species in the experiment and the compliance of the animal ethical guidelines for conducting the proposed procedures.

No animal will be used in the study.

Literature Cited

Identify all cited references to published literature in the text by number in parentheses. List all cited references sequentially as they appear in the text. For unpublished references, provide complete information in the text and do not include them in the list of Literature Cited. There is no page limit for this section, however exercise judgment in assessing the "standard" length.

References

1. Banchongaksorn T, Prajakwong S, Rooney W, Vickers P. 1997. Operational trial of ParaSight-F (dipstick) in the diagnosis of falciparum malaria at the primary health care level. *SEA J Trop Med Publ Hlth* 28:243-46.
2. Beadle C, Long GW, Weiss WR, McElroy PD, Maret SM, Oloo AJ, Hoffman SL. 1994. Diagnosis of malaria by detection of *Plasmodium falciparum* HRP-2 antigen with a rapid dipstick antigen-capture assay. *Lancet* 343:564-68.
3. Bhuiya A. Health knowledge and behaviour in five unions of Chakaria. *Special Publication No. 52. International Centre for Diarrhoeal Disease Research, Bangladesh*. ICDDR,B, Mohakhali, Dhaka, Bangladesh. 1996.
4. Chiodini PL. 1998. Non-microscopic methods for diagnosis of malaria. 1998. *Lancet* 351:80-81.
5. Da Cunha, MLON, Piovesan-Alves F, Pang LW. 2001. A community-based program for the diagnosis and treatment of malaria in the Brazilian Amazon. *Am J Trop Med Hyg* 65:883-6.
6. Dietze RM, Perkins M, Boulos F, Luz F, Reller B, Corey GR. 1995. The diagnosis of *Plasmodium falciparum* infection using a new antigen detection system. *J Trop Med Hyg* 5245-49.
7. Ekvall H, Premji Z, Bjorkman A. 1998. Chloroquine treatment for uncomplicated childhood malaria in an area with drug resistance: early treatment failure aggravates anemia. *Trans R Soc Trop Med Hyg* 92:556-60.
8. Ettling MB, Thimasarn K, Shepard DS, Krachaikln S. 1991. Economic analysis of several types of malaria clinics in Thailand. *WHO* 69:467-76.
9. Faiz MA, Yunus EB, Rahman MR, Hossain MA, Rahman E, Bhuiyan SN. Evaluation of "New Clinical Case Definition for Uncomplicated Malaria" applied in National guidelines in Bangladesh. Abstract for the 9th ASCON, Dhaka, Bangladesh. 2000. P.25.
10. Harinasuta T, Suntharassami P, P, and Viravan C. 1965. Chloroquine resistant falciparum malaria in Thailand. *Lancet*, 288: 6757-660.
11. Hossain SMM, Bhuiya A, Rasheed S. 2001. Correlates of perceived malarial episodes and treatment seeking behavior in a malaria endemic rural area in Bangladesh. *Southeast Asian J Trop Med Public Health* 32(4):1-14.

12. Kahn HA and Sempos CT. Statistical methods in epidemiology. Chapter 8: Follow-up studies: Person-years. pp.206-225. Oxford University Press 1989. New York.
13. Kodisinghe HM, Perera KLRL, Premawansa S, Naotunne TS, Wickramasinghe AR, Mendis KN. 1997. The ParaSight-F dipstick test as a routine diagnostic tool for malaria in Sri Lanka. Trans Roy Soc Trop Med Hyg 91:398-402.
14. M&PDC, Director General of Health services (DGHS), MOHFW. 1995. Guidelines for the implementation of " The Revised Malaria Control Strategy in Bangladesh." MOHFW/Nov 1995/B.H.E. press/B-700.
15. M&PDC, Director General of Health Services (DGHS), MOHFW. 1997. Report, Malaria cases detected in Bangladesh - 1963-1996.
16. M&PDC, Director General of Health Services (DGHS), MOHFW. Malaria Control Program in Bangladesh. 2000.
17. Mills CD, Burgess DCH, Taylor HJ, Kain KC. 1999. Evaluation of a rapid and inexpensive dipstick assay for the diagnosis of *Plasmodium falciparum* malaria. Bull World Health Organ 77:553-9.
18. Montanari RM, Bangali AM, Talukder KR, Baqui A, Maheswary NP, Gosh A, Rahman M, Mahmood AH. 2001. Three case definitions of malaria and their effect on diagnosis, treatment and surveillance in Cox's Bazar district, Bangladesh. Bull World Health Org 79(7):648-56.
19. Parasittisuk C, Ettling M. 1986. Cost-effectiveness research in malaria control and the need for health behaviour and socio-economic research in malaria control in Thailand. SEA J Trop Med Publ Hlth 17: 393-95.
20. Piovesan-Alves F, Da Cunha MLON, Pang LW. 2001. The economic advantage of a community based malaria management program in the Brazilian Amazon. Am J Trop Med Hyg 65:872-6.
21. Premji Z, Minjas JN, Shiff CJ. 1994. Laboratory diagnosis of malaria by village health workers using the rapid manual ParaSight-F test. Trans Roy Soc Trop Med Hyg 88:418.
22. Rahman MR, Paul DC, Rashid M, Ghosh A, Bangali AM, Jalil MA, Faiz MA. 2001. A randomized controlled trial on the efficacy of alternative treatment regimens for uncomplicated falciparum malaria in a multidrug-resistant falciparum area of Bangladesh – narrowing the options for the National Malaria Control Programme? Roy Soc Trop Med Hyg 95:661-67.
23. Ruebush TK, Zeissig R, Koplan JP, Klein RE, Godoy HA. 1994. Community participation in malaria surveillance and treatment III. An evaluation of modifications in the volunteer collaborator network of Guatemala. Am J Trop Med Hyg 50:85-98.
24. Ryan JR, Dave K, Emmerich E, Garcia L, Yi L, Coleman RE, Sattabongkot J, Dunton RF, Chan AST, Wirtz RA. 2001. Dipsticks for rapid detection of Plasmodium in vectoring Anopheles mosquitoes. Med Veterinary Entomology 15:225-230.

