Evaluation of Pilot Implementation of Seasonal Malaria Chemoprevention on Morbidity in youngChildren In Northern Sahelian Ghana

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Research

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Abstract

Background

In Sahelian Africa, the risk of malaria increases with the arrival of the rains, during which most clinical malaria occur particularly in young children. Following successful trials in 2012, the World Health Organization (WHO) recommended the use of seasonal malaria chemoprevention (SMC) in areas where there is a seasonal peak in malaria. This study evaluated the pilot implementation of SMC in Northern Ghana.

Methods

Fourteen communities each serving as clusters were selected randomly from Lawra District of Upper West Region as intervention area and West Mamprusi District in the Northern Region as the control area all in Ghana. The intervention was undertaken by the National Malaria Control Program using Sulphadoxine Pyrimethamine plus Amodiaquine and standard WHO protocols. Before and after intervention surveys for malaria parasitemia and hemoglobin levels were assessed as well as monitoring of malaria morbidity.

Results

Incidence rates of severe malaria were 10 and 20 per 1000 person-years follow up in the intervention and comparison areas respectively with P.E of 45% (p = 0.62). For mild malaria, it was 220 and 170 per 1000 person-years in intervention and comparison area respectively with PE of − 25% (p = 0.31). Differences in anemia (Hb < 11.0g/dl) from baseline to end-line was a reduction of 0.16g/dl (p = 0.000) in intervention and an increase of 0.12g/dl (p = 0.002) in the control area. Mean Hb difference between baseline and end-line was a reduction of 0. 24g/dl (p = 0.000) in control and an increase of 0.39g/dl (p = 000) in the intervention area. At the end of the intervention, the proportion of children with asexual parasites reduced by 19% (p = 0.000) in the intervention and increased by 12%(p = 0.000) in the control area.

Conclusion

The feasibility of SMC in Northern Ghana was demonstrated as evidenced by high study retention, reduction in malaria parasitemia and anemia during the wet season.

Introduction

Malaria remains a major public health concern in Sub-Saharan Africa (SSA) despite a significant reduction in the global burden of the disease in the last two decades (1). Sub-Saharan Africa still accounts for most clinical cases and malaria-related deaths, which contributes about 10% of all under-five deaths in sub-Saharan Africa. Malaria continues to exert negative social and economic impact in many endemic areas. Economically it reduces productivity due to increased worker absenteeism and increased national health care spending. Socially malaria affects individual and household behaviors resulting in broad social costs with the attendant long-term effect on growth and development (1, 2).

Currently, the World Health Organization (WHO) recommends a combination of approaches for malaria control including the use of long-lasting insecticide-treated nets, indoor residual spraying, confirmation of cases and the use of artemisinin-based combination treatment for case management. (1, 2). In addition, intermittent preventive treatment in pregnancy and infancy are recommended for specific high-risk groups (1, 2). Intermittent preventive treatment of malaria in children (IPTc) has been found to be a safe method of malaria control that reduces significant proportion of clinical malaria illness in areas of marked seasonal malaria transmission. It also has substantial protective effect against all-cause mortality. Therefore, IPTc is a valuable tool that can contribute to the control of malaria especially in areas with short and marked seasonal transmission (3).

The WHO currently recommends Seasonal Malaria Chemoprevention (SMC) as a tool to prevent malaria among young children in areas with high seasonal transmission especially in the Sahelian areas of Africa (4, 5). The SMC is the intermittent administration of full malaria treatment course to children during the malaria season. This is to check infection by sustaining therapeutic concentrations of antimalarial drugs in the blood during the period of highest malarial risk (4, 5). WHO recommends sulfadoxine-pyrimethamine plus amodiaquine as the drugs of choice in the Sahel sub-region of sub-Saharan Africa, where the *P. falciparum parasite* is sensitive to both antimalarial drugs (4, 5). Across the Sahel sub-region, most childhood malarial disease and deaths occur during the rainy season, which is generally short (3–4 months). Giving effective antimalarial treatment at monthly intervals during this period protects against uncomplicated and severe malaria in young children (6–8).

The SMC approach is cost-effective and safe, and can be administered by community-health workers. In areas where SMC has been adopted it has helped in reducing the cases of malaria and proven to be very effective (6–8). Apart from reducing infection, morbidity and mortality, malaria anaemia and child wellbeing are also improved (6–8). Several studies involving children that were treated with the SMC regimen in different countries attest that SMC is very effective in the fight against malaria. It has therefore been suggested that SMC should be scaled up in other areas that had more incident and prevalent cases of malaria (6–8).

