Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Christina M. Riley Date

Assessment of Knowledge and Adherence to the National Guidelines for Malaria Case Management in Pregnancy among Healthcare Providers and Drug Outlet Dispensers in rural, western Kenya

By

Christina M. Riley
Master of Public Health

Global Epidemiology

_____

Aryeh D. Stein, PhD
Faculty Thesis Advisor

_____

Julie R. Gutman
Thesis Field Advisor

Assessment of Knowledge and Adherence to the National Guidelines for Malaria Case Management in Pregnancy among Healthcare Providers and Drug Outlet Dispensers in rural, western Kenya

By

Christina M. Riley

B.S., Villanova University, 2011

Thesis Committee Chair: Aryeh D. Stein, PhD

Field Chair: Julie R. Gutman, MD, MSc

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Epidemiology
2014

Abstract

Assessment of Knowledge and Adherence to the National Guidelines for Malaria Case Management in Pregnancy among Healthcare Providers and Drug Outlet Dispensers in rural, western Kenya

By Christina M. Riley

Although prompt and effective treatment is a cornerstone of malaria control, information on healthcare provider adherence to malaria treatment guidelines in pregnancy is lacking. Incorrect or sub-optimal treatment can cause adverse consequences to the mother and fetus.

We conducted a cross-sectional study from September to November 2013, in all health facilities and randomly selected drug outlets in the Siaya County HDSS catchment area in western Kenya, to assess provider adherence to and knowledge of case management for uncomplicated malaria in pregnancy, including diagnosis, pregnancy assessment, and treatment. In health facilities, we used exit interviews of women of childbearing age, including pregnant women, who had been assessed for fever. Simulated clients posing as 1st trimester pregnant women or as relatives of women in 3rd trimester collected information from drug outlets. Information on treatment was recorded from prescriptions or after reviewing medications in patient's possession. Standardized questionnaires were used to assess provider knowledge of treatment guidelines.

Correct provider case management for malaria in pregnancy was observed in 32% of health facility cases and 3% of drug outlets; provider knowledge was 45% and 0%, respectively. Prescription of the correct drug for pregnancy trimester at the correct dosage was observed in 62% of cases in health facilities and 42% in drug outlets. Prescribing of correct drug and dosage was observed less often in 1st trimester than in 2nd/3rd (27% vs. 0%, $p<0.01$, and 65% vs. 32%, $p<0.01$, at health facilities and drug outlets, respectively). Sulfadoxine-pyrimethamine, which is not recommended for treatment of acute malaria, was prescribed in 3% of cases in health facilities and 18% of simulations in drug outlets ($p<0.01$). Exposure to artemether-lumefantrine in 1st trimester, which is contraindicated due to its unknown safety, occurred in 27% and 49% of cases in health facilities and drug outlets, respectively ($p=0.04$); none were a result of quinine stock-out.

This study highlights knowledge inadequacies and incorrect prescribing practices in the treatment of malaria in pregnancy. These should be addressed through comprehensive trainings and adequate supervision by the Kenya Ministry of Health to improve the quality of patient care and maximize therapeutic outcomes.

Assessment of Knowledge and Adherence to the National Guidelines for Malaria Case Management in Pregnancy among Healthcare Providers and Drug Outlet Dispensers in rural, western Kenya

By

Christina M. Riley

B.S., Villanova University, 2011

Thesis Committee Chair: Aryeh D. Stein, PhD

Field Chair: Julie R. Gutman, MD, MSc

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Epidemiology
2014

Acknowledgements

The paper presented in this thesis is the result of collaborative efforts from people across multiple institutions and countries. I would like to extend my deepest gratitude and appreciation for all researchers, staff, and friends involved in some part of this two-year long process; the success of the study and the multiple manuscripts being submitted for publication is a testament their dedication and support.

I am incredibly grateful to Julie Gutman and Stephanie Dellicour who were willing to take a chance on me in offering me the opportunity and responsibility of such an integral role in the study- possibly due to pregnancy hormones. I'd like to deeply thank each of them for their extraordinary support and expert input throughout the preparation, fieldwork, and analysis and manuscript processes; the success of the study and this thesis would not have possible without them. I'd also like to thank them for their patience and professional advice; they have been and continue to be integral in my development as a researcher and public health professional.

Many thanks to my supervisors/coauthors Meghna Desai, Peter Ouma, Simon Kariuki and Ann Buff and additional coauthors for their technical and professional support throughout the process as well as others at KEMRI-CDC and Malaria Branch of CDC, Atlanta. Thanks to Jodi Van den Eng, Ryan Weigand, and John Williamson for their statistical genius for the original study analysis and intervention study design. The design of the interventional cluster randomized trial protocol was developed in conjunction with many of the coauthors of the MiP case management manuscript. Special thanks to Ian Hennessee, Lane Ringer (Emory University – RSPH) and Nicole Yan (LSTM) for their critical thinking and troubleshooting of the design, as well as Julie Gutman and Feiko ter Kuile for their expert input. Thank you to Aryeh Stein for his trust and confidence in my thesis-producing abilities.

I'd like to especially thank the members of my fieldwork research team for their fierce dedication, spirit, and friendship. Their enthusiasm and commitment was reflected in the quality and completeness of data collection; and their compassion and humor continues to be reflected in our friendship. I'd also like thank all of my friends in the Kisumu community, which I was very happy to call home for a time, for their support, friendship, and good times. Thanks to my family and friends for all of their love, support, and encouragement.

Table of Contents

CHAPTER I

LITERATURE REVIEW

It is estimated that around 125 million pregnancies occur in areas at risk of *P. falciparum* and/or *P. vivax* infections every year; an estimated 1.3 million of these are in Kenya [1]. Malaria in pregnancy (MiP) can have devastating consequences for the woman and her unborn baby. Adverse effects of MiP include maternal anemia, fetal loss, intrauterine growth retardation, premature delivery and low birth weight (LBW); LBW associated with MiP results in an estimated 100,000 deaths each year in Africa alone [2]. In 2007, Kenya's population included about 9.1 million were women of childbearing age (WOCBA); of these women, 1.3 million were estimated to become pregnant in areas where malaria is endemic and were thus exposed to the risk of malaria [1]. In order to prevent the adverse consequences associated with MiP, the World Health Organization (WHO) and the Kenyan Ministry of Health (MoH) recommend that pregnant women in sub-Saharan Africa use long-lasting insecticidal nets (LLINs), intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP), and receive prompt and effective diagnosis and treatment of malaria infections with a safe drug.

In Kenya, following WHO recommendations, artemether-lumefantrine (AL) is the 1st-line treatment for uncomplicated *P. falciparum* malaria in the general population and women in 2nd/3rd trimester of pregnancy; due to insufficient safety data [3-5], this is not recommended in 1st trimester, and oral quinine is used instead [6,7]. In practice, this means that all women of child-bearing age (WOCBA) must be assessed for pregnancy inclusive of the trimester of pregnancy. In addition, Kenyan MoH guidelines, updated in 2010, stipulate that artemesinin combination therapies (ACTs) should only be provided for malaria cases confirmed by parasitological diagnostic test. Antimalarial treatment on the basis of clinical suspicion of malaria should only be considered in situations where a parasitological diagnosis is not accessible, particularly in vulnerable populations such as pregnant women and children [6].

There is limited data on health provider adherence to diagnostic and treatment guidelines for MiP. A review of studies of antimalarial use in the general population found that only 51% of cases were

treated with recommended antimalarials during 2004-2006 [8]. A 2008 study in Kenyan health facilities reported limited health worker compliance with the recommended treatment guidelines in patients over five years of age [9]. Although 99% of patients with a positive test received an antimalarial, only 80% received AL, the recommended first line therapy, despite the fact that the study was restricted to health facilities, which had both malaria diagnostics and AL available on the survey day. A more recent 2010 study in Kenya found improved adherence, with 90% of test-positive patients receiving the recommended first-line therapy [10]. Very few studies have looked at adherence to treatment guidelines in pregnancy. A recent systematic review and meta-analysis of MiP case management reported that only 28% and 72% of healthcare providers followed the treatment guidelines for malaria during the 1st and 2nd /3rd trimesters across 12 studies, respectively [11]. Inadvertent exposure to ACTs in first trimester and the continued use of ineffective drugs, such as SP, for treatment has been observed in a number of countries; very few providers know that ACTs are potentially teratogenic [11-16]. In Uganda, 70% of women in 1st trimester received a contraindicated antimalarial and less than 6% of 1st trimester women received quinine [16]. In Tanzania, 43% of drug dispensers in registered pharmacies offered AL regardless of the pregnant client's gestation; only 20% knew that AL was contraindicated in 1st trimester [13].

Several studies have found that less than half of those who seek care for malaria do so in the formal health system [17] (& Ndyiomugyenyi). Although data from the Kenya Demographic and Health Survey (KDHS) show that overall antenatal care (ANC) coverage remains high, many women make their first ANC visit late in pregnancy [18], indicating that early pregnancies at risk for ACT exposure may not receive a pregnancy assessment within the formal healthcare setting or may be seeking care for malaria outside of the formal health care setting and also unlikely to receive assessment.

Understanding provider prescribing behaviour in pregnant patients can play a key role in improving the prescribing, administration, and use of antimalarials while minimizing potential harmful

exposures. Given that WOCBA represent about 25% of the total population, up to 14% of whom could be pregnant at any time and one-third of them in the 1st trimester, it is crucial that providers recognize regimens that have the potential for teratogenicity and assess WOCBA for pregnancy status and gestational age. This cross-sectional study assessed healthcare provider and drug dispenser prescribing behaviors and knowledge of malaria treatment guidelines for pregnant clients in a malaria endemic region of western Kenya.

CHAPTER II

Assessment of Knowledge and Adherence to the National Guidelines for Malaria Case Management in Pregnancy among Healthcare Providers and Drug Outlet Dispensers in rural, western Kenya

Assessment of Knowledge and Adherence to the National Guidelines for Malaria Case Management in Pregnancy among Healthcare Providers and Drug Outlet Dispensers in rural, western Kenya

Christina Riley[1], Stephanie Dellicour[2], Peter Ouma[3], Urbanus Kioko[4], Feiko O. ter Kuile[2], Ahmeddin Omar[4], Simon Kariuki[3], Ann M. Buff[5,6], Meghna Desai[5], Julie Gutman[5]

1. Rollins School of Public Health, Emory University, Atlanta, USA
2. Liverpool School of Tropical Medicine, Liverpool, United Kingdom
3. KEMRI, Centre for Global Health Research, Kisumu, Kenya
4. Malaria Control Unit, Ministry of Health, Nairobi, Kenya
5. Malaria Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, US Centers for Disease Control and Prevention, Atlanta, USA and Kenya
6. US President's Malaria Initiative, Nairobi, Kenya

ABSTRACT

Although prompt and effective treatment is a cornerstone of malaria control, information on healthcare provider adherence to malaria treatment guidelines in pregnancy is lacking. Incorrect or sub-optimal treatment can cause adverse consequences to the mother and fetus.

We conducted a cross-sectional study from September to November 2013, in all health facilities and randomly selected drug outlets in the Siaya County HDSS catchment area in western Kenya, to assess provider adherence to and knowledge of case management for uncomplicated malaria in pregnancy, including diagnosis, pregnancy assessment, and treatment. In health facilities, we used exit interviews of women of childbearing age, including pregnant women, who had been assessed for fever. Simulated clients posing as 1st trimester pregnant women or as relatives of women in 3rd trimester collected information from drug outlets. Information on treatment was recorded from

prescriptions or after reviewing medications in patient's possession. Standardized questionnaires were used to assess provider knowledge of treatment guidelines.

Correct provider case management for malaria in pregnancy was observed in 32% of health facility cases and 3% of drug outlets; correct knowledge of case management was 45% and 0%, respectively. Prescription of the correct drug for pregnancy trimester at the correct dosage was observed in 62% of cases in health facilities and 42% in drug outlets. Prescribing of correct drug and dosage was observed less often in 1st trimester than in 2nd/3rd (27% vs. 0%, $p<0.01$, and 65% vs. 32%, $p<0.01$, at health facilities and drug outlets, respectively). Sulfadoxine-pyrimethamine, which is not recommended for treatment of acute malaria, was prescribed in 3% of cases in health facilities and 18% of simulations in drug outlets ($p<0.01$). Exposure to artemether-lumefantrine in 1st trimester, which is contraindicated due to its unknown safety, occurred in 27% and 49% of cases in health facilities and drug outlets, respectively ($p=0.04$); none were a result of quinine stock-out.

This study highlights knowledge inadequacies and incorrect prescribing practices in the treatment of malaria in pregnancy. These should be addressed through comprehensive trainings and adequate supervision by the Kenya Ministry of Health to improve the quality of patient care and maximize therapeutic outcomes.

INTRODUCTION

It is estimated that around 125 million pregnancies occur in areas at risk of *P. falciparum* and/or *P. vivax* infections every year; an estimated 1.3 million of these are in Kenya [1]. Malaria in pregnancy (MiP) can have devastating consequences for the woman and her unborn baby. Adverse effects of MiP include maternal anemia, fetal loss, intrauterine growth retardation, premature delivery and low birth weight (LBW); LBW associated with MiP results in an estimated 100,000 deaths each year in Africa alone [2]. In order to prevent the adverse consequences associated with MiP, the World Health Organization (WHO) and the Kenyan Ministry of Health (MoH) recommend that pregnant women in sub-Saharan Africa use long-lasting insecticidal nets (LLINs), intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP), and receive prompt and effective diagnosis and treatment of malaria infections with a safe drug.

In Kenya, following WHO recommendations, artemether-lumefantrine (AL) is the 1st-line treatment for uncomplicated *P. falciparum* malaria in the general population and women in 2nd/3rd trimester of pregnancy; due to insufficient safety data [3-5], this is not recommended in 1st trimester, and oral quinine is used instead [6,7]. In practice, this means that all women of child-bearing age (WOCBA) must be assessed for pregnancy inclusive of the trimester of pregnancy. In addition, Kenyan MoH guidelines, updated in 2010, stipulate that artemesinin combination therapies (ACTs) should only be provided for malaria cases confirmed by parasitological diagnostic test. Antimalarial treatment on the basis of clinical suspicion of malaria should only be considered in situations where a parasitological diagnosis is not accessible, particularly in vulnerable populations such as pregnant women and children [6].

There is limited data on health provider adherence to diagnostic and treatment guidelines for MiP. A review of studies of antimalarial use in the general population found that only 51% of cases were treated with recommended antimalarials during 2004-2006 [8]. A 2008 study in Kenyan health facilities reported limited health worker compliance with the recommended treatment guidelines in

patients over five years of age [9]. Although 99% of patients with a positive test received an antimalarial, only 80% received AL, the recommended first line therapy, despite the fact that the study was restricted to health facilities, which had both malaria diagnostics and AL available on the survey day. A more recent 2010 study in Kenya found improved adherence, with 90% of test-positive patients receiving the recommended first-line therapy [10]. Few studies have looked at adherence to treatment guidelines in pregnancy. A recent systematic review and meta-analysis of MiP case management reported that only 28% and 72% of healthcare providers followed the treatment guidelines for malaria during the 1st and 2nd /3rd trimesters across 12 studies, respectively [11]. Inadvertent exposure to ACTs in first trimester and the continued use of ineffective drugs, such as SP, for treatment has been observed in a number of countries; very few providers know that ACTs are potentially teratogenic [11-16]. In Uganda, 70% of women in 1st trimester received a contraindicated antimalarial and less than 6% of 1st trimester women received quinine [16]. In Tanzania, 43% of drug dispensers in registered pharmacies offered AL regardless of the pregnant client's gestation; only 20% knew that AL was contraindicated in 1st trimester [13].

Understanding provider prescribing behaviour in pregnant patients can play a key role in optimizing case management and minimizing potential harmful exposures. Given that WOCBA represent about 25% of the total population, up to 14% of whom could be pregnant at any time, with one-third of them in the 1st trimester, it is crucial that providers recognize potentially teratogenic regimens and assess WOCBA for pregnancy status and gestational age. This cross-sectional study assessed healthcare provider and drug dispenser prescribing behaviors and knowledge of malaria treatment guidelines for pregnant clients in a malaria endemic region of western Kenya.