25. Sharma VP. 1996. Re-emergence of malaria in India. *Int J Med Res* 103, 26-45.
26. Shehgal PN, Sharma MID, Sharma SI, and Gogi S. 1975. Resistance to chloroquine in *falciparum* malaria in Asam state. *J Commun Dis* 5: 175-177.
27. Shiff CJ, Minjas J, Premji Z. 1994. The ParaSight-F test: a simple rapid manual dipstick test to detect *Plasmodium falciparum* infection. *Parasitology Today* 10:494-95.
28. Verderger J. 1986. Epidemiology of emergence and spread of drug resistant *falciparum* malaria in Southeast Asia. *Southeast Asian Journal of Tropical Medicine and Public Health*, 17: 111-118.
29. Watson PA, Laidoueu AB, Kacou E, Koudou G, Traore M. 1998. Comparison of a rapid dipstick test and thick blood films for detecting parasites of *Plasmodium falciparum* used under typical conditions at a semi-rural hospital in Cote d'Ivoire. *Tropical Doctor* 28:85-88.
30. WHO. 1990. Malaria. p.32-37 In: WHO model prescribing information; Drugs used in parasitic diseases. WHO Publications, Geneva.
31. WHO. 1994. Entomological laboratory techniques for malaria control: Part II. Tutor's Guide. WHO publications, Geneva.
32. WHO. 1997. Assessment of therapeutic efficacy of antimalarial drugs for uncomplicated *falciparum* malaria. Geneva. 29.2.97.
33. WHO. 2000. New perspectives: Malaria diagnosis: Report of a joint WHO/USAID informal consultation 25-27 October, 1999. WHO Geneva WHO/CDS/RBM/2000.14.
34. WHO. 2000. WHO Expert Committee on Malaria. WHO Technical Report Series 892.
35. WHO. 2001. Drug resistance in malaria. WHO/CDS/CSR/DRS/2001.4.
36. WHO. 2001 Report on the 3rd Meeting of Technical Support Network: Insecticide-treated netting materials. WHO/CDS/RBM/2001.36
37. Wongsrichanalai C, Webster HK, Wimonwatterawatee T, Sokoto P, Chuannak, Thaimassarn K and Wernsdorfer WH. 1992. Emergence of multidrug-resistant *Plasmodium falciparum* in Thailand: in vitro tracking. *American Journal of Tropical Medicine and Hygiene* 47:112-116.

Dissemination and Use of Findings

Describe explicitly the plans for disseminating the accomplished results. Describe what type of publication is anticipated: working papers, internal (institutional) publication, international publications, international conferences and agencies, workshops etc. Mention if the project is linked to the Government of Bangladesh through a training programme.

Immediate benefit will emerge from timely dissemination of findings integrated into the service components of Chakaria Community Health Projects to continuously provide functional malaria healthcare service options with quality through community self-help organizations.

Moreover, timely dissemination of the findings from the study, technical assistance to build the capacity of the National Malaria Control Programme and improved use of data for policy decisions will be important priorities of the project. In order to achieve these objectives mechanisms of coordination with the GoB and other institutions with malaria research/control capacity will be developed. There has been a national coordination board with the central office at the Malaria & Vector Borne Disease Control (M&VBDC) in the Directorate-General of Health Services. The Malaria Working Group at Chittagong Medical College has been offering the key research roll on malaria case-management including drug resistance monitoring in the past. This project has been facilitated and will continuously strengthen such research networking capabilities and partnership on malaria control in Bangladesh. The Regional and Head Office of WHO as well as the Country Office have a good communications with the above mentions parties. Recent communications with WHO technical offices revealed that our proposed study is fitted well with their current initiatives. Since malaria is one of the most important global issues as emerging and reemerging infections, we are expected to facilitate to formulate a Steering Committee on Malaria & Vector-borne Diseases involving concerned officials from the MOHFW under the supervision of the Directorate- General of Health Services in Bangladesh.

Collaborative Arrangements

Describe briefly if this study involves any scientific, administrative, fiscal, or programmatic arrangements with other national or international organizations or individuals. Indicate the nature and extent of collaboration and include a letter of agreement between the applicant or his/her organization and the collaborating organization. (DO NOT EXCEED ONE PAGE)

This project will be implemented through the collaboration with the National Malaria Control Programme, Directorate General Health Services, the Malaria Working Group of Chittagong Medical College, Department of Zoology, Chittagong University, The Johns Hopkins University, USA, Malaria Branch, CDC, Atlanta, USA, Wellcome-Mahidol University, Oxford Tropical Medicine Research Programme, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand and others.

The Malaria Working Group in Chittagong Medical College is currently funded by WHO/TDR, Geneva and continuously works on severe malaria study since they have a strong advantage to look at the referral cases at facility level. The ICDDR,B rather has the strength on community-based uncomplicated malaria management studies as well as highly specialized laboratory studies. The ICDDR,B will be responsible for setting up the research team for malaria fever monitoring at the community level and train the health workers and malaria volunteers in the community. The National Malaria Control Office will coordinate all the related malaria activities in the country, as well as to promote the links between the collaborative organizations.

Two hospitals in Chakaria (Upazilla Health Complex and Memorial Christian Hospital) will be the collaborative institutions as referral hospitals. They will collaborate for monitoring malaria cases at hospitals. Upazilla Health and Family Planning Officer at Chakaria Upazilla Health Complex will assist coordinating the study activities in the study area.

Biography of the Investigators

Give biographical data in the following table for key personnel including the Principal Investigator. Use a photocopy of this page for each investigator.