Despite the success, the SMC strategy also has some challenges. The implementation strategy and acceptance of treatment drugs have been an issue for some time. Previous studies have shown that some mothers do not administer the antimalarial medication as prescribed. Parents give several reasons for not adhering to the medication, such as the drugs being bitter and complaints of the negative side effects they get from these drugs. The issue of implementation and the last mile distribution across hard-to-reach areas have often emerged. Despite this, there is good adherence to the SMC drugs in most areas where it has been implemented, and care givers have attested to them being beneficial by helping them in reducing the incident cases of malaria cases (9–10).

The Ghana National Malaria Control Programme (NMCP) in 2014 proposed to adopt SMC using Sulphadoxine Pyrimethamine and Amodiaquine combination in Ghana (11). The adoption was to help reduce morbidity and mortality in children in the northern Ghana where malaria transmission is seasonal. This was to also improve the wellbeing and the livelihoods of many children and parents as time and resources are spent to cater for malaria that could be channeled into other productive ventures. However, there was a need for the NMCP to undertake a pilot study to determine the feasibility and effectiveness of SMC in the Ghanaian setting to inform policy decision for its scale-up. The Navrongo Health Research Centre (NHRC) was commissioned to evaluate a pilot study and to provide evidence for introducing SMC in the northern part of Ghana.

Methodology

Study setting: The study evaluation was undertaken by the Navrongo Health Research Centre (NHRC), a field station of the Research and Development Division of the Ghana Health Service (12). The NHRC runs the Navrongo Health and Demographic Surveillance System (NHDSS) a platform designed to provide an efficient platform for evaluating health and social interventions (12). The implementation of the intervention and control was done in two administrative districts; Lawra district, Upper West Region and West Mamprusi in Northern Region both located in the northern part of Ghana (12–14). Figure 1 shows the location of the NHRC and the two administrative districts in the respective regions. The study setting is characterized by dryness due to its proximity to the Sahel and Sahara. The vegetation is predominantly Savannah grasslands with clusters of highly drought-resistant trees. There are two main seasons in the area, the dry and wet seasons. The peak of the dry season stretches from November to March and the wet season from April to October with a peak in July to September which coincides with malaria transmission. In northern Ghana cases of clinical malaria are seasonal caused mainly by *Plasmodium falciparum* and transmitted by anopheles' mosquitoes with *An. gambiae s.l.* and *An. funestus* being the predominant vector species. (15–17). As part of efforts to reduce malaria transmission in Ghana, several interventions have been put in place, including indoor residual spraying and free distribution of long-lasting insecticide-treated bed nets. Intensive education on compliance and use of the available malaria interventions have also been taking place (11). Although these efforts have contributed to the reduction in malaria deaths, high case fatalities, and decreased testing rates have still been attributed to Northern Ghana (11).

Study areas: The study districts have similar weather and vegetation types as described above making them well suited for this study. The intervention area was the Lawra district (13) which lies in the North-Western corner of the Upper West Region of Ghana between latitudes 2^0 25"W and 2°45"W and longitudes 10°20" N and 11°00"N. The total population of the area was about 100,929 people. The main ethnic group in Lawra is the Dagaaba.

The district had five health centers, 10 Community-based Health Planning and Services (CHPS) compounds (18), three pharmacy shops, one clinic and one hospital which provides health services to the people in the area. The control area was at the West Mamprusi District (14), one of twenty districts in the Northern Region of Ghana and lies within longitudes 0°35'W and 1°45'W and latitudes 9°55'N and 10°35'N. The had a total population of about 180,877. There was one polyclinic, one health center, three private clinics, 6 CHPs compounds, and 15 pharmacy shops in this area. The people are mainly of Mamprusi ethnicity in the West Mamprusi district.

Study design: The study used a quasi-experimental design with before and after cross-sectional surveys. The implementation was during the main malaria transmission season from July 2015 to the end of the study in December 2015. The duration of participation for each child was six months. Enrolment was conducted over 2 weeks period and the post-implementation evaluation surveys lasted for 2 weeks. The study population included children aged 3 months to 59 months who were eligible for enrolment in the selected households and communities. Two cross-sectional surveys, one at baseline and the other at end line after 6 months were used for evaluation. The baseline survey took place in both study areas before drug administration. The enrolled children were followed up between the two surveys for episodes of severe and mild malaria. Other parameters documented included weight, height, malaria parasitemia, hemoglobin level and temperature.

Sample size estimation and Sampling strategy: The study was designed to have at least 90% power to detect a reduction in the incidence of severe malaria of 50% assuming the incidence rate of 0.04 per child per transmission season (i.e., 8 per 1000 child-months, based on data from 2009 from district health records showing there were 290 positive cases with fever or history of fever and a positive RDT among children under five years in the district from June- December, with an estimated total population of children of 7,000. District health records from 2010 showed a higher rate of about 0.1 per child per month, or 0.5per child per 5-month transmission season. The sample size calculation was based on the impact of SMC on severe malaria as a primary outcome. Effectiveness assumption is based on studies that showed a reduction in severe malaria by 65 to 86% (6–9). To demonstrate a 75% reduction in the proportion of severe malaria cases in the intervention districts a minimum number of 14 clusters per arm were required.