METHODS

Prescribing practice was observed by a) use of simulated client approach within randomly sampled drug outlets, b) exit interviews with WOCBA (18-49 years) and pregnant clients being treated for febrile illness at all health facilities (HF) within the study area, and c) provider surveys using structured questionnaires conducted for healthcare providers and drug dispensers to assess knowledge of malaria treatment guidelines and self-reported prescribing behavior for case management of MiP. The latter surveys were administered following completion of the provider practice component so as to avoid any influence in provider behavior.

Study Site & Sampling

This study was carried out from September to November 2013, in Bondo, Gem, Rarieda, and Siaya districts/sub-counties, including the Kenya Medical Research Institute (KEMRI) and U.S. Centers for Disease Control and Prevention (CDC) Public Health Collaboration's Health and Demographic Surveillance System (HDSS) catchment area in Siaya County, Nyanza Province in western Kenya. The HDSS collects birth, death, and migration information quarterly from a large, rural area of approximately 700 km^2 with 220,000 inhabitants [19]. Malaria transmission is perennial and holo-endemic with peaks following the two rainy seasons, from March through May and October through December. In the study area, approximately 20% of pregnant women coming for the first antenatal clinic visit are parasitemic, 70% are anemic [20], and 18% of women delivering in Siaya District Hospital had placental malaria [21].

Health Facility Selection

All facilities in the HDSS study area and within a 5 km buffer zone were eligible if they were operational, stocked antimalarials, and were visited by WOCBA for treatment of potential febrile illness. After excluding 9 facilities due to ongoing studies that could have influenced study results,

52 health facilities, including hospitals, health centers, and dispensaries, were eligible for the study; 50 consented to participate.

Drug Outlets Selection

Prior to the start of data collection, a census was conducted of all registered and unregistered entities selling antimalarial drugs within the HDSS border (Kioko et al., unpublished). Of the 181 DOs identified, excluding 27 homesteads, 152 consented to participate in this study, and 39 were randomly selected. This sample size allowed estimation of the proportion of providers with adequate knowledge with 14% precision at 80% power, assuming that 45% of providers have adequate knowledge and prescribing practice [13].

Data Collection

Training

Fieldworkers underwent two weeks of training, including interviewing techniques, data recording, and piloting survey tools. Four fieldworkers (two women and two men) were trained on the methodology behind the simulated client approach and piloted the standardized, pre-determined scenarios for an additional week in outlets outside the study area prior to implementation.

Exit Interviews in Health Facilities

Patients were approached for eligibility assessment after completing a provider consultation in either outpatient department (OPD) or antenatal care clinic (ANC) and receiving all prescribed medications. Eligible patients included any WOCBA, either pregnant or non-pregnant, that presented with febrile illness and consented to participate in the study. Fieldworkers tried to interview at least one of each of the following categories of patients per facility: 1) WOCBA who could potentially be pregnant, 2) women in early pregnancy (1st trimester, defined as up to 14 weeks inclusive), and 3) women in late pregnancy (2nd/3rd trimester, defined as 15 weeks gestation or

greater). Pregnancy status was based on patient report; gestational age and trimester were later confirmed by calculation from patient reported date of last menstrual period (LMP).

After obtaining informed consent, exit interviews were conducted following a standard format. In cases where an antimalarial contraindicated for pregnancy had been prescribed, the patient was informed of the national treatment guidelines for MiP. The field supervisor (a Kenyan clinician) and study coordinator were immediately informed and the recommended treatment was given to the patient with appropriate dosage instructions and information.

Simulated Clients in Drug Outlets

The simulated client (also known as mystery clients or shoppers [22,23]) approach was used to assess prescribing practice within drug outlets. Female fieldworkers presented themselves as either WOCBA or in early pregnancy, and male fieldworkers presented as the husband of a WOCBA or woman in third trimester of pregnancy. All simulated clients initially complained of general malaise, and, if prompted, complained of fever, headache, chills, joint or muscle pain, and nausea. The simulated clients were trained not to disclose pregnancy status unless it was asked about by the dispenser. If dispensers failed to assess pregnancy status, following receipt of a prescription the simulated clients would then disclose pregnancy status (either first or third trimester, using local language to convey early or late pregnancy depending on the pre-set scenario) and note any changes in the prescribed treatment or advice given. Simulated clients were able to purchase medications up to an allotted 250 KSh (3.00 USD), but were instructed not to take pregnancy or malaria diagnostic tests or treatment, if offered. The study coordinator and/or field supervisor were in the vicinity at the time of simulation in case the simulated client was uncovered, though this never occurred. Immediately following completion of the scenario, the checklist for simulated client interaction was completed under guidance of the study coordinator and/or field supervisor.

Provider Surveys in Health Facilities & Drug Outlets

Following the completion of exit interviews/client simulations at each facility or outlet, a separate fieldworker administered a structured questionnaire to the provider to assess knowledge and self-reported prescribing practice, including: training, knowledge of symptoms, diagnosis, availability of the most recent treatment guidelines, and treatment/preventive regimens for a variety of different scenarios including pregnant women and the general population.

Data Management & Analysis

Information for the drug outlet census and mapping and the provider survey components was collected via personal digital assistant (PDA), and data for the simulated client and exit interview components was collected via scannable form.

All datasets were cleaned and analyzed using SAS 9.3 (SAS Institute, Cary, NC, USA). Descriptive statistics were performed on all data to identify the extent of adherence to and knowledge of Kenyan National Treatment Guidelines as they pertain to MiP across the provider study population. Exit interview and simulated client data were analyzed to describe provider prescribing and dispensing behavior in reference to pregnancy status, malaria diagnosis prior to treatment, correct treatment and dosage, and provision of appropriate information as pertaining to treatment advice. Provider survey data was also analyzed across these categories pertaining to the malaria treatment guidelines. Variables within these categories were coded to give a threshold for dichotomous correct/incorrect practice or knowledge for each category.

Correct practice and adequate knowledge definitions (Table 1) were based on the 2010 Kenyan National Malaria Treatment Guidelines (MTGs) [7]; where these were insufficient, the 2010 WHO Malaria Treatment Guidelines [6] were used. For exit interviews and client simulations, treatment was considered correct if either first- or second-line treatment was prescribed.

Chi square test or Fisher exact test were used to assess statistical significance ($p \leq 0.05$) of comparisons between categorical variables; $p \leq 0.05$ indicates statistical significance. The total proportion of providers (clustering on facility) who met adequate pregnancy assessment standards, adequate malaria diagnostic standards, and correctly prescribed drug and dosage was calculated; these measures were used to define overall correct prescribing practice. Significant provider characteristic predictors ($p<0.1$) of correct case management practice and adequate knowledge were controlled for in the multivariate models. Correlations between MiP case management practice and knowledge scores were run to assess provider knowledge level as a predictor of practice. Principal component analysis was used to validate case management practice and knowledge scores.

Ethics

This study was approved by the ethical and institutional review boards of the U.S. Centers for Disease Control and Prevention (CDC), the Kenya Medical Research Institute (KEMRI), Liverpool School of Tropical Medicine (LSTM), and Emory University prior to the start of study. In addition, permission to operate within the study area was obtained via meetings with the Siaya County Director of Health and the District Health Management Teams. Verbal consent was obtained from health facility in-charges prior to any interview activities at the respective facility; informed consent regarding future potential participation in a study for MiP treatment assessment was obtained from the dispenser during the drug-outlet mapping and census. Written, informed consent was obtained from all providers and patients interviewed during the study period in the participants' preferred language of Dholuo, Kiswahili, or English. Study participants were free to withdraw from the study at any time.

RESULTS

Prescribing Practice and Dispensing Behaviours: Exit Interviews in Health Facilities

A total of 210 patients were interviewed across 51 health facilities (HFs): 108 non-pregnant women, 19 women in 1st trimester of pregnancy, 77 women in second or third trimester of pregnancy, and 6 women who were unsure of their pregnancy status; one interview with a woman in her second trimester of pregnancy with severe malaria was excluded from the analysis. The average age of the patients was 26 years; 26% of respondents had completed secondary school (Table 2).

Malaria Diagnosis in Health Facilities

Of the 209 women analyzed, 160 (77%) women were tested for malaria (RDT or microscopy). Of those women who were not tested, 28 women were appropriately clinically diagnosed in facilities that did not have the capacity to perform malaria diagnostics. Taking this into account, 90% were properly assessed for malaria according to the facility diagnostic capability (Table 3).

Pregnancy Assessment in Health Facilities

Overall, 92 (44%) of 209 patients were asked about their potential pregnancy status; inquiry was more common among pregnant patients than among non-pregnant patients (64% for pregnant versus 26% for non-pregnant, $p<0.01$) (Table 4). Only 43% of women were asked about their LMP; this occurred with much greater frequency in pregnant versus non-pregnant patients (63% v. 24%, $p<0.01$). Only 20 (10%) women were offered a pregnancy test; 80% of these women were pregnant (9 in the 1st, 5 in the 2nd and 2 in the 3rd trimester). Twenty-three women who reported to the fieldworker that they were not pregnant had a last menstrual period (LMP) of greater than six weeks, and thus should have been tested for pregnancy. Overall, 52% of patients were correctly assessed for pregnancy status (Table 4); however this was significantly higher in pregnant women versus self-reported non-pregnant women (83% vs. 24%, $p<0.01$).

Treatment Prescribed in Health Facilities

An antimalarial medication was prescribed to 205 (98%) of the 209 women; the most frequently prescribed was AL (82%), followed by quinine (14%), and sulfadoxine-pyrimethamine (SP) (3%). Overall, 62% of providers prescribed the correct treatment and dosage to the patient across all pregnancy scenarios (Table 5). AL was incorrectly prescribed in 1st trimester to 6/22 (27%) women. The majority of prescriptions for AL and SP were for the correct dosage (73% and 71%, respectively); in contrast, the correct dose of quinine was prescribed only 31% of the time. The correct drug and dosage was prescribed more frequently to non-pregnant patients (68%) and those in the 2nd/3rd trimester of pregnancy (63%) than to those in 1st trimester (27%, p=0.001). The first dose of antimalarial was directly observed in 25% of cases. Very few patients (7%) were informed of potential side effects.

Correct case management (diagnosis, treatment and pregnancy assessment) was observed in only 32% of patients, with no significant difference across outlet types (Table 6).

Predictors of Correct Practice in Health Facilities

Significant predictors of correct prescribing and diagnostic practice in HFs were respondent cadre and dispensing medication (Table 7). Pharmacists were more likely to correctly prescribe and diagnose patients then their clinical counterparts [RNs, COs, MDs] (OR=8.8 [95% CI 1.0-78.5]). Strictly among clinical providers, those that reported dispensing medicines were more adherent to correct practice than their counterparts who did not dispense medicines (OR=2.2 [95% CI 1.2-4.1]). Neither malaria diagnostic training nor MiP training within the last five years was statistically significant predictors of correct provider practice in HFs.

Prescribing Practice and Dispensing Behaviours: Simulated Clients in Drug Outlets

Simulations were completed at 41 drug outlets (DOs); two facilities were homesteads (individuals selling antimalarials from their residence) and were excluded from analysis. There were 77 simulated client-providerinteractions with 147 total scenarios simulated (Figure 1). DO providers were a mean of 32 years old, and 56% were female. The majority had completed only primary (19%) or secondary school (43%). Between 34 and 38 simulations per scenario were completed (Table 8).

Malaria Diagnosis in Drug Outlets

DO providers assessed for malaria in 34% of all interactions (Table 9). Providers had a higher proportion of diagnosis-associated practices when interacting with female clients that were seeking treatment for themselves versus male clients seeking treatment on behalf of their wife. 33% of providers asked about symptoms;less than half of these inquired about specific symptoms. RDTs were offered in 5% of interactions where the client was present. A prescription was requested by the provider in only 5% of interactions.

Pregnancy Assessment in Drug Outlets

There were only four unprompted pregnancy inquiries across 77 total interactions (5%); none were offered a pregnancy test. Gestation was inquired in two of four interactions. DO providers were informed of positive pregnancy status in 70 interactions where there was no initial inquiry on the part of the provider; in 57% of these interactions the provider followed up with gestational age or LMP inquiry. Inquiry about pregnancy timing (most often via gestational age [95%]) was highest in registered pharmacies (77%) and informal drug shops (73%), with general shops significantly lower (31%, $p<0.01$); this did not differ between interactions where the client was the patient versus the patient's relative (Table 10).

Treatment Dispensed in Drug Outlets

Antimalarials were dispensed in 83% of all interactions; AL was most commonly dispensed (76%), followed by SP (21%). Quinine was not dispensed in the DOs (Table 11). There were highly significant differences in correct treatment and dosage across pregnancy status, with 71% of non-pregnant, 54% of 3rd trimester, and 0% of 1st trimester client simulations receiving the appropriate treatment ($p<0.01$). DO providers were 7.6 times more likely to prescribe SP for treatment of acute malaria to pregnant versus non-pregnant women ($p<0.0001$). About half (51%) of the 39 1st trimester clients were prescribed AL; all but 1 of the remaining clients were prescribed SP. AL was initially prescribed to over 90% of simulated client patients; in 27% of cases treatment was changed from AL to SP after finding out the patient was pregnant, regardless of trimester, and in another 17% AL was withdrawn and the patient was referred to a health facility.

Of 27 clients not given an antimalarial, 17 (63%) were referred to the hospital, and 8 (30%) clients did not receive a medication due to antimalarial stock out. Other reasons for not receiving treatment included refusal to treat without a prescription, diagnostic test, or clinical evaluation. Prior to dispensing, only 16% of DO providers questioned the simulated client if any previous treatment had been given for the current illness and only 5% asked about potential allergies. Dosage directions were given to 87% of simulated clients.

Correct MiP case management practice was observed in only 3% of the 147 interactions in DOs, with no significant difference across outlet types (Table 12). It was not possible to accurately assess for DO provider predictors of correct MiP case management practice given the rare occurrence of this outcome.

Knowledge of the National Malaria Treatment Guidelines among Providers

Characteristics of Respondents

We surveyed 112 providers across 86 facilitiess; 75 in HFs and 39 in DOs. 44% of respondents were nursing staff, 16% were COs/MDs, 18% pharmacists, and 13% were shopkeepers. 69% of providers stated that they both prescribed and dispensed medication (Table 13a-b).

National Malaria Treatment Guidelines Awareness

75% of all providers said they were aware of the National Malaria Treatment Guidelines (MTGs); 67% had read the MTGs, 56% were in possession of them, and 58% were aware of the government initiative to disseminate them (Table 14). However, HF providers were much more likely to respond in the affirmative to all MTG-related questions compared to DO providers. Fifty-five percent of all providers had attended a malaria management workshop (93% within the past five years), however only 31% of all providers had attended a workshop specific to MiP. Over 89% of those that reported attending any workshop within the past five years were HF providers.

Malaria in Pregnancy Consequence and Diagnosis Knowledge

98% of all providers surveyed knew that MiP can cause adverse effects; 90% were able to cite at least one adverse effect. 90% of all providers suspected malaria in cases of fever; other clinical symptoms cited included headache (84%), vomiting (82%), body ache (67%), and chills (65%). HF providers had statistically significant greater knowledge of both MiP consequences and clinical symptoms versus DO providers. 84% of HF providers reported utilizing laboratory diagnosis (81% RDT, 70% microscopy); 25% of those that did not use lab diagnostics reported always treating clinically (versus regularly, sometimes, and never). In DOs where diagnostics are not widely available, 33% reported utilizing RDTs or microscopy while 33% reported that they always treat clinically. Fifty-nine percent of providers reported ‘always’ or ‘sometimes’ performing a

pregnancy assessment; 79% of which reported asking for LMP and 48% reported offering a pregnancy test.

Malaria Treatment & Treatment Contraindication Knowledge

Thirty-five (47%) HF providers knew the correct 1st-line treatment and dosage for all pregnancy scenarios compared to none of the 37 drug dispensers. Correct knowledge for 1st trimester patients was given by 56% of HF providers and none of drug dispensers ($p<0.01$). Correct treatment knowledge for 2nd/3rd trimester patients was reported in 85% of HF and 41% of drug outlets ($p<0.01$). Overall provider knowledge was considerably higher for 1st-line treatment versus 2nd-line treatment ($p<0.01$) (Table 15).