- 1 Name: Yukiko Wagatsuma
- 2 Present position: Scientist, Public Health Sciences Division, ICDDR, B
Assistant Scientist, Division of Disease Control, Department of International Health,
Johns Hopkins University School of Hygiene and Public Health
- 3 Educational background (last degree and diploma & training relevant to the present research proposal)
M.D., University of Tsukuba, Japan, 1987
D.T.M., Tropical Medicine, University of Tokyo, Japan, 1987
M.P.H., International Health, Johns Hopkins University, USA, 1990
Dr. P.H., International Health, Johns Hopkins University, 1996
Certificate in Health Economics, Joint Programme of London School of Economics and London School
of Hygiene and Tropical Medicine, 1999

4. List of ongoing research protocols (start and end dates; and percentage of time):

2000-023: Emergency research programme to enhance dengue prevention and control programs in Bangladesh; vector surveillance and control component.
#2000-025: Combined interventions to promote maternal and infant health.
#2000-026: Drug resistance monitoring and community-based case-management using dipstick for malaria diagnosis in Bangladesh.
#2000-028: Population-based evaluation of *Shigella* infection in an urban area of Dhaka, Bangladesh.
#2001-021: Community-based epidemiologic study of visceral leishmaniasis in Bangladesh.
#2002-006: Community-based study of bronchial asthma among children in an urban slum in Dhaka, Bangladesh.

4.1. As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
#2000-023	16/08/2000	31/12/2001	20%
#2000-026	3 years after starting (not yet started)		30%
#2001-021	01/12/01	30/12/05	3%
#2002-006	14/03/02	31/03/03	5%

4.2. As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time
#2000-025	01/11/2000	30/10/2005	30%
#2000-028	01/07/2001	30/06/2003	5%

5 Publications

Types of publications	Numbers
a) Original scientific papers in peer-review journals	12
b) Peer reviewed articles and book chapters	2
c) Papers in conference proceedings	9
d) Letters, editorials, annotations, and abstracts in peer-reviewed journals	2
e) Working papers	6
f) Monographs	1

6 Five recent publications including publications relevant to the present research protocol

- 1) Richter J, Wagatsuma Y, Aryeetey ME, Feldmeier H. Sonographic screening for urinary tract abnormalities in patients with *Schistosoma haematobium* infection; pitfalls in examining pregnant women. *Bull World Health Org* 1996;74(2):217-221.
- 2) Abdel-Wahab MF, Campagne G, Doehring E, Garba A, Hammou A, Hatz C, Homeida MMA, Kardorff R, Magak PW, Mbaye A, Olveda RM, Qurashi MA, Ramarokoto CE, Richter J, Traore M, Wagatsuma Y, Zhongdao W. WHO Niamey Working Group. Ultrasound in schistosomiasis: A practical guide to the standardized use of ultrasonography for the assessment of schistosomiasis-related morbidity. *World Health Organization TDR/STR/SCH/00.1*.
- 3) Wagatsuma Y, Aryeetey ME, Sack DA, Morrow RH, Hatz C, Kojima S. Resolution and resurgence of *S. haematobium*-induced pathology following community-based chemotherapy in Ghana as detected by ultrasound. *J Inf Dis* 1999;179(6):1515-1522.
- 4) Aryeetey ME, Aholu C, Wagatsuma Y, Bentil G, Nkrumah FK. Health education and community participation in the control of urinary schistosomiasis in Ghana. *East African Medical J* 1999; 76(6): 324-329.
- 5) Nsowah-Nuamah NNN, Mensah G, Asryeetey ME, Wagatsuma Y, Bentil G. Urinary schistosomiasis in southern Ghana: a logistic regression approach to data from a community-based integrated control program. *Am J Trop Med Hyg* 2001; 65(5):484-490.

CURRICULUM VITAE OF CO-PRINCIPAL INVESTIGATOR

- 1 Name : Abbas Bhuiya
- 2 Present position : Head, Social and Behavioural Sciences Unit
- 3 Educational background : BA (Honours) MA in Statistics
(last degree and diploma & training relevant to the present research proposal) MA, Ph.D. in Demography

List of ongoing research protocols
(start and end dates; and percentage of time)

4.3. As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
2001-013	1-7-01	31-12-02	10
SBSP	1-7-93	30-6-02	55
94-002	1-1-94	31-12-02	10

4.4. As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
92-028	1-09-00	31-8-02	15

4.5. As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time
2000-001	1-9-00	31-8-02	10

5 Publications

Types of publications	Numbers
a) Original scientific papers in peer-review journals	32
b) Peer reviewed articles and book chapters	12
c) Papers in conference proceedings	many
c) Letters, editorials, annotations, and abstracts in peer-reviewed journals	
d) Working papers	many
b) Monographs	some

6 Five recent publications including publications relevant to the present research protocol

1. Hossain SMM, Bhuiya A. Rasheed S. 2001. Correlates of perceived malarial episodes and treatment seeking behaviour in a malaria endemic rural area in Bangladesh. *The Southeast Asian Journal of Tropical Medicine and Public Health*, 32:1-14
2. Bhuiya A., Aziz A., and Chowdhury M. (2001) Ordeal of women for induced abortion in a rural area of Bangladesh. *Journal of Health, Population and Nutrition*, 19:281-290.
3. Bhuiya A., Chowdhury M., Ahmed F. and Adams A. M. (2001) Bangladesh: An intervention study of factors underlying increasing equity in child survival. In Evans *et al.* (eds.) *Challenging Inequities in Health: From Ethics to Action*. New York: Oxford University Press, pp: 227-239.
4. Bhuiya A. and Chowdhury M. (2002) Beneficial effects of a woman-focused development programme on child survival: evidence from rural Bangladesh. *Social Science and Medicine* (in press).
5. Ahmed SM, Chowdhury M. and Bhuiya A. (2001) Micro-credit and emotional well-being: experience of poor rural women from Matlab, Bangladesh. *World Development*, 29:1957-1966.