SP was incorrectly cited as the appropriate treatment in the following scenarios: a) 1st and 2nd line treatment for adults by 4% of providers, b) in 1st trimester pregnant patients by 19% of providers, c) in 2nd/3rd trimester by 7% of providers, and d) for treatment of severe malaria in pregnancy by 5% of providers. Two-thirds cited IPTp with SP as a preventive measure for MiP; however, only 54% knew that SP could only be used as preventive therapy and not as treatment. Additionally, 6% of all providers thought AL could be used as preventive therapy and another 14% were not able to cite a drug for preventive treatment. An ACT was incorrectly cited as the appropriate treatment in 1st trimester pregnancies by 5% of HF providers and 18% of drug outlet providers.

The majority of providers stated the reason behind their chosen antimalarial for 1st and 2nd-line treatment was either due to the observed effectiveness of the drug in their practice (45% and 36%, respectively) or due to national guidelines (35% and 30%, respectively). However, of the providers that cited the national guidelines as the reason, 83% and 74% had chosen an antimalarial not recommended by the national MTGs for 1st-line and 2nd-line, respectively. 71% of HF providers and 28% of drug outlet dispensers cited 1st trimester as a contraindication for AL treatment

($p<0.0001$). 37% of HF providers cited 'allergy' as a contraindication for both 1st and 2nd line treatments versus 13% ($p<0.01$) and 3% ($p<0.01$) of drug outlet providers, respectively.

Correct treatment knowledge for severe malaria in pregnancy was given by 84% of HF providers and 23% of drug outlet providers ($p<0.0001$). Overall adequate knowledge of MiP (inclusive of diagnostics, pregnancy assessment, and treatment knowledge) was reported by 34 providers (30%), all of which were HF based.

Malaria in Pregnancy Comprehensive Care Knowledge

85% of HF providers reported giving any type of comprehensive care practices to pregnant patients with malaria versus 22% of drug outlet providers ($p<0.01$). Fetal monitoring (60% HF, 14% drug outlet) and anemia treatment (61% HF, 11% drug outlet) were the most commonly cited practices, followed by hypoglycaemia prevention (43% HF, 0% drug outlet) and guidance on antipyretic usage (32% HF, 3% drug outlet). 87% of all providers reported that they give pregnant patients instructions on treatment; 57% reported informing a pregnant patient of potential side effects, 52% reported telling the patient to return if symptoms continued, and 7% reported informing the patient of danger signs to look out for. A greater proportion of HF providers than drug outlet-based providers reported giving such information to a pregnant patient ($p<0.001$), with the exception of danger signs (Table 16).

Knowledge Predictors of Case Management for Malaria in Pregnancy

Univariate provider characteristic predictors of adequate knowledge of MiP case management included facility type, malaria diagnostic training and continuing medical education (CME) as a source of information (Table 17). Correct knowledge of treatment and dosage in 1st trimester patients was removed from the adequate knowledge definition for logistic regression with DO providers because none of those interviewed were able to provide the correct response. In the fully adjusted provider characteristic model, HF providers were more likely to possess adequate

knowledge than their DO counterparts (OR=2.8 95% CI [0.9-8.4]). Provider that had attended trainings on malaria management were more likely to possess adequate knowledge than those who had not (OR=3.6 95% CI [1.3-9.7]).

Providers that were able to identify the 1st trimester as a contraindication for ACT-treatment, advised the women to return to the facility if there was no improvement, advised on ITN-usage, or knew that SP was only prescribed for preventive purposes (versus treatment) were also more likely to possess correct MiP case management knowledge (Table 18).

Correlations between Provider Practice Scores and Provider Knowledge Scores for MiP Case Management

There was a medium degree of overall correlation between provider case-management practice scores and knowledge scores ($r=0.49$, $p<0.01$). When stratified for pregnancy status, the correlation between provider practice and knowledge in pregnant patients was much stronger than in non-pregnant patients (1st trimester [$r=0.66$, $p<0.01$], 2nd/3rd trimester [$r=0.54$, $p<0.01$], versus non-pregnant patients [$r=0.24$, $p<0.01$]). The level of correlation weakened between practice and knowledge when MiP case-management scores were broken down into malaria diagnostics, pregnancy assessment, and treatment & dosage scores, regardless of stratification (Table 19).

DISCUSSION

This study found that correct provider MiP case management for uncomplicated malaria in Siaya County is low overall, particularly in the 1st trimester. Providers consistently failed to assess for pregnancy, despite knowing that this was necessary; practice was considerably worse in DOs than HFs. Although women in 2nd/ 3rd trimester generally received appropriate therapy, less than one third of women in 1st trimester were treated appropriately. Of particular concern, incorrect prescribing practice included provision AL in early pregnancy, suboptimal dosing of quinine, and

use of SP for treatment. Consistent with what was observed in practice, knowledge of treatment guidelines was also unacceptably low. These observations highlight the urgent need to monitor and ensure delivery of quality MIP case management.

Pregnancy assessment was very poor. Although 79% of providers reported assessing for pregnancy, less than half of the women in HFs and none of the female simulated clients in DOs were assessed for pregnancy, indicating that providers know they should assess WOCBA for pregnancy but consistently fail to do so. It is notable that while HF providers assessed for gestational age of pregnancy, DO providers almost never did so, even when made aware that the woman was pregnant. The failure of providers to assess for pregnancy in a large proportion of women is problematic and may result in inadvertent exposure to potential teratogens, such as ACTs, in early pregnancy. This additionally represents a missed opportunity to refer women for early antenatal care in an area where most women initiate ANC late in pregnancy [24].

Women in the 1st trimester were significantly less likely to receive the correct treatment than women in later pregnancy or non-pregnant women. Overall, contraindicated regimens were prescribed in 65% of 1st trimester, consistent with previous observations in this area (Dellicour personal communication) and Uganda [16]. This likely reflects a lack of knowledge by healthcare providers regarding potential teratogenicity as evidenced by the fact that only 56% of providers reported that ACTs were contraindicated in the 1st trimester. Among providers that were aware of ACT contraindication in 1st trimester a number incorrectly cited SP as the correct treatment. There was a tendency among DO providers to withdraw AL and refer the woman to a health facility upon learning of pregnancy status. While this may reflect an inadequate knowledge of how to treat pregnant women, and delays receipt of appropriate therapy, referral is preferable to giving an incorrect drug, and allows for a complete assessment of the pregnant woman. Clear guidelines are needed for correct MiP case management in DOs.

Quinine, the recommended treatment for 1st trimester, was almost never offered, and when it was, dosage was generally incorrect. Quinine was not offered to any of the simulated clients in DOs. At HFs, only 31% of women in 1st trimester were offered quinine, and over 70% of those that were prescribed quinine were given an insufficient supply or incorrect instructions. In contrast, only 25% of women given AL received an incorrect dose. These errors resulted in quinine prescriptions ranging from 10-70% of the full dose, increasing the risks of treatment failure and the development of drug resistance [25,26]. This is particularly troubling given that quinine is currently the only safe and effective treatment available to women in early pregnancy. Poor knowledge of correct quinine dosage versus that of other commonly prescribed antimalarials such as AL was likewise observed in the provider survey. In DOs, not a single provider cited quinine as the correct drug of choice, consistent with the observed practices. SP was given preferentially to pregnant women in both HFs and DOs. Nearly 30% of DO providers who initially prescribed AL changed the prescription to SP upon learning that a client was pregnant; almost 90% of SP prescription in HFs was for treatment of pregnant clients. This practice highlights a worrying gap in knowledge- 49% of DO providers and 33% of HF providers incorrectly reported that SP could be used for both treatment and preventive purposes, and the fact that providers switched therapy from AL to SP indicates that not only did they incorrectly believe that SP can be used as treatment, but that they felt it was a better treatment option for pregnant women. This is alarming given that Kenya changed its recommendation for first-line treatment for uncomplicated malaria from SP to ACTs in 2004, and by 2006, the new ACT guidelines were implemented countrywide [3,9]. Using SP as treatment is associated with a high risk of treatment failure, given the high level of SP resistance in this area, which could have serious health consequences for both the mother and fetus [27,28].

Although almost all HF providers reported a high rate of awareness of the national MTGs versus only slightly more than a quarter of drug outlet dispensers, provider knowledge in both settings was poor and were reflective of the low levels of correct case management observed in practice. The

greatest knowledge deficiencies were observed in pregnancy assessment, and correct treatment and drug regimen. Although a number of providers were aware of contraindications in 1st trimester, knowledge of the correct treatment for 1st trimester patients was low for both HFs and especially drug outlets, where not a single provider cited quinine as the correct drug of choice, consistent with the observed practices.

Stronger correlation between provider practice score and knowledge score is likely reflective of the low provider performance for MiP case management. Though a higher percentage of correct outcomes for provider practice and knowledge in non-pregnant women was observed, the weak correlation between provider practice and knowledge for non-pregnant women may suggest that providers are not consciously following a specific algorithm when treating patients in general.

HF providers had statistically significant greater knowledge of MiP consequences, clinical symptoms, pregnancy assessment, and treatment regimens versus DO providers; however provider knowledge in both settings was poor and was reflective of the low levels of observed correct case management practice. The only significant indicators for correct knowledge was malaria management training and provider professional cadre, which was reflected in the differences by facility type, consistent with previous findings [11]. Training alone has been shown to have limited impact on provider case management practice [11]. A different combination of approaches and interventions are likely to work for HFs versus DOs.

The use of mobile phone text-message reminders has been shown improve malaria case management practice for children in Kenya, and could be combined with training to improve case management in pregnancy [29]. Team based quality improvement has been suggested as another method to improve provider practice [30]. The role of DOs in management of MIP needs to be clarified, and updated guidance disseminated along with targeted MiP trainings. In addition, community education and governmental regulation are recommended to improve case management practices [11,30,31]. Governmental recognition and regulation of informal drug outlets is relevant

given that informal DO practice levels were consistently at or above those of registered pharmacies. A registration system for informal DOs, similar to that of the accredited drug dispensing outlets in Tanzania, may increase competition with registered pharmacies and incentivize both entities to improve their practice [32].

Improvement of pregnancy assessment is needed but will be a challenge due to socio-cultural factors that influence both a woman's willingness to disclose pregnancy status and a provider's willingness to ask. Adequate guidelines and interactive trainings must be available so that providers are well-informed and feel comfortable inquiring about potential pregnancy. Providers must clearly explain the purpose of the pregnancy assessment (i.e. to ensure adequate and safe treatment) and be prepared to refer the patient for ANC services. [33].

Multiple coordinated approaches and overall capacity building will be key to the improvement of MiP case management practice across facilities and has been shown to be effective in the region [30,31].

Limitations & Challenges

The relatively short time-frame of the overall study limited the number of exit interviews completed at each facility. In particular, the identification of febrile patients in 1st trimester for interview was challenging, possibly due to shortcomings in early pregnancy detection. Gestational age assessment was based on reported LMP which could have led to pregnancy trimesters misclassification for late 1st trimester pregnancies. Unless the provider had an alternative approach to assess gestation (such as fundal height) it is unlikely that assessment of correct practice would have been affected.

It is likely that correct diagnostic practice was overestimated as the diagnostic capacity of health facilities or drug outlets was not collected at the time of exit interviews nor simulated client

interactions. It was assumed that drug outlets, health centers and dispensaries didn't have access to diagnostic tests and clinical diagnosis in these facilities was considered correct.

Exit interviews and provider surveys were susceptible to courtesy or social-desirability bias, meaning that respondents may have provided answers they thought were 'more correct' or that the interviewer wanted to hear. Information obtained from exit interviews may also be biased due to patient recall/information loss, although this was minimized by conducting the interview immediately upon completion of the consultation. In addition, errors may have been introduced if the patient did not understand the information given or procedures done when in the presence of the provider.

CONCLUSION

We observed very poor malaria in pregnancy case management practice and knowledge in both HFs and DOs. Particularly concerning findings were the general failure of providers to assess WOCBA for pregnancy and incorrect treatment with SP, inadequate QN dosage, and prescription of AL in 1st trimester. Similar issues have been reported elsewhere [11]. Multifaceted approaches, including trainings, mHealth, team-based quality improvement, and community education, should be explored to improve provider adherence and knowledge. These approaches should be tailored specifically for HFs and DOs given the unique provider qualifications and patient health-seeking behaviours that characterize the two entities. Improving practice in the informal sector is critical, as it comprises a large part of health service provision for malaria treatment and has little to no institutional oversight. Optimizing treatment of WOCBA and pregnant women is critical to prevent adverse consequences of MiP.

Disclaimer

The findings and conclusions presented in this manuscript are those of the authors and do not necessarily reflect the official position of the U.S. President's Malaria Initiative, United States Agency for International Development, or U.S. Centers for Disease Control and Prevention.

Acknowledgements

We are grateful to the communities of Asembo, Gem and Karemo for their participation in and support of the HDSS. We also thank numerous field, clinical, data and administrative staff, without whom, this work would not have been possible. We thank INDEPTH for their ongoing collaboration to strengthen and support health and demographic surveillance systems; the KEMRI/CDC Research and Public Health Collaboration is a member of the INDEPTH Network. This paper is published with the permission of the Director, KEMRI.

Financial support

This publication was made possible through support provided by the United States President's Malaria Initiative, U.S. Agency for International Development and U.S. Centers for Disease Control and Prevention (CDC), under the terms of an Interagency Agreement with CDC and through a Cooperative Agreement between the CDC and the Kenya Medical Research Institute (KEMRI). The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all of the data in the study and had final responsibility for the decision to submit for publication.

Potential conflicts of interest

All authors: No reported conflicts.

REFERENCES

1. Dellicour S, Tatem AJ, Guerra CA, Snow RW, ter Kuile FO (2010) Quantifying the number of pregnancies at risk of malaria in 2007: a demographic study. PLoS Med 7: e1000221.

2. Desai M, ter Kuile FO, Nosten F, McGready R, Asamoa K, et al. (2007) Epidemiology and burden of malaria in pregnancy. Lancet Infect Dis 7: 93-104.

3. Ward SA, Sevene EJ, Hastings IM, Nosten F, McGready R (2007) Antimalarial drugs and pregnancy: safety, pharmacokinetics, and pharmacovigilance. Lancet Infect Dis 7: 136-144.

4. WHO (2003) Assessment of the safety of artemisinin compounds in pregnancy. Report of two informal consultations convened by WHO in 2002. Geneva: WHO.

5. WHO (2007) Assessment of the safety of artemisinin compounds in pregnancy: report of two joint informal consultations convened in 2006. Geneva: WHO.

6. WHO (2010) Guidelines for the treatment of malaria. Geneva: World Health Organisation.

7. DOMC (2010) Division of Malaria Control National guidelines for the diagnosis treatment and prevention of malaria in Kenya.: Ministry of Public Health and Sanitation, Nairobi.

8. WHO (2009) Medicines use in primary care in developing and transitional countries: Fact Book summarizing results from studies reported between 1990 and 2006 Geneva: World Health Organization.

9. Zurovac D, Njogu J, Akhwale W, Hamer DH, Larson BA, et al. (2008) Effects of revised diagnostic recommendations on malaria treatment practices across age groups in Kenya. Trop Med Int Health 13: 784-787.

10. Nyandigisi A, Memusi D, Mbithi A, Ang'wa N, Shieshia M, et al. (2011) Malaria case-management following change of policy to universal parasitological diagnosis and targeted artemisinin-based combination therapy in Kenya. PLoS One 6: e24781.

11. Hill J, D'Mello-Guyett L, Hoyt J, van Eijk AM, ter Kuile FO, et al. (2014) Women's access and provider practices for the case management of malaria during pregnancy: a systematic review and meta-analysis. PLoS Med 11: e1001688.

12. Aviv RI, Chubb K, Lindow SW (1993) The prevalence of maternal medication ingestion in the antenatal period. S Afr Med J 83: 657-660.

13. Kamuhabwa A, Jalal R (2011) Drug use in pregnancy: Knowledge of drug dispensers and pregnant women in Dar es Salaam, Tanzania. Indian Journal of Pharmacology 43: 345-349.

14. Kebede B, Gedif T, Getachew A (2009) Assessment of drug use among pregnant women in Addis Ababa, Ethiopia. Pharmacoepidemiol Drug Saf 18: 462-468.

15. Rohra DK, Das N, Azam SI, Solangi NA, Memon Z, et al. (2008) Drug-prescribing patterns during pregnancy in the tertiary care hospitals of Pakistan: a cross sectional study. BMC Pregnancy Childbirth 8: 24.