Detailed Budget for New Proposal

Project Title: Epidemiological and socioeconomic factors related to malaria in endemic communities of Bangladesh

Protocol Number: _____ Name of PI: Yukiko Wagatsuma Division: PHSD

Funding Source: DFID
Amount Funded (direct): \$22,800 Overhead (indirect): 25% \$5,700 Total: \$28,500

Starting Date: 25/04/2002 Closing Date: 31/08/2002

Personnel (No. personnel)	Position	Effort%	Salary	Two months
1 Yukiko Wagatsuma, PI	P-4	10%	8,659	1,731
2 Abbas Bhuiya, Co-PI	P-4	5%	10,024	1,002
3 Robert Breiman	P-5	2%	-	-
4 A.K.M. Siddique	P-4	2%	10,192	408
3 Rashidul Haque	NO-C	10%	1,332	266
4 Shakil Ahmed	NO-B	10%	900	180
5 Entomologist	GS-5	80%	-	-
6 Medical Anthropologist	GS-5	50%	373	373
7 Sr. Research Assistant (2)	GS-4	100%	317	(1 mo. only) 634
8 Study physician (1) -Chakaria	No-A	10%	757	151
9 Chief Field Research Officer (1)	GS-6	10%	522	104
10 Field Research Officer (1)	GS-5	10%	373	75
11 Data Management Assistant (1)	GS-3	100%	260	520
12 Community Health Workers (30)	GS-1	100%	120	7,200
Sub Total				12,644
Travel				
Local Travel				1,000
Transport charge from Chakaria Research Centre				1,000
Transportation charge (Dhaka Transportation Office)				200
Sub Total				2,200
Supplies and Materials (Description of Items)				
Dipsticks (seed money for revolving fund)				2,580
Drugs for patients				200
Chemicals, reagents, dipsticks for detecting malaria parasites in mosquitoes and other laboratory supplies				3,000
Stationeries and other office supplies				300
Sub Total				6,080
Other Contractual Services				
Communications, Utilities				100
Trainings and Seminars				300
Printing, photocopy, publication, etc.				300
Chakaria Research Centre Charges				600
Sub Total				1300
Other Operating Costs				
				576
TOTAL DIRECT COST				22,800
25 % INDIRECT COST				5,700
TOTAL PROJECT COST				28,500

16/4/2002
Md. Bozior Rahman
Manager, Budget & Costing
ICDDR,B: Centre for
Health & Population Research
Mohakhali, Dhaka-1212
Bangladesh

Budget Justifications

Please provide one page statement justifying the budgeted amount for each major item. Justify use of man power, major equipment, and laboratory services.

Personnel:

Y. Wagatsuma, PI will take overall responsibility of study implementation (10%). A. Bhuiya will be responsible to supervise Chakria Research Centre's activities related to the study as well as work for the components on household malaria expenditure study (5%). A.K.M. Siddique will share take responsibility of epidemiological component of the study (2%). Dr. R. Haque (parasitologist) will do overall parasitological and laboratory technical and scientific aspects of the study (10%). Dr. S. Ahmed (health economist) will supervise and analyze the household expenditure component (10%). One entomologist at GS-5 level will offer 80% of time for two months for mosquito collection and laboratory work (his salary will not be charged for this study). One medical anthropologist will work for two months with 50% efforts to supervise group discussions and key interviews. Two Senior Research Assistants will conduct group discussions and key interviews in one month period (GS-4 level).

From Chakaria research team, one Study Physicians of 10% effort will be employed to be a main coordinator/supervisor stationed in Chakaria. One Chief Field Officer (GS-6) and one Field Research Officers (GS-5) currently employed and working at the Chakaria Research Centre will be continuously employed for their efforts of 10% for this study. One Data Management Assistants will be employed for 100% effort at the level of GS-3 only for two months. Community Health Workers (CHWs) will be continuously visit households in the study area for two-month data collection period (30 CHWs).

Dipstick: The total 10,000 population will be in the study area. The study expects 3,000-4,000 dipsticks would require for the study. We charge initial 3,000 dipstick cost as seed money for revolving funds (the study will do cost-recovery to continuously supply for the field needs; $\$0.76/\text{dipstick} \times 3,000 \text{ dipsticks plus shipping cost } (\$300) = \$2,580$).

Laboratory component

Supplies, reagents, dipsticks to detect parasites in mosquitoes: Some reagents and chemicals will be required for laboratory work. The study will procure the materials require for detecting the sporozoites in mosquitoes. One of the promising technique would be a dipstick detection. We are still negotiating the price, but we estimate approximately \$3,000. One microscope will be brought from Dhaka entomology lab to Chakaria for study period.

Training: 1-2 day training session will be held for community health workers. Malaria microscopist training is currently on going (3 weeks) in Dhaka and plan to complete before the initiation of study in April 2002.

Other Support

Describe sources, amount, duration, and grant number of all other research funding currently granted to PI or under consideration. (DO NOT EXCEED ONE PAGE FOR EACH INVESTIGATOR)

Wagatsuma, Y

ACTIVE

- | | | |
|--|---------------------|------------|
| 1. USAID/W/ID | Jan 2000–Dec 2003 | 50% effort |
| Responsible: Coordination, Infectious Disease Initiatives | | \$150,000 |
| 2. Government of Japan | Apr 2000–Mar 2003 | 30% effort |
| Low Birth Weight Study | | |
| Fetal ultrasound component (PI: Y Wagatsuma) was integrated into the umbrella protocol of “Combined Interventions to Promote Maternal and Infant Health” funded by UNICEF and NIH. | | |
| 3. IVI | July 2001–June 2003 | 5% effort |
| DOMI-Shigellosis: Population-based evaluation of <i>Shigella</i> infection in an urban area of Dhaka, Bangladesh | | \$940,246 |
| 4. CDC | Dec 2001–Sep 2004 | 3% effort |
| Community-based epidemiologic study of visceral leishmaniasis in Bangladesh | | \$103,913 |