16. Sangare LR, Weiss NS, Brentlinger PE, Richardson BA, Staedke SG, et al. (2011) Patterns of anti-malarial drug treatment among pregnant women in Uganda. Malar J 10: 152.

17. Bigogo G, Audi A, Aura B, Aol G, Breiman RF, et al. (2010) Health-seeking patterns among participants of population-based morbidity surveillance in rural western Kenya: implications for calculating disease rates. Int J Infect Dis 14: e967-973.

18. Ochako R, Fotso JC, Ikamari L, Khasakhala A (2011) Utilization of maternal health services among young women in Kenya: insights from the Kenya Demographic and Health Survey, 2003. BMC Pregnancy Childbirth 11: 1.

19. Odhiambo FO, Laserson KF, Sewe M, Hamel MJ, Feikin DR, et al. (2012) Profile: the KEMRI/CDC Health and Demographic Surveillance System--Western Kenya. Int J Epidemiol 41: 977-987.

20. Ouma P, van Eijk AM, Hamel MJ, Parise M, Ayisi JG, et al. (2007) Malaria and anaemia among pregnant women at first antenatal clinic visit in Kisumu, western Kenya. Trop Med Int Health 12: 1515-1523.

21. Perrault SD, Hajek J, Zhong K, Owino SO, Sichangi M, et al. (2009) Human immunodeficiency virus co-infection increases placental parasite density and transplacental malaria transmission in Western Kenya. Am J Trop Med Hyg 80: 119-125.

22. Huntington D, Schuler SR (1993) The simulated client method: evaluating client-provider interactions in family planning clinics. Stud Fam Plann 24: 187-193.

23. Madden JM, Quick JD, Ross-Degnan D, Kafle KK (1997) Undercover careseekers: simulated clients in the study of health provider behavior in developing countries. Soc Sci Med 45: 1465-1482.

24. Kenya National Bureau of Statistics (KNBS) and ICF Macro (2011) Kenya Demographic and Health Survey 2008-09. Calverton, Maryland, USA. http://www.measuredhs.com/pubs/pdf/FR229/FR229.pdf.

25. Cheruiyot J, Ingasia LA, Omondi AA, Juma DW, Opot BH, et al. (2014) Polymorphisms in Pfmdr1, Pfcrt, and Pfnhe1 Genes Are Associated with Reduced In Vitro Activities of Quinine in Plasmodium falciparum Isolates from Western Kenya. Antimicrob Agents Chemother 58: 3737-3743.

26. Tarning J, Kloprogge F, Dhorda M, Jullien V, Nosten F, et al. (2013) Pharmacokinetic properties of artemether, dihydroartemisinin, lumefantrine, and quinine in pregnant women with uncomplicated plasmodium falciparum malaria in Uganda. Antimicrob Agents Chemother 57: 5096-5103.

27. McCollum AM, Schneider KA, Griffing SM, Zhou Z, Kariuki S, et al. (2012) Differences in selective pressure on dhps and dhfr drug resistant mutations in western Kenya. Malar J 11: 77.

28. Iriemenam NC, Shah M, Gatei W, van Eijk AM, Ayisi J, et al. (2012) Temporal trends of sulphadoxine-pyrimethamine (SP) drug-resistance molecular markers in Plasmodium falciparum parasites from pregnant women in western Kenya. Malar J 11: 134.

29. Zurovac D, Sudoi RK, Akhwale WS, Ndiritu M, Hamer DH, et al. (2011) The effect of mobile phone text-message reminders on Kenyan health workers' adherence to malaria treatment guidelines: a cluster randomised trial. Lancet 378: 795-803.

30. Hanson C, Waiswa P, Marchant T, Marx M, Manzi F, et al. (2014) Expanded Quality Management Using Information Power (EQUIP): protocol for a quasi-experimental study to improve maternal and newborn health in Tanzania and Uganda. Implement Sci 9: 41.

31. Brantuo MN, Cristofalo E, Mehes MM, Ameh J, Brako NO, et al. (2014) Evidence-based training and mentorship combined with enhanced outcomes surveillance to address the leading causes of neonatal mortality at the district hospital level in Ghana. Trop Med Int Health 19: 417-426.

32. Bruxvoort K, Festo C, Kalolella A, Cairns M, Lyaruu P, et al. (2014) Cluster randomized trial of text message reminders to retail staff in tanzanian drug shops dispensing artemether-lumefantrine: effect on dispenser knowledge and patient adherence. Am J Trop Med Hyg 91: 844-853.

33. Perlman SE, Postlethwaite D, Stump S, Bielan B, Rudy SJ (2001) Taking a sexual history from and counseling women on teratogenic drugs. J Reprod Med 46: 163-168.

TABLES

Table 1. Definitions of Correct Practice & Adequate Knowledge

Correct Malaria Diagnosis	
Utilization of microscopy or RDT	
Clinical diagnosis when diagnostic test unavailable	
Correct Pregnancy Assessment	
Inquired about pregnancy and/ or offered pregnancy test	
Inquiry on LMP or gestational age	
Correct Treatment & Dosage	
Acceptable Knowledge Answers	*Acceptable Prescriptions in Practice*
Non-pregnant	***Non-pregnant***
1st-line: Artemether-lumefantrine (4x2x3)	Artemether-lumefantrine (4x2x3)
2nd-line: DHA-piperaquine (3x1x3 or 4x1x3)	DHA-piperaquine (3x1x3 or 4x1x3)
	Quinine (2x3x7)
1st Trimester	***1st Trimester***
Quinine (2x3x7)	Quinine (2x3x7)
2nd/3rd Trimester	***2nd/3rd Trimester***
Quinine (2x3x7)	Quinine (2x3x7)
Artemether-lumefantrine (4x2x3)	Artemether-lumefantrine (4x2x3)
	DHA-piperaquine (3x1x3 or 4x1x3)
Treatment regimens:	
Artemether-lumefantrine tablets (20/120 mg): 4 tablets, 2 times daily for 3 days (4x2x3)	
DHA-piperaquine tablets (40/320 mg): 3 or 4 tablets, once daily for 3 days (3x1x3) (4x1x3)	
Quinine: 2 tablets of 300 mg, 3 times daily for 7 days (2x3x7)	

Acronyms: RDT, rapid diagnostic test; LMP, date of last menstruation period; DHA, dihydroartemisnin

Table 2a. Exit Interview: Health Facility Characteristics

	Total Facilities		*Total Interviews*	
District	**N**=*51*	**%**	**N=209**	**%**
Bondo	6	11.8	18	8.6
Gem	20	39.2	89	42.6
Rarieda	9	17.6	28	13.4
Siaya	16	31.4	74	35.4
Facility Type				
Hospital	4	7.8	18	8.6
Health Center	19	37.3	83	39.7
Dispensary	28	54.9	108	51.7
Facility Managing Authority				
Government	44	86.3	188	90.0
Mission	2	3.9	4	1.9
Private	5	9.8	17	8.1

Table 2b. Health Facility Exit Interview: Respondent Characteristic

	Overall		*Non-Pregnant*		*1st trimester***		*2nd/3rd trimester*	
	N=209	***%***	***N=111***	***%***	***N=22***	***%***	***N=76***	***%***
Respondent Characteristics								
Education Level								
No Education	16	7.7	14	12.6	1	4.5	1	1.3
Primary	138	66.0	70	63.1	16	72.7	52	68.4
Secondary	38	18.2	20	18.0	2	9.1	16	21.1
Higher Education	17	8.1	7	6.3	3	13.6	7	9.2
Age mean *(range)* & Std. Deviation	26.4 *(17-48)*	7.2	28.2 *(18-48)*	7.8	25.6 *(18-45)*	6.5	23.9 *(17-40)*	5.6
Symptoms Reported to provider*								
Fever	138	66.0	78	70.3	15	68.2	45	59.2
Headache	183	87.6	101	91.0	19	86.4	63	82.9
Pain	104	49.8	54	48.6	10	45.5	24	31.6
Nausea	72	34.4	27	24.3	7	31.8	31	40.8
Malaise	80	38.3	39	35.1	7	31.8	34	44.7
Chills	17	8.1	9	8.1	2	9.1	6	7.9
Stomach Pain	23	11.0	12	10.8	3	13.6	8	10.5
Cough	18	8.6	7	6.3	3	13.6	8	10.5
Dizziness	3	1.4	0	0.0	0	0.0	3	3.9
Diarrhea	2	1.0	0	0.0	1	4.5	1	1.3
Gravidity	n=156		n=64		n=21		n=71	
0	33	21.2	12	18.8	3	14.3	18	25.4
1	31	19.9	11	17.2	7	33.3	13	18.3
2	33	21.2	12	18.8	3	14.3	18	25.4
3-4	32	20.5	12	18.8	6	28.6	14	19.7
5+	27	17.3	17	26.6	2	9.5	8	11.27
Missing	*53*		*47*		*1*		*5*	

**2 reported no symptoms to provider*

***Patients with gestational age of up to 14 weeks, 6 days were included in 1st trimester given that treatment guidelines use 'quickening' as a treatment indicator*

Table 3. Malaria Diagnostics practice in Health Facilities as observed through exit interviews stratified across facility type

	Overall			Hospital			Health Center			Dispensary			
	N	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**P-value**
Diagnostically Tested for Malaria	209			18			83			108			
Yes	160	76.6	(64.9, 88.3)	16	88.9	(68.2, 100.0)	75	90.4	(77.9, 100.0)	69	63.9	(46.0, 81.8)	0.02
No	48	23.0	(8.0, 38.0)	2	11.1	(0.0, 31.8)	8	9.6	(0.0, 25.2)	38	35.2	(10.7, 59.7)	
Don't Know	1	0.5	(0.0, 1.4)	0	0.0		0	0.0		1	0.9	(0.0, 2.7)	
Malaria Test Results	160			16			75			69			
Positive	151	94.4	(90.4, 98.3)	14	87.5	(68.3, 100.0)	70	93.3	(87.3, 99.4)	67	97.1	(93.6, 100.0)	
Negative	3	1.9	(0.0, 4.5)	2	12.5	(0.0, 31.7)	1	1.3	(0.0, 3.6)	0	0.0		
Don't Know	6	3.8	(0.7, 6.8)	0	0.0		4	5.3	(0.0, 10.8)	2	2.9	(0.0, 6.4)	
Test Location	160			16			75			69			
OPD	28	17.5	(5.6, 59.4)	0	0.0		3	4.0	(0.0, 10.3)	25	36.2	(13.3, 59.2)	
Lab	131	81.9	(69.6, 94.1)	16	100.0		72	96.0	(89.7, 100.0)	43	62.3	(38.8, 85.9)	
Pharmacy	1	0.6	(0.0, 1.9)	0	0.0		0	0.0		1	1.4	(0.0, 4.4)	
No Diagnostic Test	49	23.3		2	11.1		18	21.7		57	52.3		
Correct Clinical Diagnosis*	28	57.1	(37.2, 77.1)	0	0.0		4	50.0	(3.3, 96.7)	24	61.5	(40.1, 82.6)	0.45
Incorrect Diagnosis**	21	42.9	(22.9, 62.8)	2	100.0		4	50.0	(3.3, 96.7)	15	38.5	(17.0, 59.9)	
CORRECT Malaria Diagnosis	**188**	**90.0**	**(85.2, 94.7)**	**16**	**88.9**	**(68.2, 100.0)**	**79**	**95.2**	**(90.4, 99.9)**	**93**	**86.1**	**(79.2, 93.0)**	**0.20**

**Tested via Rapid Diagnostic Test (RDT) or microscopy*

***Correct Clinical Diagnosis indicates women presenting with fever, multiple symptoms, and/or were pregnant with symptom(s) at facilities without diagnostic capacity*

****Incorrect Diagnosis indicates patients treated for malaria without diagnostic testing at facilities where it was available or without clinical presentation if at a facility with no diagnostic capacity*

Table 4. Pregnancy assessment practice in Health Facilities as observed in exit interviews stratified across pregnancy status

	Overall			Non-Pregnant			1st Trimester			2nd/3rd Trimester			
	N	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**P-value**
All Patients	209			111			22			76			
Pregnancy Status Inquiry	92	44.0	(35.6, 52.4)	29	26.1	(16.9, 35.4)	17	77.3	(57.1, 97.5)	46	60.5	(49.2, 71.8)	<0.01
Pregnancy Test Offered	20	9.6	(5.5, 13.6)	4	3.6	(0.3, 6.9)	9	40.9	(19.3, 62.5)	7	9.2	(2.3, 16.1)	<0.01
LMP Inquiry	89	42.6	(33.9, 51.7)	27	24.3	(14.6, 34.0)	16	72.7	(51.8, 93.7)	46	60.5	(49.9, 71.2)	<0.01
Pregnancy Duration/Timing	67	68.4	(57.0, 79.7)	NA			14	63.6	(40.4, 86.9)	53	69.7	(58.1, 81.4)	0.59
Additional Confirmation*	41	41.8	(30.5, 53.2)	NA			5	22.7	(3.7, 41.7)	36	47.4	(35.2, 59.6)	0.03
Correct pregnancy assessment	**108**	**51.7**	**(42.2, 61.1)**	**27**	**24.3**	**(14.6, 34.0)**	**18**	**81.8**	**(62.5, 100.0)**	**63**	**82.9**	**(75.0, 90.8)**	**<0.01**

* *Additional confirmation included palpation in 1st trimester, and palpation or observation in 2nd/3rd trimester cases.*

Table 5. Malaria treatment practice in Health Facilities as observed through exit interviews stratified across pregnancy status

	Overall			Non-Pregnant			1st Trimester			2nd/3rd Trimester			
	N	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**P-value**
	209			**111**			**22**			**76**			
Prescribed Antimalarials	205	**98.1**		**110**	**99.1**		**21**	**95.5**		**74**	**97.4**		
Proper Dosage (tabs x doses x days)					**0.00**			**0.0**					
Artemether lumefantrine	172	82.3	(76.9, 87.7)	105	94.6	(90.2, 98.9)	**6**	27.3	(3.5, 51.0)	61	80.3	(70.8, 89.8)	<0.01
(4x2x3)	125	59.8	(50.7, 68.9)	74	66.7	(55.4, 77.9)	**5**	22.7	(2.5, 42.9)	46	60.5	(47.5, 73.6)	<0.01
DHA-Piperaquine	2	1.0	(0.0, 2.3)	2	1.8	(0.0, 4.5)	0	0.0		0	0.0		
(3x1x3)	1	0.5	(0.0, 1.5)	1	0.9	(0.0, 2.8)		0.0			0.0		
Quinine	29	13.9	(9.3, 18.4)	4	3.6	(0.0, 8.1)	13	59.1	(48.0, 88.9)	12	15.8	(7.0, 24.6)	
(2x3x7)	8	3.8	(1.4, 6.3)	0	0.0		6	27.3	(11.1, 52.0)	2	2.6	(0.0, 6.3)	<0.01
(150mgxN)	1	0.5	(0.0, 1.5)	1	0.9	(0.0, 2.8)	0	0.0		0	0.0		
Sulfadoxine Pyremethamine	7	3.3	(0.4, 6.3)	**1**	0.9	(0.0, 2.8)	**2**	9.1	(0.0, 24.0)	**4**	5.3	(0.0, 11.3)	
(3x1x1)	5	2.4	(0.0, 4.8)	**0**	0.0		**2**	9.1	(0.0, 24.0)	**3**	3.9	(0.0, 9.6)	0.42
Artemether Injection	1	0.5	(0.0, 1.5)	1	0.9	(0.0, 2.8)	0	0.0		0	0.0		
(60mg)	1	0.5	(0.0, 1.5)	1	0.9	(0.0, 2.8)		0.0			0.0		
Correct Drug	195	93.3		111	100.0		13	59.1		74	97.4		
Correct Drug & Dosage	130	62.2	(52.5, 71.9)	**76**	68.5	(57.2, 79.7)	**6**	27.3	(8.2, 46.3)	**48**	63.2	(49.6, 76.7)	<0.01
Concomitant Medications		0.0											
Analgesic	148	70.8	(61.3, 80.3)	79	71.2	(59.3, 83.0)	17	77.3	(59.5, 95.1)	52	68.4	(55.7, 81.1)	0.72
Antibiotic	75	35.9	(26.8, 45.0)	37	33.3	(21.9, 44.8)	7	31.8	(13.1, 50.5)	31	40.8	(28.9, 52.6)	0.48
Treatment Advice		0.0											
Reason for Prescription	58	27.8	(20.7, 35.9)	32	28.8	(20.9, 38.3)	5	22.7	(5.3, 42.3)	21	27.6	(16.6, 38.7)	0.82
Side Effects	14	6.7	(3.1, 10.5)	5	4.5	(0.5, 8.8)	4	18.2	(1.2, 38.8)	5	6.6	(1.2, 12.3)	0.04
Any other advice	46	22.0	(15.4, 28.6)	21	18.9	(11.0, 26.8)	6	27.3	(6.3, 48.2)	19	25.0	(14.0, 36.0)	0.54
Any treatment Advice	**83**	39.7	(31.5, 47.9)	**42**	37.8	(27.5, 48.2)	**11**	50.0	(27.4, 72.6)	**30**	39.5	(27.0, 52.0)	0.59