PENDING

- | | |
|---|------------|
| 1. Chakaria Community Health Research | 30% effort |
| Drug resistance monitoring and community-based case-management using dipstick for malaria diagnosis in Bangladesh | |
| | \$700,000 |

OVERLAP

None

International Centre for Diarrhoeal Disease Research, Bangladesh

Voluntary Consent Form

Title of the Research Project:

Epidemiological and socioeconomic factors related to malaria in endemic communities of Bangladesh

Principal Investigator: Yukiko Wagatsuma

Before recruiting into the study, the study subject must be informed about the objectives, procedures, and potential benefits and risks involved in the study. Details of all procedures must be provided including their risks, utility, duration, frequencies, and severity. All questions of the subject must be answered to his/ her satisfaction, indicating that the participation is purely voluntary. For children, consents must be obtained from their parents or legal guardians. The subject must indicate his/ her acceptance of participation by signing or thumb printing on this form.

We are currently conducting a malaria study in communities having many malaria patients in Chakaria. This study aims at improving the case-management of those with symptoms of uncomplicated malaria using rapid simple dipstick diagnosis. We think that only about one of every three patients with symptoms of malaria actually have malaria. The results of this study will help us to improve the quality of malaria control in your community. We invite you to participate in our study. You may help us in our efforts by participating in the study. If you agree to participate in our study:

We will ask some questions individually and as a group session regarding to malaria. We will ask you about money spent for malaria treatment, how long the illness disturbed your normal life and if someone has to nurse you during illness. This information will assist the country to improve how to control malaria problem in the community. The study ask you to record all fever episodes for two months, and a trained malaria community volunteers will perform rapid diagnosis test for possible malaria infection. Using the small paper strips, we will test your blood for malaria. Very small amount of blood will be taken by a finger pricking with a disposable lancet. The procedure only involves a little pain when we prick your finger, but no other harm will be involved. The Village Health Post will treat you with effective second line drugs that are usually prescribed after the observed failure of the first choice of oral chloroquine tablets according to the current government guideline. This drug is very effective but more expensive than the first line drug. We therefore need the accurate diagnosis before we will give this treatment. There are two types of malaria parasites cause malaria in Bangladesh. Without accurate diagnosis we cannot distinguish these two types of malaria. One type (*falciparum*) can be very serious and needs special drugs. The other type (*vivax*) can be treated with chloroquine. Results of the rapid test can be informed to you within several minutes while you wait for a result. Once you are diagnosed with one specific type called *falciparum* malaria, you will be given specific treatment. The drugs are tablets and can be taken orally. There are two types of drugs that have to be taken to get a good cure from malaria. The first one called quinine has to be taken for three days. The other one called sulfadoxine/primethamine has to be taken once on the fourth day. To complete all four-day course is very important for curing malaria. We will give you a piece of paper "malaria drug sheet" for you to mark for your drug taking record for four days. Some of you may be asked to come back after 28 days to dipstick spots to assure the cure by testing again by a dipstick. If you are not cured from the treatment, you will be referred to our collaborated hospitals in Chakaria.

Our rapid dipstick test can only detect falciparum and if your test is negative we will treat you with chloroquine. Before treatment community health worker will take a blood smear simultaneously with a dipstick test. As you may have seen in a hospital, a malaria blood smear will be prepared by placing the small amount of blood taken by finger pricking and spread the blood on the glass for microscopic examination. By doing this examination, we can only know if you have other type of malaria (vivax malaria). Since microscopic examination takes time and result can be informed only the next day, you will be treated immediately after blood smear is taken.

You will be directly benefited from the participation in this study since we will diagnose with the quick and accurate method and provide the appropriate treatment at the Village Health Post. Although they charge the minimum cost for drugs, but that are usually less expensive than private drug sellers. This case-management by completing with appropriate drug with confirmed diagnosis will also prevent transmission of malaria to others. Additionally, the results of this study will benefit the society. There is no physical risk involved in this study. If you do not participate in this study, you may go for treatment at clinics and hospitals. You would be able to withdraw your consent at anytime during the study period without causing any penalty to you and without affecting your further treatment at clinics and hospitals.

All of your medical information including the results of the diagnosis test will be kept confidential, and no one other than the investigators of this study and the Ethical Review Committee that overseas protection of human rights would be able to see them. We will be happy to answer to your questions, now and a later time.

If you agree to participate in this study, please indicate that by putting your signature or left thumb impression on the specified space below. If you have less than 18 years child in your family and you will allow him/her to participate in the study, please list all the children's names and sign or thumb impression next to his/her name.

Thank you very much for your cooperation.

Signature of Investigator/ or agents

Date:

Signature or thumb impression of Subject/
Parents or Guardian

Date:

A. List of the children less than 18 years old for permission of participation:

<u>Name of the Child</u>	<u>Parents'/guardian's Signature</u>
1.	
2.	
3.	
4.	
5.	
6.	
7.	

Household costs of malaria care in Chakaria Thana

(Check whether any member of the household is eligible: administer this questionnaire)

Other instruments will collect information on socio-economic & demographic characteristics

101. Please mention your name/ Who has been suffering from fever during the last two weeks?

Name of Respondent: _____ | | | Please verify the ID.

102. Occupation of the respondent _____ | | |

103. What was the total duration of illness at a stretch?

[If duration is less than one day then write 1]

| | | Days (write 95 if still suffering)

104. Did the sickness cause you/your child to lose any days of routine work, normal functioning of school?

Yes

No

0-60 months of age

1

2

3

→ Skip to q. 106

105. If yes, how many days of routine work, normal functioning, schooling days, did you/your child lose?

| | | Days (write 95 if he/she was not able to do right now)

106. What was the course of action taken? (there may be more than one answer)

Did not do anything

01

Took some remedial measures at home without any drugs

02

Took some remedial measures at home with drugs

03

Taken to health care provider/facility

04

Doctor was called at home

05

Others _____ (specify)

07

→ Skip to q. 201

107. Why did not you seek any care from health care provider/facility? (there may be more than one answer)

The condition was not serious

01

Need not think to go to the doctor

02

Home remedy is enough/better

03

Do not know where else to go for such treatment

04

Do not have enough money to seek provider's care

05

The health care facility is far away from home

06

Experienced bad treatment/care from the provider's around

07

Better treatment/care not available

08

Others (specify) _____

09

→ Skip to q.319

PROVIDER'S SECTION:

201. Place/person last visited for Treatment (there may be more than one answer)

Name _____ Address _____

Public Sector

a. Zilla Hospital

01

b. Upazilla Health Complex

02

c. Health and Family Welfare Centre

03

d. Community clinic

04

e. Satellite/EPI Clinic

05

f. Doctor/Paramedic

06

Medical Private Sector

- g. Private Clinic/Doctor 07
 h. Village doctor 08
 i. Pharmacy 09
 j. Homeopath 10

NGOs

- k. Village Health Posts (VHPs) 11
 l. Clinic 12
 m. Satellite clinic 13
 n. Field worker 14

Other private sector

- o. Shop 15
 p. Friend/Relative 16
 q. TBA/Dai 17

Others (specify) _____ 18

202. Why did you select this particular provider /facility? (there may be more than one answer)

- a. The facility is near 01
 b. Fees/treatment is cheap 02
 c. Convenient 03
 d. Always used this source 04
 e. The providers are well-behaved 05
 f. The providers are efficient/well-trained 06
 g. Drugs are dispensed free 07
 h. The facility is clean 08
 i. The waiting time is less 09
 j. Better treatment experienced previously 10
 k. Registered facility 11
 l. Others (specify) _____ 12

PATIENT'S COST SECTION:

301. Did anybody assist / accompany you during your travel to reach the particular provider?

Yes
 No

1
 2 → Skip to q. 303

302. _____ (Specify) Age | | S | | Occupation | | |
 _____ (Specify) Age | | S | | Occupation | | |
 _____ (Specify) Age | | S | | Occupation | | |

303. How did you / they get there, how long did it take, and how much did it cost?

From	To	Means	Time	Cost

304. How did you/ they come back, how long did it take, and how much did it cost?

From	To	Means	Time	Cost

305. How long did you have to wait to receive and complete services at that particular place?

____ Hr. ____ Min. (write 97 if does not know)

306. Did you pay for the services you took? Yes

1

No

DK

2

7

→ Skip to q. 310

→ Skip to q. 310

307. How much did you pay for the service in total? ____ Taka
(write 997 if does not know)

308. For which of the following services did you pay this money?
(more than one answer is possible)

a. Registration/card

b. Visit/Consultation

c. Laboratory tests

g. Medicine

h. Staying at the hospital

i. Others (specify) _____

j. Paid all together

k. Don't know

309. Do you think that the amount of money that was charged were appropriate with respect to the services you received?

High 1

Just right 2 (skip to q.311)

Less 3

Don't know 7

310. You said you have not paid for the services. Why did you not have to pay? (only one answer)

a. You were exempted from the fee

1

b. The service was available free

2

c. You will pay in your next visit

3

d. Others (specify) _____

..... 4

311. After leaving the <PROVIDER'S> place, did you/they have to spend more time and money for getting drugs or laboratory tests?

Yes 1

No 2 → Skip to q. 314

DK 7 → Skip to q. 314

312. How long? ____ Hr. ____ Min. (write 97 if does not know)

313. How much? ____ Taka (write 997 if does not know)

314. Did you/ they have to spend the night away from home either going there or coming back?

Yes, on the way

1

Yes, clinic/hospital

2

No

3

DK

7

→ Skip to q. 316

→ Skip to q. 316

315. How much did you/they spend for lodging?

____ Taka (write 997 if does not know)

316. Did you / they have to spend money to buy food or drinks while you were away for the consultation ?

Yes 1
No 2 → Skip to q. 318
DK 7 → Skip to q. 318

317. How much did you/they spend for lodging ?

_____ Taka (write 997 if does not know)

318. To make sure I got everything right, can you tell me again how much time you/they spent between leaving home and getting back after the consultation ?

_____ Day _____ Hr. _____ Min.

319. Did you have to spend any extra drug cost or on anything else due to malaria illness since the last onset?

Yes 1
No 2 → Skip to q. 321
DK 7 → Skip to q. 321

320. How much? _____ Taka (write 997 if does not know)

321. Do you take any preventive measures for malaria at the household ?

Yes 1
No 2 → Skip to q. 324
DK 7 → Skip to q. 324

322. What are those?

Using mosquito net	01
Using mosquito coil	02
Using aerosol	03
Using any traditional materials	04
Others _____	07

323. How much did you spend for those preventive measures in the last month ?

_____ Taka (write 997 if does not know)

324. How did you finance your treatment during the episode of malaria?

Sold out / Mortgaged household asset	01
Advanced labor payment	02
Loan from neighbors / friends	03
Loan on interest	04
Used own savings	05
Others _____	07

401. Did anybody assist (or assisting you) you during your illness at home.?

Yes 1
No 2 → Stop interview
DK 7

402. FOR EACH PERSON WHO ACCOMPANIED THE CHILD TO THE PROVIDER:

#	Household person	Age	Sex	Occupation / Principal activity	Average time spent on principal activity (Normal time)	Average time spent on principal activity (During illness)	Number of days assisted by the person	Number of loss full functioning days (if there)
	Person 1							
	Person 2							
	Person 3							
	Person 4							

Principal Investigator: Last, first, middle Wagatsuma, Yukiko

Mosquito Collection Recording Sheet

Man Biting Condition (Outdoor and indoor)

Union:..... Village:Village Code: House NO.