**Unsure pregnancy status refers to women who self-reported as not knowing if they were pregnant or not, correct prescribing practice was not assessable for those; these women are not included in the 'Correct Drug' or 'Drug & Dosage' denominator.*

***Percentage for correct dosage is based on the numbers receiving the specific antimalarial.*

****Any other advice includes patient-reported advice by the provider including emphasis of complete medication regimen, eating prior to taking medication, sleeping under ITNs, etc.*

Table 6. Malaria Case Management Practice in Health Facilities as observed through Exit Interviews, stratified across Health Facility Type

	Overall			Hospital			Health Center			Dispensary			
	N	***%***	***95% CI***	***N***	***%***	***95% CI***	***N***	***%***	***95% CI***	***N***	***%***	***95% CI***	***P-value***
	209			18			83			109			
Malaria Diagnostics	188	90.0	(85.2, 94.7)	16	88.9	(68.2, 100.0)	79	95.2	(90.4, 99.9)	93	85.3	(79.2, 93.0)	0.20
Pregnancy Assessment	108	51.7	(42.2, 61.1)	14	77.8	(62.3, 93.2)	45	54.2	(33.9, 74.5)	49	45.0	(36.7, 54.0)	0.10
Treatment & Dosage	130	62.2	(52.5, 71.9)	10	55.6	(19.2, 91.9)	54	65.1	(49.9, 80.2)	66	60.6	(47.5, 74.7)	0.86
Non-pregnant *n=111*	76	68.5	(57.2, 79.7)	7	77.8	(49.6, 100.0)	31	72.1	(57.5, 83.4)	38	67.9	(47.2, 83.6)	0.75
1st Trimester *n=22*	6	27.3	(7.0, 47.5)	0	0.0		3	60.0	(0.0, 87.3)	3	25.0	(0.0, 46.9)	
2nd/3rd Trimester *n=76*	49	64.5	(49.5, 76.8)	3	42.9	(0.0, 86.7)	20	62.5	(39.1, 85.9)	26	68.4	(50.4, 84.8)	0.58
Correct Practice	**66**	**31.6**	**(22.3, 40.9)**	**7**	**38.9**	**(13.9, 63.9)**	**29**	**34.9**	**(15.5, 54.4)**	**30**	**27.5**	**(18.3, 37.2)**	**0.65**

Table 7. Predictors of correct prescribing and diagnostic practice in health facilities

Provider Characteristic	**N**	%	**Crude OR**	**95% CI**	**Pr >|Z|**	**Adjusted OR**	**95% CI**	**Pr >|Z|**
Dispenses Medicine (ref='No')	**156**							
No	19	12.2	--	--	--	--	--	--
yes	137	87.8	2.2	(1.2, 4.1)	0.01			

**Logistic regression includes only respondents in nursing and clinical officer/medical doctor cadres due to sparse data in other cadres.*

Table 8. Drug Outlet & Simulation Characteristics

Drug Outlets	*Total Facilities*		Registered Pharmacy		Informal Drug Outlet		General Shop	
	N	%	N	%	N	%	N	%
District	*39*	100	9	23.1	13	33.3	17	43.6
Gem	13	33.3	3	33.3	6	46.2	4	23.5
Rarieda	8	20.5	2	22.2	3	23.1	3	17.6
Siaya	18	46.2	4	44.4	4	30.8	10	58.8
Provider Gender	*39*							
Male	17	43.6	5	55.6	5	38.5	7	41.2
Female	22	56.4	4	44.4	8	61.5	10	58.8
Education Level	*37*		9		13		15	
Primary School	7	18.9	0	0.0	0	0.0	7	41.2
Secondary School	16	43.2	5	55.6	6	46.2	5	29.4
Higher Education	6	16.2	2	22.2	2	15.4	2	11.8
Clinical Officer/MD	1	2.7	0	0.0	1	7.7	0	0.0
Registrd Midwife/Nurse	2	5.4	1	11.1	1	7.7	0	0.0
Enrolled Midwife/Nurse	1	2.7	0	0.0	1	7.7	0	0.0
Pharmacist	3	8.1	1	11.1	1	7.7	1	5.9
Other technical	1	2.7	0	0.0	1	7.7	0	0.0
	mean *(range)*	Std. Dev						
Age	32.1 *(19-60)*	9.2	28.0 *(19-46)*	8.5	31.1 *(20-48)*	7.1	35.5 *(21-60)*	10.5
Simulation Characteristics	*147*							
WOCBA	38	25.9	9	100.0	13	100.0	16	94.1
1st Trimester Pregnancy	37	25.2	9	100.0	12	92.3	16	94.1
Husband of WOCBA	34	23.1	8	88.9	10	76.9	16	94.1
Husband of 3rd Trimester	38	25.9	9	100.0	13	100.0	16	94.1

**There were 2 homesteads visited; these were included as Informal Drug Outlets.*

***Education level was obtained from matched provider surveys (39 of 41 dispensers were interviewed) and this is missing for 2 providers in the general shop*

Table 9. Malaria Diagnostics practice in drug outlets as observed through simulated clients across pregnancy status

	Overall			WOCBA /1st Tri			Relative: 2nd/3rd Tri			
	N	***%***	***95% CI***	***N***	***%***	***95% CI***	***N***	***%***	***95% CI***	***P-value***
Symptoms	**77**			**38**			**39**			
Any Inquiry	25	32.5	(21.6, 43.3)	15	39.5	(23.2, 55.7)	10	25.6	(11.3, 40.0)	0.20
Specific	12	15.6	(7.1, 24.1)	4	10.5	(0.3, 20.7)	8	20.5	(7.3, 33.8)	0.23
Fever	7	9.1	(1.7, 16.5)	6	15.8	(3.7, 27.9)	1	2.6	(0.0, 7.8)	0.02
Chills	3	3.9	(0.0, 8.3)	3	7.9	(0.0, 16.9)	0	0.0		
Headache	10	13.0	(5.7, 20.2)	8	21.1	(7.5, 34.6)	2	5.1	(0.0, 12.4)	0.05
Nausea	6	7.8	(0.7, 14.9)	4	10.5	(0.3, 20.7)	2	5.1	(0.0, 12.4)	0.30
Pain	3	3.9	(0.0, 8.3)	2	5.3	(0.0, 12.7)	1	2.6	(0.0, 7.8)	0.55
Prescription	4	5.2	(0.0, 11.5)	1	2.6	(0.0, 8.0)	3	7.7	(0.0, 16.4)	0.17
Temperature	0	0.0		0	0.0		0	0.0		
Diagnostic Test or Test Inquiry	4	5.2	(0.0, 11.5)	2	5.3	(0.0, 12.7)	2	5.1	(0.0, 12.4)	0.35
Any Malaria Diagnostic	**26**	**33.8**	**(22.4, 45.2)**	**16**	**42.1**	**(25.7, 58.5)**	**10**	**25.6**	**(11.3, 40.0)**	**0.12**

Table 10. Pregnancy assessment practice in drug outlets as observed through simulated clients across pregnancy status

	Overall			WOCBA/1st Trimester			Husband of WOCBA/3rd Trimester			
	N	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**P-value**
Pregnancy Inquiry	77			38			39			
Unprompted Pregnancy Inquiry	4	5.2	(3.7, 11.1)	0	0.0		4	10.3	(3.5, 24.2)	0.29
Confirmation										
Timing	2	50.0	(0.0, 100.0)	0	0.0		2	50.0	(0.0, 100.0)	
LMP	*0*	*0.0*		*0*	*0.0*		*0*	*0.0*		
Gestation	*2*	*50.0*	*(0.0, 100.0)*	*0*	*0.0*		*2*	*100.0*		
Pregnancy Test Offered	0	0.0		0	0.0		0	0.0		
None	2	50.0	(0.0, 100.0)	0	0.0		2	50.0	(0.0, 100.0)	
Informed Provider of Pregnancy Status	70			36			34			0.72
Confirmation										
Timing	40	57.1	(45.6, 69.4)	21	58.3	(41.4, 75.2)	19	55.9	(39.0, 72.2)	1.00
LMP	*2*	*5.0*	*(0.0, 11.5)*	*2*	*5.6*	*(0.0, 22.9)*	*0*	*0.0*		
Gestation	*38*	*95.0*	*(88.5, 100.0)*	*19*	*52.8*	*(77.1, 100.0)*	*19*	*100.0*		
Pregnancy Test Offered	0	0.0		0	0.0		0	0.0		
None	30	42.9	(30.6, 54.4)	15	41.7	(24.0, 57.1)	15	44.1	(61.0, 27.8)	1.00
Correct Pregnancy Assessment*	**48**	**62.3**	**(53.1, 65.5)**	**23**	**57.5**	**(48.8, 66.3)**	**25**	**61.0**	**(51.6, 69.4)**	**0.93**

**Correct Pregnancy Assessment indicates that the provider confirmed pregnancy status via LMP, gestational inquiry, or pregnancy test*

Table 11. Correct Treatment and Dosage Characteristics by Pregnancy Status in Drug Outlets

	Overall			WOCBA			1st Trimester			2nd/3rd Trimester			
	N	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**N**	**%**	**95% CI**	**P-value**
	147			**72**			**37**			**38**			
Prescribed Antimalarials	122	**83.0**		65	90.3		29	78.4		28	73.7		
Correct Dosage (tabs x doses x days)													
Artemether lumefantrine	93	76.2	(66.3, 86.2)	59	90.8	(81.3, 100.0)	18	62.1	(43.5, 80.6)	16	57.1	(37.9, 76.4)	<0.01
(4x2x3)	75	61.5	(51.1, 71.9)	46	70.8	(59.5, 82.0)	14	48.3	(29.1, 67.4)	15	53.6	(34.1, 73.0)	0.04
Artesunate amodiaquine	1	0.8	(0.0, 2.5)	1	1.5	(0.0, 4.7)	0	0.0		0	0.0		
(4x1x3)	0	0.0		0	0.0		0	0.0			0.0		
Amodiaquine	2	1.6	(0.0, 5.0)	1	1.5	(0.0, 4.7)	1	3.4	(0.0, 10.4)	0	0.0		
(3x1x1)	2	1.6	(0.0, 5.0)	1	1.5		1	3.4	(0.0, 10.4)		0.0		
Quinine	0	0.0		0	0.0		0	0.0		0	0.0		
(2x3x7)	0	0.0			0.0			0.0			0.0		
Sulfadoxine Pyrimethamine	26	21.3	(13.1, 29.5)	4	6.2	(0.0, 13.6)	10	34.5	(16.3, 52.7)	12	42.9	(23.6, 62.1)	<0.01
(3x1x1)	20	16.4	(8.8, 24.0)	4	6.2	(0.0, 13.6)	6	20.7	(5.2, 36.2)	10	35.7	(17.0, 54.4)	<0.01
Correct Drug	77	63.1		61	93.8		0	0.0		16	57.1		
Correct Drug & Dosage	**61**	**50.0**	**(42.5, 57.5)**	**46**	**70.8**	**(59.5, 82.0)**	**0**	**0.0**		**15**	**53.6**	**(34.1, 73.0)**	
Concomittant Medications													
Analgesic	90	73.8	(61.2, 86.4)	47	72.3	(59.5, 85.1)	24	82.8	(68.3, 97.2)	19	67.9	(49.7, 86.1)	0.14
Multivitamin	2	1.6	(0.0, 4.8)	0	0.0		0	0.0		2	7.1	(0.0, 17.2)	
Treatment Advice													
Dosage Directions	106	86.9	(79.2, 94.6)	55	84.6	(68.3, 97.2)	24	82.8	(68.3, 97.2)	27	96.4	(89.2, 100.0)	0.12
Visual Instructions	69	56.6	(43.9, 69.2)	34	52.3	(38.4, 66.2)	18	62.1	(43.5, 80.6)	17	60.7	(41.7, 79.7)	0.47
Emphasize need to finish Dose	8	6.6	(0.0, 13.4)	3	4.6	(0.0, 9.9)	1	3.4	(0.0, 10.4)	4	14.3	(0.7, 27.9)	0.01
Side Effects	2	1.6	(0.0, 4.0)	1	1.5	(0.0, 4.7)	0	0.0		1	3.6	(0.0, 10.8)	
Advice if Symptoms Persist	5	4.1	(0.0, 9.0)	3	4.6	(0.0, 9.9)	2	6.9	(0.0, 16.6)	0	0.0		
Any Treatment Advice	106	86.9	(79.2, 94.6)	55	84.6	(76.2, 93.1)	24	82.8	(68.3, 97.2)	27	96.4	(89.2, 100.0)	0.12

**Percentage for correct dosage is based on the numbers receiving the specific antimalarial*

Table 12. Malaria Case Management practice in drug outlets as observed via simulated clients stratified across Drug Outlet Type

	Overall			Registered Pharmacy			Informal Drug Shop			General Shop			
	N	***%***	***95% CI***	***N***	***%***	***95% CI***	***N***	***%***	***95% CI***	***N***	***%***	***95% CI***	***P-value***
	147			35			48			64			
Malaria Diagnostics	48	32.7	(21.5, 43.8)	13	37.1	(11.3, 63.0)	21	43.8	(22.6, 64.9)	14	21.9	(9.3, 34.5)	0.20
Pregnancy Assessment	43	29.3	(23.0, 35.5)	14	40	(30.3, 49.7)	18	37.5	(27.2, 47.8)	11	17.2	(9.8, 24.5)	<0.01
Treatment & Dosage	61	41.5	(33.2, 49.8)	18	51.4	(42.7, 60.2)	25	52.1	(39.7, 64.4)	18	28.1	(14.8, 41.4)	<0.01
Non-pregnant *n=72*	46	63.9	(51.6, 76.2)	14	82.4	(65.7, 99.0)	19	82.6	(67.5, 97.7)	13	40.6	(22.4, 58.9)	<0.01
1st Trimester *n=37*	0	0.0		0	0.0		0	0.0		0	0.0		
2nd/3rd Trimester *n=38*	15	39.5	(23.2, 55.8)	4	44.4	(10.4, 78.5)	6	46.2	(17.8, 74.5)	5	31.3	(7.5, 55.0)	0.67
Correct Practice	**4**	**2.7**	**(0.1, 5.4)**	**1**	**2.9**	**(0.0, 8.5)**	**1**	**2.1**	**(0.0, 6.3)**	**2**	**3.1**	**(0.0, 7.4)**	**0.94**

Table 13. Facility characteristics from the provider survey on national malaria treatment guidelines

Facility Characteristics	*Total Facilities*		*Total Providers*	
	N=86	%	N=112	%
District				
Bondo	6	7.0	9	8.0
Gem	32	37.2	42	37.5
Rarieda	15	17.4	17	15.2
Siaya	33	38.4	44	39.3
Facility Type				0.0
Hospital	4	4.7	6	5.4
Health Center	19	22.1	28	25.0
Dispensary	26	30.2	41	36.6
Total Health Facilities	**49**	**57.0**	**75**	**67.0**
Registered Pharmacy	9	10.5	9	8.0
Informal Drug Shop	13	15.1	13	11.6
General Shop	15	17.4	15	13.4
Total Drug Outlets	**37**	**43.0**	**37**	**33.0**
Facility Managing Authority				0.0
Government	42	48.8	67	59.8
Mission	4	4.7	2	1.8
Private	43	50.0	43	38.4

Table 13b. Provider characteristics from the provider survey on national malaria treatment guidelines

	Overall		Health facilities		Drug Outlets	
Provider/Dispenser Characteristics	**N**	%	N	**%**	N	**%**
	112		75		37	
Sex						
Male	54	48.2	39	52.0	15	40.5
Female	58	51.8	36	48.0	22	59.5
Respondent Cadre						
Registered Nurse	33	29.5	32	42.7	1	2.7
Enrolled Nurse	16	14.3	16	21.3	0	0.0
Clinical Officer/MD	18	16.1	17	22.7	1	2.7
Pharmacist	20	17.9	5	6.7	15	40.5
Shopkeeper	15	13.4	0	0.0	15	40.5
CHW/VR/other*	10	8.9	5	6.7	5	13.5
Professional Qualification						
Primary School	9	8.0	2	2.7	7	18.9
Secondary School	23	20.5	7	9.3	16	43.2
Higher Education	19	17.0	13	17.3	6	16.2
Clinical Officer/MD	14	12.5	13	17.3	1	2.7
Registered Midwife/Nurse	22	19.6	20	26.7	2	5.4
Enrolled Midwife/Nurse	11	9.8	10	13.3	1	2.7
Pharmacist	4	3.6	1	1.3	3	8.1
Other technical	10	8.9	9	12.0	1	2.7

* *Other included clerk, economist, statistical clerk, and support staff*

Table 14. Malaria Treatment Guideline Awareness, comparing Health Facilities vs. Drug Outlets

	Total			Health Facilities			Drug Outlets			
MTGs	n=112	%	95% CI	n=75	%	95% CI	n=37	%	95%CI	P-value
Awareness of Government Initiative	65	58.0	(47.7, 68.4)	62	82.7	(72.6, 92.7)	3	8.1	(0.0, 17.1)	<0.01
Read the MTGs	75	67.0	(57.3, 76.6)	67	89.3	(82.3, 96.4)	8	21.6	(8.1, 35.2)	<0.01
In Possession	63	56.3	(45.9, 66.6)	60	80.0	(70.1, 89.9)	3	8.1	(0.0, 17.1)	<0.01
Additional Materials	73	65.2	(55.2, 75.1)	71	94.7	(89.6, 99.8)	2	5.4	(0.0, 12.8)	<0.01
Awareness of MTGs	**84**	**75.0**	**(66.1, 83.9)**	**74**	**98.7**	**(96.0, 100.0)**	**10**	**27.0**	**(12.4, 41.6)**	<0.01
Addtl Sources of Information										
Training/CME	63	56.3	(46.4, 66.1)	52	69.3	(57.9, 80.8)	11	29.7	(14.7, 44.8)	<0.01
DHMT/health facility memos	46	41.1	(31.5, 50.7)	38	50.7	(38.8, 62.5)	8	21.6	(8.1, 35.2)	<0.01
Colleagues	40	35.7	(26.0, 45.4)	28	37.3	(25.1, 49.6)	12	32.4	(17.0, 47.8)	0.6215
Media	55	49.1	(38.7, 59.5)	33	44.0	(30.9, 57.1)	22	59.5	(43.3, 75.6)	0.1405
Medical Journals	19	17.0	(8.6, 25.3)	19	25.3	(13.2, 37.5)	0	0.0		
Medical Reps	17	15.2	(8.2, 22.1)	11	14.7	(6.2, 23.1)	6	16.2	(4.1, 28.3)	0.8322
Other*	10	8.9	(3.5, 14.4)	3	4.0	(0.0, 8.5)	7	18.9	(6.0, 31.8)	<0.01
Training Workshops										
Malaria Training	61	54.5	(45.2, 63.7)	51	68.0	(58.0, 78.0)	10	27.0	(12.4, 41.6)	<0.01
within past 5 years	57	50.9	(41.3, 60.5)	50	66.7	(56.1, 77.3)	7	18.9	(6.0, 31.8)	<0.01
MIP Training	34	30.4	(22.4, 38.3)	30	40.0	(30.2, 49.8)	4	10.8	(0.6, 21.0)	<0.01
within past 5 years	31	27.7	(19.9, 35.5)	28	37.3	(27.3, 47.3)	3	8.1	(0.0, 17.1)	<0.01

**P-values from Chi-square test*

***Other includes community meetings (Barazas), CDC staff, NGOs, & Village Reporters*

Acronyms: MTGs, malaria treatment guidelines; CME, continuing medical education; DHMT, district health medical team; MiP, malaria in pregnancy

Table 14 Extended. Malaria Treatment Guideline Awareness, comparing all facility types

	Total		**Health Facilities**		Hospitals		Health Centers		Dispensaries		**Drug Outlets**		Rgstrd Pharmacies		Informal Drug		General Shop	
MTGs	**n=112**	**%**	**n=75**	**%**	n=6	%	n=28	%	n=41	%	**n=37**	**%**	n=9	%	n=13	%	n=15	%
Awareness of Government Initiative	65	58.0	**62**	**82.7**	6	100.0	23	82.1	33	80.5	3	8.1	1	11.1	0	0.0	2	13.3
Read the MTGs	75	67.0	**67**	**89.3**	5	83.3	26	92.9	36	87.8	8	21.6	5	55.6	1	7.7	2	13.3
In Possession	63	56.3	**60**	**80.0**	4	66.7	23	82.1	33	80.5	3	8.1	1	11.1	1	7.7	1	6.7
Additional Materials	73	65.2	**71**	**94.7**	5	83.3	26	92.9	40	97.6	2	5.4	1	11.1	1	7.7	0	0.0
Awareness of MTGs	**84**	**75.0**	**74**	**98.7**	6	100.0	27	96.4	41	100.0	**10**	**27.0**	6	66.7	1	7.7	3	20.0
Addtl Sources of Information																		
Training/CME	63	56.3	**52**	**69.3**	4	66.7	22	78.6	26	63.4	11	29.7	4	44.4	3	23.1	4	26.7
DHMT/health facility memos	46	41.1	**38**	**50.7**	3	50.0	14	50.0	21	51.2	8	21.6	2	22.2	3	23.1	3	20.0
Colleagues	40	35.7	**28**	**37.3**	3	50.0	12	42.9	13	31.7	12	32.4	4	44.4	5	38.5	3	20.0
Media	55	49.1	**33**	**44.0**	1	16.7	15	53.6	17	41.5	22	59.5	4	44.4	10	76.9	8	53.3
Medical Journals	19	17.0	**19**	**25.3**	3	50.0	10	35.7	6	14.6	0	0.0	0	0.0	0	0.0	0	0.0
Medical Reps	17	15.2	**11**	**14.7**	0	0.0	8	28.6	3	7.3	6	16.2	1	11.1	3	23.1	2	13.3
Other*	10	8.9	**3**	**4.0**	0	0.0	3	10.7	0	0.0	7	18.9	2	22.2	2	15.4	3	20.0
Training Workshops																		
Malaria Training	**61**	**54.4**	**51**	**68.0**	4	66.7	20	71.4	27	65.9	**10**	**27.0**	3	33.3	4	30.8	3	20.0
within past 5 years	**57**	**93.4**	**50**	**98.0**	4	100.0	20	100.0	26	96.3	**7**	**70.0**	1	33.3	3	75.0	3	100.0
training prior to 2008	**4**	**6.6**	**1**	**2.0**	0	0.0	0	0.0	1	3.7	**3**	**30.0**	2	66.7	1	25.0	0	0.0

MIP Training	**34**	**30.4**	**30**	**40.0**	2	33.3	9	32.1	19	46.3	**4**	**10.8**	1	11.1	3	23.1	0	0.0
within past 5 years	**31**	**91.2**	**28**	**93.3**	1	50.0	9	100.0	18	94.7	**3**	**75.0**	0	0.0	3	100.0	0	0.0
training prior to 2008	**3**	**8.8**	**2**	**6.7**	1	50	0	0	1	5.3	**1**	**25.0**	1	100	0	0.0	0	0.0

Table 15. Adequate Provider Knowledge of Malaria in Pregnancy based on National treatment guidelines comparing HFs to DOs

	Overall			Health Facilities			Drug Outlets			P-value
	n=112	%	95% CI	n=75	%	95% CI	n=37	%	95% CI	
Consequences of MiP	110	98.2	(95.7, 100.0)	74	98.7	(96.0, 100.0)	36	97.3	(92.0, 100.0)	0.61
Awareness of MTGs	84	75.0	(66.1, 83.9)	74	98.7	(96.0, 100.0)	10	27.0	(12.4, 41.6)	<0.01
Malaria Diagnostics	104	92.9	(88.0, 97.7)	73	97.3	(93.7, 100.0)	31	83.8	(71.7, 95.9)	<0.01
Pregnancy Assessment	88	78.6	(70.7, 86.4)	70	93.3	(87.9, 98.8)	18	48.6	(32.2, 65.1)	<0.01
Treatment & Dosage	35	31.3	(22.0, 40.5)	35	46.7	(34.4, 59.0)	0	0.0		<0.01
NP-1st Line	92	82.1	(74.9, 89.4)	69	92.0	(86.1, 97.9)	23	62.2	(46.2, 78.1)	<0.01
NP-2nd Line	18	16.1	(8.9, 23.2)	15	20.0	(10.6, 29.4)	3	8.1	(0.0, 17.1)	<0.01
1st Tri- 1st Line	**42**	**37.5**	**(27.6, 47.4)**	**42**	**56.0**	**(43.6, 68.4)**	**0**	**0.0**		<0.01
2nd/3rd Tri- 1st Line	**79**	**70.5**	**(61.7, 79.3)**	**64**	**85.3**	**(77.1, 93.6)**	**15**	**40.5**	**(24.4, 56.7)**	<0.01
Severe MiP	69	61.6	(52.1, 71.1)	61	81.3	(71.8, 90.9)	8	21.6	(8.1, 35.2)	<0.01
Adequate Knowledge	**34**	**30.4**	**(21.3, 39.4)**	**34**	**45.3**	**(33.2, 57.5)**	**0**	**0.0**		<0.01

**P-values from Chi-square test and Fisher Exact used for strata with <5 observations*

Acronyms: MTG, malaria treatment guidelines, MiP, malaria in pregnancy, NP, non-pregnant; Tri, trimester of pregnancy

Table 16. Comprehensive Care Practices Provided during Pregnancy, comparing Health Facilities vs. Drug Outlets

	Overall			Health Facilities			Drug Outlets			
	n=112	**%**	**95% CI**	**n=75**	**%**	**95% CI**	**n=37**	**%**	**95% CI**	**p-value**
Care Practices in Pregnancy										
Prevent Hypoglycemia	32	28.6	(18.4, 38.7)	32	42.7	(29.2, 56.1)	0	0.0		<0.01
Fetal Monitoring	50	44.6	(34.2, 55.1)	45	60.0	(46.9, 73.1)	5	13.5	(2.3, 24.8)	<0.01
Anemia Treatment	50	44.6	(34.8, 54.5)	46	61.3	(49.5, 73.2)	4	10.8	(0.6, 21.0)	<0.01
Antipyretics	25	22.3	(14.2, 30.5)	24	32.0	(21.1, 42.9)	1	2.7	(0.0, 8.0)	<0.01
None	8	7.1	(2.2, 12.1)	0	0.0		8	21.6	(8.1, 35.2)	<0.01
Other*	53	47.3	(38.5, 57.2)	25	33.3	(21.9, 44.8)	28	75.7	(61.6, 89.8)	<0.01
Give Preg Pts Info w/ Trtmnt										
Instructions	97	86.6	(80.2, 93.0)	71	94.7	(89.7, 99.6)	26	70.3	(55.2, 85.3)	<0.01
Side Effects	64	57.1	(46.4, 67.9)	57	76.0	(64.0, 88.0)	7	18.9	(6.0, 31.8)	<0.01
Return if Symptoms Continue	58	51.8	41.4, 62.2)	47	62.7	(49.3, 76.0)	11	29.7	(14.7, 44.8)	<0.01
Danger Signs**	8	7.1	(2.4, 11.9)	5	6.7	(1.1, 12.3)	3	8.1	(0.0, 17.1)	0.78
Other	12	10.7	(4.7, 16.7)	3	4.0	(0.0, 8.5)	9	24.3	(10.2, 38.4)	<0.01
Any Information Given	**102**	**91.1**	**(85.5, 96.6)**	**74**	**98.7**	**(96.0, 100.0)**	**28**	**75.7**	**(61.6, 89.8)**	<0.01

**Included nutritious diet, ITNs, IPTp, and medication compliance.*

*** Danger signs included death, convulsions, dizziness, spotting, & fetal movement*

****P-values from Chi-square test and Fisher Exact used for strata with <5 observations*

Table 17. Provider Characteristic Predictors of Adequate Knowledge of Malaria in Pregnancy Case-Management

Provider Characteristic	N	%	Crude OR	95% CI	P	Adjusted OR	95% CI	P
Facility Type	**112**							
Health Facilites	**75**	67.0	4.3	(1.6, 11.7)	<0.01	2.8	(0.9, 8.4)	0.07
Drug Outlets (ref)	**37**	33.0	--	--	--	--	--	--
Malaria Management Training								
None	51	45.5	--	--	--	--	--	--
Yes	61	54.5	4.8	(1.9, 12.1)	<0.01	3.6	(1.3, 9.7)	0.01
Sources of Information (ref='No')								
CME as a source of info	63	56.3	1.5	(1.8, 10.4)	<0.01	--	--	--

**Adjusted model included facility type and Malaria diagnostic training. CME dropped from multivariate model due to non-significance.*

***Facility type is stratified at the health facility versus drug outlet level; the fully stratified model was unstable due to quasi-complete separation of data points.*

Table 18. Other Knowledge Predictors of Adequate Case-Management Knowledge of Malaria in Pregnancy

Provider Characteristic	N	%	Crude OR	95% CI	P	Adjusted OR	95% CI	P
Facility Type	**112**							
Health Facilites	**75**	67.0	4.3	(1.6, 11.7)	<0.01	0.7	(0.2, 3.2)	0.67
Drug Outlets (ref)	**37**	33.0	--	--	--	--	--	--
Malaria Management Training								
None	51	45.5	--	--	--	--	--	--
Yes	61	54.5	4.8	(1.9, 12.1)	<0.01	4.7	(1.4, 15.7)	0.01
Knowledge Variable (ref='Not Known')								
1st Trimester as Contradindication	63	56.3	6.1	(2.1, 17.8)	<0.01	8.2	(2.3, 29.0)	<0.01
Return to Facility if no Improvement	58	51.8	2.7	(1.2, 5.9)	0.02	4.5	(1.7, 11.9)	<0.01
Sleep under ITN	103	92.0	3.7	(0.9, 14.8)	0.07	12.4	(1.9, 82.6)	<0.01
SP can only be used for MiP Prevention	62	55.4	2.6	(1.0, 6.5)	0.05	1.9	(0.6, 5.6)	0.26

**Crude model for each knowledge variable included facility type and Malaria diagnostic training. Adjusted model included all covariates..*

***Facility type is stratified at the health facility versus drug outlet level; the fully stratified model was unstable due to quasi-complete separation of data points.*