Date of Collection: Team NO. Supervisor:

Sl. NO.	Time of Collection	Type of Aspirator	Collection NO.(after collection)	Remarks
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				

Mosquito Identifications Recording Sheet

Determined By: Date:

Village Code	Container NO.	Date of Collection	Collected from (Man/Animal)	<i>Anopheles</i> mosquito species	Other mosquito	NO. of Female <i>Anopheles</i>	NO. of Male <i>Anopheles</i> (if any)	Remarks

FOCUS GROUP GUIDE
COMMUNITY PERCEPTIONS, BELIEFS AND TREATMENT FOR MALARIA

1. Common illness in this community
2. Which are most important? Why? (Prevalence? Severity? Disability? Mortality?)
3. Which affect children/adults?
4. Local name for 'malaria'?
IF NO TERM IS MENTIONED FOR A FEBRILE ILLNESS, PROBE FOR TERMS. CHECK FAMILIARITY WITH TERM 'MALARIA.'
5. Different types of febrile illnesses? Name them.
6. What are the signs and symptoms of [malaria]*?
7. How do you treat [malaria]* in this community?
PROBE TO ENSURE ALL TREATMENTS ARE MENTIONED.
Which are most effective? Why?
When is [malaria] treated?
PROBE: ONSET? LATER?
8. What causes [malaria]* Can [malaria]* be spread? How?
IF MOSQUITOES ARE NOT MENTIONED, PROBE.
9. Can it be prevented? How?
PROBE: INSECTICIDES? BEDNETS? COILS? REASONS FOR USE.
10. Do people use bednets here?
PROBE: ARE THEY AVAILABLE? IF AVAILABLE AND NOT USED, WHY NOT?
How many people use them? Few, many? Who?
PROBE: WOMEN, CHILDREN, EDUCATED PEOPLE, RICH PEOPLE, THOSE WHO'VE BEEN TO BIGGER TOWNS.
Do any of you use bednets? If so, why?
Advantages/disadvantages of the nets? When are they used?
11. Are mosquitoes a problem? How are they kept away?
IF NETS HAVE BEEN MENTIONED, ask if there other things people do to avoid mosquitoes?

Note: * We ask questions using the local terms where [malaria] is written.

Key Informant Interview Schedule: Perceptions, beliefs and treatment for [malaria]

1. What are the common illnesses in this community?
2. Which of these do you think are the most important? Why?
3. Which of these affect adults? Which affect children?
4. Which is the local name for [malaria]*?
Use local term if appropriate.
Are there different types of febrile illness? List names of different types. Clarify difference between [malaria] and other febrile illnesses? Explore overlap or difference between malaria and local categories of febrile illness.
5. What are the signs of [malaria]? Do people distinguish disease in terms of severity?
6. How do you treat [malaria]? When do you treat it?
Probe to check all treatments are mentioned, and that information is given on first line treatment (self-medication, drugs bought without seeking medical advice) as well as treatment if the person does not respond to first treatment.
Are different treatments followed depending on signs and symptoms?
Differences in treatment for adults and children?
Which treatment is most effective? Why
7. What causes [malaria]?
Check that there are no other causes. Check frequency, seasonality.
8. Can [malaria] be spread (transmitted)? How?
9. Can it be prevented? How?
Probe: Insecticides? Bednets? Coils? Reasons for use.
Who uses them in the household? Frequency? Effectiveness?
IF BEDNETS HAVE NOT BEEN MENTIONED, ASK
Do people use bednets here?
IF YES, probe: how many do you own? How many people share?
Why?
Probe: prevent mosquito bites, stop nuisance effect of other insects, prestige
IF NO, probe: are they available? If available and not used, why not?
10. Do you have/use a bednet?
Probe time of day - morning, afternoon, evening, night
Check for other household members - do all have nets? Sleeping patterns?
Advantages/disadvantages?
How acquired: Government? NGO? Sewn in the house? bought/ other?

* Note: We ask questions using the local terms where [malaria] is written.

FAMILY FEVER MONITORING CARD (Any episodes of fever to be recorded; kept with family; this card to be translated in Bangla; to be made like a small booklet with attractive cover with picture)

Head of Household:
MCV:

House No.:
CHW:

Village:

FOR OFFICE USE ONLY: RKB Transfer Complete RKB No.

Date of Fever Started (dd/mm/yy)	Name of Patient	Symptoms (Tick for all symptoms)	Action Taken (Tick for all actions)	Date of Action(s) (dd/mm/yy)
---/---/---		1. ☐ Fever 2. ☐ Headache 3. ☐ Backache 4. ☐ Generalized myalgia 5. ☐ Others (specify)	1. ☐ Nothing 2. ☐ Self-medication 3. ☐ Village doctor 4. ☐ Homeopathic Doctor 5. ☐ Public clinic (HFWC) 6. ☐ THC Hospital 7. ☐ Memorial Christian Hospital 8. ☐ Other hospital (specify)	2. ---/---/--- 3. ---/---/--- 4. ---/---/--- 5. ---/---/--- 6. ---/---/--- 7. ---/---/--- 8. ---/---/---
FOR OFFICE USE ONLY: ID No.: Age: years Sex: 1. Male 2. Female				

FOR OFFICE USE ONLY: RKB Transfer Complete RKB No.