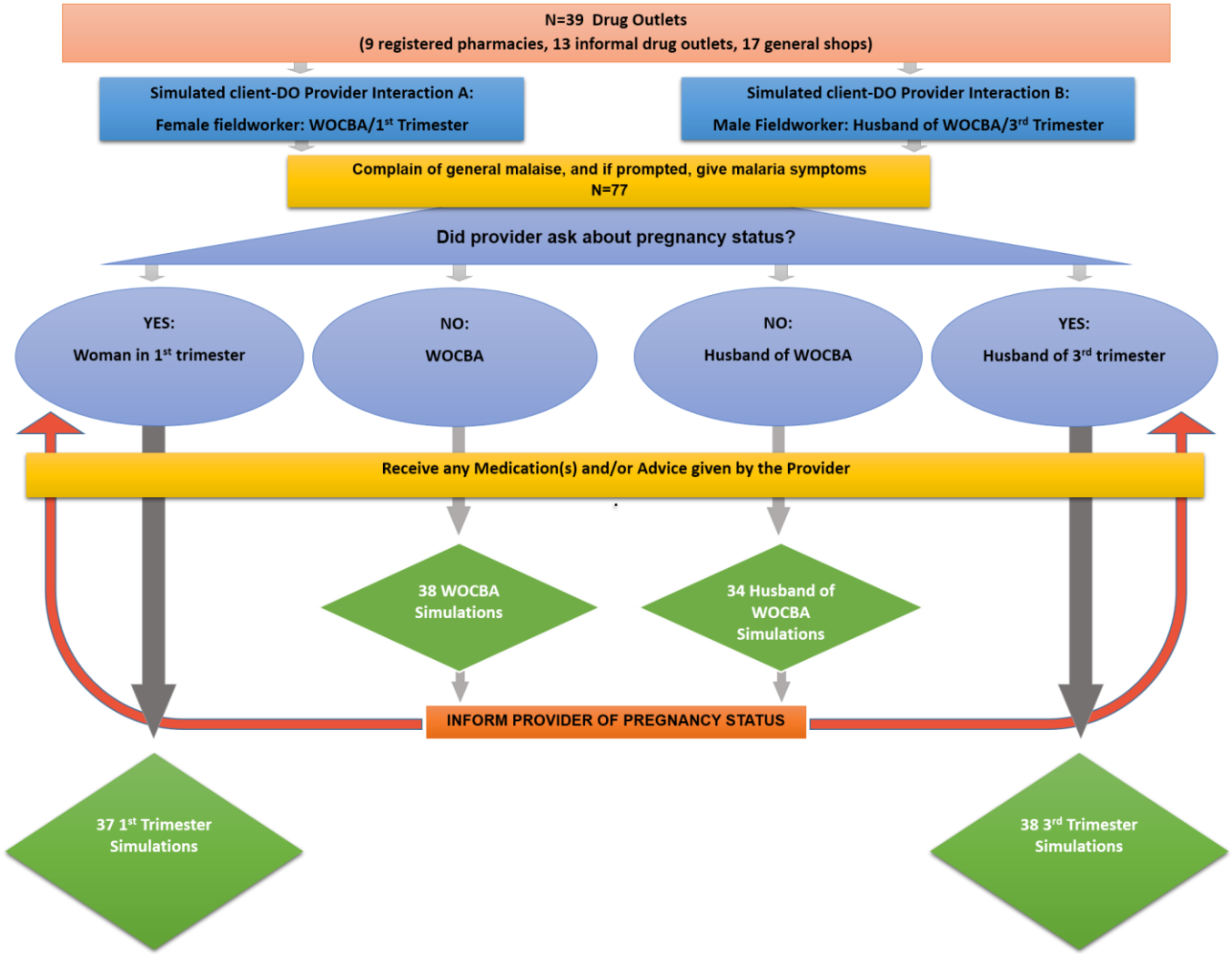
Table 19. Pearson Correlation Coefficients for Provider Practice Scores vs Provider Knowledge Scores for all Providers, stratified by Pregnancy

	Total Practice Score			
	Overall	Non-Pregnant	1st Trimester	2nd/3rd Trimester
Knowledge Score	n=290	n=150	n=46	n=94
	r	r	r	r
Case Management	**0.49251**	**0.24105**	**0.66380**	**0.54243**
Malaria Diagnostics	**0.44794**			
Pregnancy Assessment	**0.30837**			
Treatment & Dosage	**0.43364**			

**All P-values are <0.01*

FIGURES

Figure 1. Drug Outlet & Simulation Algorithm



CHAPTER III

Summary, Public Health Implications, Possible Future Directions

Improving Healthcare Provider Case Management Practices for Malaria in Pregnancy in Western Kenya: A Clustered Randomized Control Trial

Background Information and Scientific Rationale

Background Information

Malaria in Pregnancy (MiP) can have devastating consequences for the woman and her unborn baby including maternal anemia, fetal loss, intrauterine growth retardation, premature delivery, and low birth-weight (LBW) [2]. In Kenya, an estimated 1.3 million pregnancies occur in areas at risk for P. falciparum malaria infection annually [1]. MiP transmission in rural, western Kenya remains particularly high. An annual cross-sectional survey conducted in this area at peak transmission time in 2012 found about 19% of women of childbearing age (WOCBA) positive for malaria parasitemia [19] and is consistent with similar studies conducted in previous years [20,21].

As of 2012, the World Health Organization (WHO) and Kenyan Ministry of Health recommend that pregnant women use long-lasting insecticidal nets (LLINs), intermittent preventive treatment (IPTp) with Sulfadoxine pyrimethamine (SP), and receive prompt diagnosis and appropriate treatment of malaria with a safe and effective drug [6]. In 2009, the Kenyan Ministry of Health enacted the New Malaria Strategy to conduct nationwide training for front-line health workers on malaria case management [10]. However, correct case management of MiP remains suboptimal as the strategy was heavily focused on prevention of MiP and the distribution ITNs and LLINs [7].

Correct case management for MiP is defined as a woman of child-bearing age having been tested and diagnosed with malaria via rapid diagnostic test or blood slide microscopy, having been assessed for pregnancy, including gestational age, and having received the correct drug and dosage for respective trimester [7].

Rationale

Although prompt and effective treatment is a cornerstone of malaria control, there are still extensive knowledge gaps and poor adherence in Kenya to the National Guideline for the Diagnosis, Treatment and Prevention of Malaria with respect to case management of pregnant women, particularly for women in the first trimester of pregnancy [6]. A recent study by KEMRI-CDC showed that correct case management for malaria in pregnancy was only 32% among healthcare providers in the study area [Riley]. Treatment with a contraindicated drug (i.e. ACT) can lead to potential teratogenicity in the first trimester of pregnancy; this may also occur inadvertently if the provider fails to assess for pregnancy status. Treatment with ineffective drugs or inadequate dosage of the correct drug can lead to malaria treatment failure and further exacerbate emerging drug resistance of certain antimalarials in sub Saharan Africa. Timely, significant efforts to increase pregnancy assessment and correct prescribing practices are required to improve the safe and effective case management for MiP [Riley].

A variety of methods have been proposed to improve general case management including revised registers, informational memos, text message reminders, and mHealth solutions [29,30]. However, these methods have not been implemented specifically for MiP because provider adherence to MiP guidelines has not previously been studied. KEMRI-CDC is uniquely positioned to address this issue given our long-term presence in this area of Kenya, recent novel research on provider adherence to MiP guidelines, and existing partnerships with the National Malaria Control Program (NMCP) and district health management teams in the study area.

There is an immediate need for information on the effectiveness of techniques to increase provider adherence to MiP case management guidelines to reduce morbidity and mortality related to MiP. Therefore we are proposing a cluster randomized controlled trial to test the hypothesis that implementation of improved registers and/or introduction of SMS text message reminders to health facility staff will improve provider adherence to and knowledge of case management guidelines for MiP. The trial will be conducted in 50 health facilities in Siaya County in western Kenya and will take place over 14 months, exclusive of analysis and results dissemination.

This study aims to improve overall case management of MiP in Kenya and ultimately reduce morbidity and mortality related to incorrect treatment. On a larger scale, these results could contribute to strategies for improving MiP case management in malaria affected countries around the world and inform strategies for improving general provider case management in low resource settings.

Objectives

Study Objectives

In this study, we aim to assess three strategies to improve knowledge and adherence to the national guidelines for malaria in pregnancy. The three strategies include:

Objective 1

To assess the effect of case management aids on improvement of provider adherence to case management guidelines for MiP

Aim 1a: To evaluate the effectiveness of a memo with simple clinical algorithm

Aim 1b: To evaluate the effectiveness of improved facility registers in the Antenatal Care Clinic (ANC) & Outpatient Department (OPD)

Aim 1c:To evaluate the effectiveness of improved facility registers in ANC & OPD and SMS text message reminders for providers

Objective 2

To assess the effect of case management aids on improvement of provider knowledge to case management guidelines for MiP

Aim 1a: To evaluate the effectiveness of a memo with simple clinical algorithm

Aim 1b: To evaluate the effectiveness of improved facility registers in ANC & OPD

Aim 1c:To evaluate the effectiveness of improved facility registers in ANC & OPD and SMS text message reminders for providers

Objective 3

To evaluate the feasibility of adoption of interventions to improve knowledge and adherence to MiP case management guidelines through providers' self-reported use

Study Outcome Measures

Primary Outcome Measures

Outcome 1- Correct provider MiP case management practice for pregnancy status as specified in the Kenya National Guidelines

Secondary Outcome Measures

Outcome 1- Correct provider MiP case management knowledge for pregnancy status as specified in the Kenya National Guidelines

Outcome 2- Provider usage level of respective interventions

Study Design

This will be a step-wise, cluster randomized trial in and around the KEMRI/CDC Health and Demographic Surveillance System (HDSS) area in Siaya County, western Kenya. This will be a two-phase trial with three main interventional components studied. Clustering will occur at the health facility level. Facilities will be split into strata to account for the variation in correct MiP case management practices between facilities based on the 2013 baseline study. In Phase 1, all facilities will receive the memo with simplified clinical algorithm. In Phase 2 facilities within each strata will then be randomized to one of two treatment arms. Facilities in Arm 1 will receive revised facility registers for ANC and OPD; facilities in Arm 2 will receive revised facility registers for ANC and OPD and providers in these facilities will receive various SMS text message reminders 3 times per week that detail correct MiP case management practice. An assessment of provider case management practice and knowledge will be performed at the end of each phase; the 2013 study will be used as the baseline.

Study Area

The study will be carried out in and around the KEMRI and CDC Health and Demographic Surveillance System (HDSS) catchment area in Siaya County, Nyanza Province in western Kenya. The HDSS collects birth, death, and migration information quarterly from a large, rural area of approximately 700 km^2 with 220,000 inhabitants [19]; it is culturally homogeneous, with 95% of people being ethnically Luo. The HDSS serves as a platform for a variety of studies including cross-sectional surveys, cohort studies and large clinical trials. Malaria transmission is perennial and holo-endemic in this region with peaks following the two rainy seasons, from March through May and October through December. Nationally, Siaya County bears the highest burden of malaria with an estimated population prevalence of 38% [24]. In the study area,

approximately 20% of pregnant women coming for the first antenatal clinic visit are parasitemic [20], and 18% of women delivering in Siaya District Hospital had placental malaria [21].

Study Population

The study population receiving the intervention will consist of healthcare providers and pharmacists in public and private health facilities in the study area. The study population involved in the assessment component will consists of providers and pharmacists in the aforementioned facilities, as well as women of child bearing age being treated for febrile illness in these facilities at the time of assessment.

Methodology

The goal is to determine whether these strategies improve adherence to standard malaria treatment guidelines for pregnant women in Kenya. Successful strategies to improve adherence to treatment guidelines are expected to reduce morbidity and mortality due to malaria, in support of the revised Kenya Malaria Strategy, 2009-2017, which aims to reduce malaria related morbidity and mortality by two-thirds of the 2007/2008 level by the year 2017.

Phase 1

Before-and-after comparison of a simplified memo to improve provider adherence to treatment guidelines for malaria in pregnancy in health facilities

A 2013 KEMRI-CDC study observed correct MiP case management practice in only 32% of providers in health facilities; we will use this study as the baseline for comparison of our intervention [Riley]. To improve adherence to treatment guidelines, we will introduce a one-page memo detailing algorithms simplifying the correct diagnostic and treatment guidelines for malaria in pregnancy. The memo will be reviewed and delivered via a Ministry of Health supervisory team to each health facility. This is currently the standard of care (SoC) for improvement of

provider practice in this region of Kenya. A previous study delivering a similar memo with simplified guidelines for IPTp in health facilities was successful in improving coverage of IPTp from 21% to 52% [KEMRI-CDC unpublished data].

Phase 2

Before-and-after comparison and between-arm comparison of improved registers and improved registers plus SMS text message reminders to improve provider adherence to treatment guidelines for malaria in pregnancy in health facilities

Arm 1- Improved Registers in ANC & OPD

Following the second baseline assessment of MiP case management, health facilities will receive new registers[1] for ANC and OPD that capture pregnancy status and gestational age, screening for fever within past 48 hours, any malaria diagnostics done and any malaria treatment prescribed with details for drug and dosage regimen. These registers will be implemented by the Siaya County's Department of Health and the Malaria Control and Elimination Program in Africa (MACEPA). After six months of introducing the memo and register, we will compare adherence to treatment guidelines with that before the introduction of memos and registers.

Arm 2- Improved Registers in ANC & OPD and SMS Text Message Reminders sent to Providers

Following the second baseline assessment of MiP case management, health facilities will receive the new registers for ANC and OPD described above and will also receive 3 times weekly text message reminders of correct prescribing practice. A recent study in coastal Kenya showed 24.5% (CI: 8.1-41.0) improvement in pediatric malaria case management in rural health facilities

[1] Facility registers are already standard practice. We are implementing improved registers to promote adherence to MiP case management guidelines.

after 6 months of 2 daily text messages to health providers [29]. Another study in Papua New Guinea showed that 2 daily text message reminders of malaria treatment guidelines was acceptable and feasible though there was a stronger preference for messages delivered in the morning and there was some indication of saturation [12]. In light of this, we believe 3 times weekly is a good balance between exposure and saturation.

A final assessment for provider adherence and knowledge to MiP case management guidelines will be completed following 6 months of phase 2 interventions. Outcome variables will be compared to the second baseline assessment of MiP case management and between intervention and control arms.

Data Collection

All survey-related data collection will be carried out in the participants' preferred language of Dholuo, Kiswahili, or English.

Assessment of Correct MiP Case Management Practice in Health Facilities

Exit Interviews (CRF 1)

Exit interviews with clients (18-49 years) presenting with febrile episode will be conducted by trained fieldworkers. We will capture women with the following criteria at each facility during the assessment period:

1) Women of childbearing age who could potentially be pregnant

2) Women in their 1st trimester of pregnancy

3) Women in 2nd/3rd trimester of pregnancy

Women will be asked questions related to provider inquiries on symptoms, pregnancy status, allergies, etcetera, as well as any tests performed, treatment(s) provided, and advice given by the provider.

Assessment of MiP Case Management Knowledge and Interventional Tool-Usage in Health Facilities

Provider Survey (CRF 2)

A standardized questionnaire administered by trained interviewers at the end of each intervention period will be used to assess provider knowledge of several scenarios related to the treatment of malaria in pregnancy and assess provider usage and attitudes towards respective interventional-tools. Scenarios related to treatment of MiP will include questions on parasitological diagnosis, pregnancy assessment, 1st and 2nd line treatment regimens and contraindications for given pregnancy status and trimesters as applicable. Providers will also be asked the same questions from the Interim Interventional Tool-Usage Assessment detailed below.

Interim Interventional Tool-Usage Assessment in Health Facilities

Provider Survey (CRF 2.1)

A short, standardized questionnaire administered by trained interviewers after the first 3 months of Phase 2 will assess provider usage details related to use, ease of use, and attitudes toward improved practice regarding the respective Phase 2 intervention employed at their facility. This will be used for monitoring purposes and to compare usage at 3-months and 6-months.

Data Management

Data for all case reporting forms (CRFs) will be collected electronically via smart phones equipped with ODK software; each ODK programmed form will have in-built range checks and skip-patterns to minimize errors. Data will be backed up daily to cloud-based storage. The data

manager will run data queries on a weekly basis to assess if there are any issues with the data (looking at ranges and consistency between the questions).

Study Enrollment and Withdrawal

This will be a step-wise, cluster randomized trial in and around the KEMRI/CDC Health and Demographic Surveillance System (HDSS) area in Siaya County, western Kenya. Clustering will occur at the health facility level. To account for the variation in correct MiP case management practices between facilities, facilities will be split into two strata, 1) facilities with an average correct provider practice above 32%, and 2) facilities with an average correct provider practice below 32%.

Subject Inclusion Criteria

The health facility:

- within the HDSS boundaries and surrounding areas (within 5km of the HDSS border)
- be operational
- stock antimalarials

The provider:

- be a nurse (enrolled or registered), clinical officer, medical doctor, or pharmacist
- work in OPD, ANC, facility pharmacy, or work in a Dispensary-level health facility

For the exit interviews:

- Any woman (18-49 years) presenting at OPD, ANC, or Dispensary-level health facility for a febrile episode and is able to provide informed consent

Subject Exclusion Criteria

We will exclude any health facility or person who:

- Does not consent to participate
- Does not meet the inclusion criteria above

Treatment Assignment Procedures

All eligible health facilities in the study area will receive the memo with clinical algorithm (SoC) in Phase 1 of the trial and data will be collected via Assessment 1. At the start of Phase 2, all health facilities will be stratified on rate of primary outcome (correct MiP case management practice) observed in the 2013 baseline study:

1) Facilities with an average correct provider practice at or above 33%, and

2) Facilities with an average correct provider practice below 33%

The percentage of providers at a health facility with correct MiP case management practice is not normally distributed and is positively skewed to the right. The 32% cut-off was chosen based on comparable number of facilities per strata and deemed to be appropriate after discussion with a biostatistician.