Date of Fever Started (dd/mm/yy)	Name of Patient	Symptoms	Action Taken (Multiple actions can be ticked)	Date of Action(s) (dd/mm/yy)
---/---/---		1. ☐ Fever 2. ☐ Headache 3. ☐ Backache 4. ☐ Generalized myalgia 5. ☐ Others (specify)	1. ☐ Nothing 2. ☐ Self-medication 3. ☐ Village doctor 4. ☐ Homeopathic Doctor 5. ☐ Public clinic (HFWC) 6. ☐ THC Hospital 7. ☐ Memorial Christian Hospital 8. ☐ Other hospital (specify)	2. ---/---/--- 3. ---/---/--- 4. ---/---/--- 5. ---/---/--- 6. ---/---/--- 7. ---/---/--- 8. ---/---/---
FOR OFFICE USE ONLY: ID No.: Age: years Sex: 1. Male 2. Female				

RECORD KEEPING BOOK (RKB) (This is the page design of the RKB; kept with CHWs; records to be updated by fortnightly home visits; to be made like a registration notebook for each CHW catchment area)

CHW catchment area)

Head of Household:

House No.:

Village:

MCV:

CHW:

Date of Recording (dd/mm/yy):

Date of Fever Started (dd/mm/yy)	Name of Patient	Symptoms	Action Taken (Multiple actions can be ticked)	Date of Action(s) (dd/mm/yy)
...../...../.....		1. ☐ Fever 2. ☐ Headache 3. ☐ Backache 4. ☐ Generalized myalgia 5. ☐ Others (specify)	1. ☐ Nothing 2. ☐ Self-medication 3. ☐ Village doctor 4. ☐ Homeopathic Doctor 5. ☐ Public clinic (HFWC) 6. ☐ THC Hospital 7. ☐ Memorial Christian Hospital 8. ☐ Other hospital (specify)	2.-/-/- 3.-/-/- 4.-/-/- 5.-/-/- 6.-/-/- 7.-/-/- 8.-/-/-
Date of Fever Ended (dd/mm/yy)	ID No.: Age: years Sex: 1. Male 2. Female			
...../...../.....*	*Community Dipstick Post Result: 1. Yes 2. No			
Patient died on/...../..... at: 1. Home 2. Hospital	Treatment Compliance Sheet returned? 1. Yes 2. No			

* If fever continuing, fill the date later.

Date of Medical consultation	Diagnosis	Treatment	Date of Treatment Started	Duration of Treatment	Costs
2.-/-/- 3.-/-/- 4.-/-/- 5.-/-/- 6.-/-/- 7.-/-/- 8.-/-/-	1. ☐ Clinical only 2. ☐ Blood Film taken by village doctor 3. ☐ Blood film taken at hospital 4. ☐ Blood film taken at commercial pathology lab 5. ☐ Community Dipstick Post* 6. ☐ Other (specify)	1. ☐ CQ 2. ☐ CQ+primaquine 3. ☐ SP 4. ☐ Q7 5. ☐ Q3+SP 6. ☐ Artemisinin 7. ☐ Other (specify)	1./...../..... 2./...../..... 3./...../..... 4./...../..... 5./...../..... 6./...../..... 7./...../.....	1.days 2.days 3.days 4.days 5.days 6.days 7.days	Consultation: Tk Diagnosis(blood film): Tk..... Drugs: Tk..... Transportation: Tk..... Wage lost: Tk ... x ...days School days lost:days Any other cost incurred (explain):Tk.....

IF PATIENT ADMITTED TO THE HOSPITAL, CONFIRM THE FOLLOWINGS:

Which hospital?	Costs
1. THC Hospital 2. Memorial Christian Hospital 3. Other (specify)	Hospitalization (bed and food): Tk; Drugs: Tk; Transportation: Tk; Wage lost Tk; School days lostdays; Any other cost incurred during the hospitalization (specify):..... Tk

TREATMENT COMPLIANCE SHEET

(This sheet should be given for all dipstick positive patients; and to be returned by themselves or collected by MCVs at home; this sheet will be translated into Bangla.)

Instruction to MCVs: Please fill out Part A and then write the exact dates for each dose with number of tablets in Part B before you deliver to the patient. Number of tablets will follow according to the national guideline for children and adults. Please explain how the patient should follow this regimen (i.e., when and how many of which tablets should be taken). Quinine (Q) will be taken every after meal (every 8 hours) for consecutive 3 days and followed by SP one dose. Please assist the patients whenever necessary during the course.

Part A:

Name of Patient: Age: Sex: IDNo:
 Sheet Delivered (dd/mm/yy):/...../..... Delivered by (MCV Name):
 Sheet Returned (dd/mm/yy):/...../.....
 Returned by: 1. Patient/family member 2. MCV: Name: 3. Other (specify):
 Date of Treatment Crosschecked with his/her "Family Fever Monitoring Card"? 1. Yes 2. No
 IF NO, Reason for "No":
 Action for re-checking: 1. Yes 2. No
 Final Crosscheck: 1. Yes (Date:...../...../.....) 2. No

Part B:

	Treatment Date	Number of Tablet(s)	Time of the Day		
			Morning	Lunch	Evening
Q3 First Dose on	/...../.....		☐ **	☐	☐
Q3 Second Dose on	/...../.....		☐	☐	☐
Q3 Third Dose on	/...../.....		☐	☐	☐
SP Treatment on	/...../.....		☐		

** The patient or his/her family member will tick in ☐ when tablet(s) specified are taken. Quinine tablets should be taken every after meal in the morning, lunchtime and evening.

Check List

After completing the protocol, please check that the following selected items have been included.

- | | |
|--|-------------------------------------|
| 1. Face Sheet Included _____ | ☒ |
| 2. Approval of the Division Director on Face Sheet _____ | ☒ |
| 3. Certification and Signature of PI on Face Sheet, #9 and #10 | ☒ |
| 4. Table on Contents _____ | ☒ |
| 5. Project Summary _____ | ☒ |
| 6. Literature Cited _____ | ☒ |
| 7. Biography of Investigators _____ | ☒ |
| 8. Ethical Assurance _____ | ☒ |
| 9. Consent Forms _____ | ☒ |
| 10. Detailed Budget _____ | ☒ |