Randomization Procedures

Using Excel, facilities within each strata will then be assigned a random number between zero and one using the RAND function and then numerically sorted (using SORT function); the first 50% in each strata will be allocated to Arm 1 and the remaining 50% will be allocated to Arm 2.

Study Schedule

Before starting any study-related activities a series of meetings will be held with community representatives to present the proposed study and get feedback as well as any concerns or queries. The meetings will involve the County Minister of Health, District Ministers of Health, and full District Health Management Teams (DHMTs).

The fieldwork portion of the study, inclusive of Phase 1 and Phase 2 and exclusive of data analysis and follow-up, will take place over a consecutive 14-month period. 'Study Schematic' and 'Schedule of Events' located in the appendix provide visual representation.

Screening

All health facilities within the study area will be visited and screened for eligibility over a one-month period by a district MOH representative and the study coordinator prior to the Phase 1 memo delivery component. Verbal consent will be obtained from the In-Charge at the facility for a) Phase 1 memo delivery, and b) Phase 2 interventions.

Enrollment/Baseline

All consenting facilities will be enrolled at the time of screening. All providers present at the facility on the day of screening visit will be informed of Phase 2 interventional procedures and those providers that agree will provide written consent and provide their mobile number(s) with the understanding that they may or may not receive text messages. A baseline assessment at this point is unnecessary given that baseline data was captured in 2013.

Follow-up

Data will be disseminated to county and district health management teams in a joint feedback meeting, and presented to the national malaria in pregnancy technical working group and to the case management technical working groups through scheduled Malaria Control Unit meetings. In addition, data will be presented internationally at various meetings.

Assessment of Safety

Specification of Safety Parameters

There is no foreseen interventional-related risk.

Interview-related risk is minimal. However, there is potential for a patient to receive a contraindicated or ineffective treatment. If this occurs it will be dealt with on-site immediately via notification of patient, provider, and correction of prescription and future practice.

Methods and Timing for Assessing, Recording, and Analyzing Safety Procedures

Adverse Events

In case during an exit interview, it is noticed that a woman has been given a non-recommended antimalarial for her trimester of pregnancy, the fieldworker will inform the patient of the national treatment guidelines and the patient will be given the appropriate antimalarial according to the national guidelines. On the same day, the fieldworker will assess the drug stocks in order to ascertain whether the recommended medications are in stock, and whether any substitutions were made as a result of stock-outs.

Reporting Procedures

Any errors in prescribing practice found during an assessment phase will be brought to the attention of the respective provider and the national guidelines for management of malaria in all trimesters of pregnancy emphasized. If it is noticed that a provider continues to prescribe

contraindicated or ineffective treatment when the appropriate drug is available, the provider will be reported to the facility In-Charge.

Type and Duration of Follow-up of Subjects after Adverse Events

Any errors in prescribing practice found during an assessment phase will be brought to the attention of the patient, the correct drug, dosage regimen, and applicable advice will be given and the the national guidelines for management of malaria in all trimesters of pregnancy emphasized.

Halting Rules

We do not currently foresee any reasons (safety-related) or otherwise for the study to be halted. However, if an applicable issue or event arises the study will be halted immediately and postponed until the issue has been fully reviewed and resolved by the study team and community partners.

Safety Oversight

Given the nature of the study there are no safety-related concerns. The study coordinator will act as NON-independent Safety Monitor at biweekly follow-up visits per facility to address any concerns the facility in-charge or facility staff may have.

Statistical Considerations

Study Hypotheses

All alternative hypotheses are superiority comparisons.

Phase 1

H_o: Introduction of the memo with clinical algorithm (SoC) at the health facility level will have no effect on provider MiP case management practices.

H_a: Introduction of the memo with clinical algorithm (SoC) at the health facility level will have a positive effect on provider MiP case management practices.

Phase 2

H_o: Introduction of improved registers at the health facility level will have no effect on provider MiP case management practices.

H_a: Introduction of improved registers at the health facility level will have a positive effect on provider MiP case management practices.

H_o: Introduction of improved registers at the health facility level and SMS Text Message reminders at the provider level will have no effect on provider MiP case management practices.

H_a: Introduction of improved registers at the health facility level and SMS Text Message reminders at the provider level will have a positive effect on provider MiP case management practices.

H_o: Introduction of improved registers at the health facility level and SMS Text Message reminders at the provider level will have not have a greater effect on provider MiP case management practices than just the introduction of improved registers.

H_a: Introduction of improved registers at the health facility level and SMS Text Message reminders at the provider level will have a greater effect on provider MiP case management practices than just the introduction of improved registers.

Sample Size Considerations

All facilities in the study area (N=51) will receive the memo with clinical algorithm in Phase 1. We assume that the overall proportion of correct case management in the study area will be approximately 40% following the introduction of simplified memo in Phase 1. We very minimal loss to follow-up (not exceeding 2%) at the facility level given that all facilities have expressed interest in being part of the study, have historically been compliant with facility-level interventions, and the interventional period is relatively short.

Due to observed inter-cluster variation (i.e. between facilities) at baseline in the primary outcome, and intra-cluster variation due to the range in number of providers (1-7 providers) working in eligible departments at a health facility, it was difficult to calculate an accurate k or ICC. Back-calculated values were well below 0.25. To be conservative, we chose to use a within-stratum coefficient of variation (k_s) of 0.25, to detect an improvement in adherence from 40% to 70% with 80% power at 0.05 significance, 50 facilities will be needed with an average of 3 providers per facility using the intervention. We will interview 3-4 patients and all providers utilizing the intervention per facility. The following formula was used:

$$c = 2 + (z_{\alpha/2} + z_{\beta})^2 \frac{\pi_0(1-\pi_0)/m + \pi_1(1-\pi_1)/m + k_m^2\ (\pi_0^2\ + \pi_1^2)}{(\pi_0 - \pi_1)^2}$$

In Phase 2 there will be approximately 75 providers across 25 facilities will be enrolled in each arm with the intervention introduced at the facility level. We will conduct 150-200 exit interviews with women of child-bearing age (both pregnant and non-pregnant) at the time of each assessment, exclusive of interim interventional-tool usage assessment. We will conduct approximately 150 provider surveys at the time of each assessment, including the interim interventional-tool usage assessment.

Planned Interim Analysis

Safety Review

Unless indicated otherwise, a safety review is unnecessary given that there is no foreseen interventional-related risk.

Efficacy Review

Interim analysis will be done via short provider survey at the three-month mark in Phase 2 of the study to assess interventional-tool usage and any problems associated with usage.

Final Analysis Plan

Frequencies, Chi-square, and logistic regression will be conducted for all binary outcomes, controlling for clustering at the health facility level and stratifying on base-outcome levels observed in the 2013 baseline study. Statistical analyses will be done using SAS (version 9.4).

Intention-to-treat analysis will be conducted on all primary endpoints regardless of interventional-compliance level. Per-protocol analysis will be conducted only on observations from health facilities with an average interventional-compliance at 75% or above, regardless of an individual provider's compliance at those facilities.

Objective 1

To assess the effect of case management aids on improvement of provider adherence to case management guidelines for MiP, each of the following will be analyzed:

- Proportion of providers inquiring about the pregnancy status and gestation of the client
- Proportion of providers using parasitological diagnosis & confirmation before treatment
- Proportion of providers providing the correct treatment and dosage for pregnancy status

- Proportion of providers who have performed all steps appropriately according to the current malaria treatment guidelines

With respect to:

- Memo with simple clinical algorithm
- Improved facility registers in ANC & OPD
- Improved facility registers in ANC & OPD and SMS text message reminders for providers

Objective 2

To assess the effect of case management aids on improvement of provider knowledge to case management guidelines for MiP, each of the following will be analyzed:

- Proportion of providers with correct knowledge regarding pregnancy status and gestational age inquiry methodology
- Proportion of providers with correct knowledge regarding parasitological diagnosis
- Proportion of providers with correct drug and dosage knowledge regarding prevention, treatment and contra-indications for a client's pregnancy status

With respect to:

- Memo with simple clinical algorithm
- Improved facility registers in ANC & OPD
- Improved facility registers in ANC & OPD and SMS text message reminders for providers

Objective 3

To evaluate the feasibility of adoption of interventions to improve knowledge and adherence to MiP case management guidelines through providers' self-reported use, each of the following will be analyzed:

- Proportion of providers who used the intervention (frequency-of-use scale)
- Proportion of providers who felt the intervention was easy to use (ease-of-use scale)
- Proportion of providers who felt the intervention improved their practice (likert scale)

With respect to:

- Memo with simple clinical algorithm
- Improved facility registers in ANC & OPD
- Improved facility registers in ANC & OPD and SMS text message reminders for providers

All data collected from the Assessment 1 performed at the end of Phase 1 (regarding memo with clinical algorithm will be comparatively analyzed with the 2013 baseline study. Assessment 2 outcome-related data collected at the end of Phase 2 will be comparatively analyzed to the Assessment 1 dataset and internally between Arm 1 and Arm 2. Usage data collected at the Interim Analysis point will be used for monitoring purposes and also compared to usage data collected via Assessment 2.

Ethics/Protection of Human Subjects

Ethics Standard

We foresee very low potential for breach of ethics in this study. All participating health facilities receive standard of care at a minimum and are eligible for participation in secondary intervention

during phase 2. Proposed interventions pose no perceived risk to the health facility, healthcare provider, or patient. Data collection procedures are observational in nature and are of minimal risk to the participants. The only inconvenience will be the time required to participate in the interview.

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6; 62 Federal Regulations 25691 (1997).

Institutional Review Board

Institutional Review Board (IRB) clearance (or equivalent ethics review clearance) will be obtained from all institutions affiliated with the co-investigators. CDC Atlanta and all other IRBs out of country will defer to the Ethics Committees for KEMRI-CDC and Kenya Ministry of Health. Any protocol or CRF amendments must be approved by all IRB and ethics review committees affiliated with study investigators prior to implementation.

Informed Consent Process

All healthcare workers at a facility included in the study will be informed of the intervention(s) being implemented at the respective facility. The information provided will include the purpose of the study, study procedures, target population, the risks and benefits to those who participate, confidentiality of the data and the voluntary basis of participation.

Informed Consent/Assent

Intervention

All providers that meet the inclusion criteria will be informed of and trained on the applicable intervention, and (in the case of SMS messaging) will provide their mobile number(s) after providing verbal consent. They will not be forced to adhere to any of the interventions and are free to withdraw from the SMS messaging component (if applicable) by notifying the study coordinator. At this point a questionnaire on intervention withdrawal will be employed if the provider consents.

Interviews

Written informed consent will be obtained from the respondent prior to beginning the exit interview or provider survey. The trained fieldworker will do their best to put participants at ease and give them the option of "don't know" where applicable. The respondent is free to withdraw from the interview at any time.

Exclusion of Women, Minorities, and Children (Special Populations)

All persons under 18 years are excluded from participating in the study. Children (under 12 years) are not a relevant population for this study. Female minors (12-17 years) who are present with febrile illness at a health facility are excluded from this study because questions surrounding pregnancy status may be culturally insensitive.

Subject Confidentiality

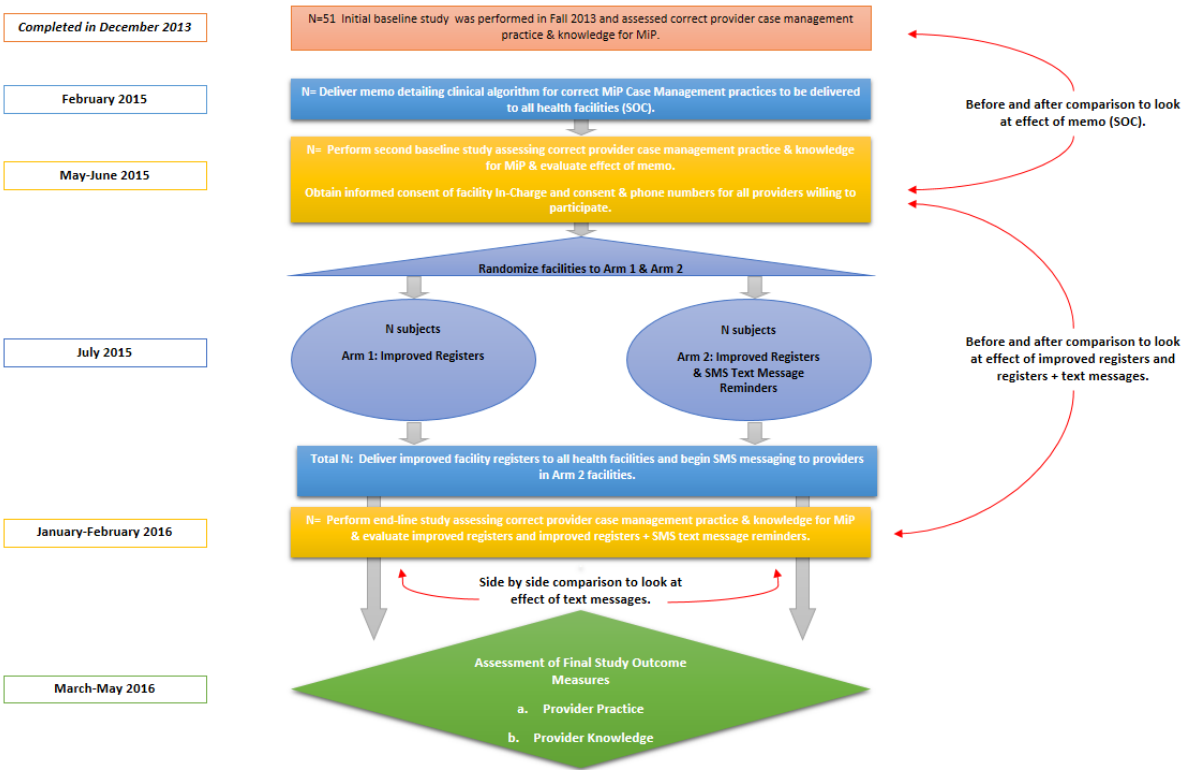
All data will be kept securely (consent forms and paper questionnaires in lockable area, all electronic data will be kept on password protected computers). Study staff will be trained on good clinical practice (GCP) and the importance of ensuring confidentiality. Health facilities and providers will be assigned unique identifiers during the time of informed consent; names of staff and facilities will not be mentioned in connection with the study's results.

Study Discontinuation

We do not currently foresee any reasons (safety-related) or otherwise for study discontinuation. However, if an applicable issue or event arises the study will be halted immediately and postponed until the issue has been fully reviewed and resolved by the study team and community partners, or the study will be discontinued.

Appendix A

Study Design Schematic



Schedule of Events

Time	Activity
January 2015	*Screening and Enrollment Period*
February 2015	*Delivery of simple memo to all health facilities in study area with MOH supervision*
May-June 2015	*2nd Assessment of correct prescribing practice & knowledge*
July 2015	*Introduction of improved facility register into ANC & OPD at facilities in Arm 1* *Introduction of improved facility register into ANC & OPD and SMS Text Message reminders to providers at facilities in Arm 2*
October 2015	*Interim Assessment of Interventional Tool-Usage for Phase 2*
January-February 2016	*3rd Assessment of correct prescribing practice & knowledge (Endline)*
March-May 2016	*Data analysis*
June 2016	*Dissemination of results*

National Guidelines for MiP Case Management

Kenyan National Guidelines for Diagnosis and Treatment of Uncomplicated Malaria		
All women of child-bearing age should be assessed for pregnancy via LMP, gestational inquiry, or pregnancy test		
Malaria Diagnosis	-Parasitological diagnosis via RDT or microscopy -Vulnerable groups (i.e. pregnant women) should only be treated on basis of clinical suspicion in facilities without diagnostic capacity	
	1st Trimester	**2nd/3rd Trimesters & Non-pregnant**
Treatment†	Quinine- 2 tabs, 3x day, 7 days	1st line: Artemether lumefantrine- 4 tabs, 2x day, 3 days 2nd line: Dihydroartemisinin piperaquine- 3 tabs, 1x day, 3 days
†Sulfadoxine-pyrimethamine, used for intermittent preventive therapy (IPTp), is not an effective treatment for acute malaria		