A cluster was taken as the community of residence as outlined by the Ghana Health Service District Health Directorate. Each community was a well-delineated area with defined boundaries. Using an average proportion of 0.36 of children under 5 years developing severe malaria and 50 children per cluster with an inter-cluster variation of 0.26, approximately 14 clusters were needed per arm to demonstrate a 75% reduction in the proportion of under-five children developing severe malaria at a power of 90 percent and a two-sided significance level of 5%.

All districts in the Upper West region were listed and one district (Lawra) was selected at random for evaluation of SMC. The control district, West Mamprusi, was selected at random from the Northern Region which had the same interventions against malaria as the Upper West Region apart from SMC. All communities in the selected districts were subsequently listed and fourteen out of 141 and 152 communities from Lawra District and West Mamprusi Districts respectively were randomly selected using the random sample selection command in STATA 12 statistical software to form` the study clusters. Each selected community was defined as the cluster, the unit of analysis. All the households in each selected community were labeled and listed. All households with eligible children were listed and 40 households randomly selected. In each selected household all eligible children were selected for participation and out of these the children whose guardians gave parental consent and were available for the 4-month duration of the study were selected for inclusion. Those children whose guardians could not give consent or were not likely to stay in the community for the duration of the study were excluded. A minimum of 50 children per village and 700 children per arm were recruited into the study. Where the community was too small to provide a minimum of 50 participants, the nearest community was added to it to make up a bigger community.

Study drug administration: Study drugs were supplied by National Malaria Control Programme. Formulations of Sulphadoxine -Pyrimethamine 500/25mg tablet (SP) and Amodiaquine (AQ) 153mg tablet were used. Infants 3–11 months old were dosed with half of a 153mg tablet of Amodiaquine given once daily for three consecutive days and a single dose of half of 500/25mg tablet of SP. Children 12–59 months were given a full tablet of 153mg Amodiaquine base given once daily for three consecutive days and a single dose of a full tablet of 500/25mg tablet of SP. The administration was done by direct observation therapy and given by community health volunteers. Children received medication for four consecutive months at monthly intervals between July and November.

To determine the proportion of children who experienced an adverse event, study participants in the intervention district were visited at home daily for three days during the administration of SMC and two days after the last

dose in each round of drug administration and a side effects questionnaire was completed to document and quantify adverse events that might have occurred since receiving the trial medication. Grading of the severity of adverse events was done by trained field workers. An adverse reaction was graded as mild (grade 1) if it was easily tolerated and moderate to severe (grade 2) if it interfered with normal activity or required treatment.

Malaria surveillance: A passive surveillance system to monitor malaria episodes was set up at the district hospitals and health centers in the study areas. Fieldworkers were stationed at health facilities as well as in the communities in both the intervention and control districts to pick up any episodes of mild or severe malaria by checking for malaria parasitemia before treatment was given. Participants were visited every fortnight to maintain their interest in the study and encourage them to seek health care promptly if any sickness developed. Field workers visited the children once a week during the period of drug administration to enquire about their health and completed a morbidity form if a child had any illness. If a child had a history of fever or vomiting within the past 48 hours the parents were advised to take their child to the nearest health facility for examination and treatment. Any mortality that occurred outside the health facility was to be investigated and a verbal autopsy questionnaire administered to help ascertain the cause of death at the Navrongo Health Research Centre (12).

Field workers were recruited and trained to do home visitations and in addition, they were trained to prepare thick and thin films, which were collected by the trial team for microscopic examination to crosscheck the RDT results. They were also trained to record and report any adverse events. In each community, trained community health workers (CHW) provided malaria case management services. Persons with fever were encouraged to attend the health post or health centre to be tested with an RDT and were treated with artemether-lumefantrine if tested positive. Consultations were recorded in a health facility register to document the test results and treatment given. In the intervention area, if a child was unwell on the day of the SMC visit, caregivers were asked to bring the child to the health post or hospital for testing with malaria RDT; those who tested positive were treated with artemether-lumefantrine and those who tested negative received SMC and were then referred to the nearest hospital.

Participants who presented at the health facilities with fever were similarly tested with an RDT and had thin and thick blood films taken by the nurse, which were read later. Treatment of study participants seen at the health facilities for other conditions was carried out per national guidelines. Registers for recording SMC administration with a list of all children enrolled in each village were made available for each field worker. In SMC villages, the dose of SP and AQ administered to each child was recorded in a register. All consultations for illness were also recorded in the registers and other details including date, symptoms, RDT results and treatment in case report forms. Besides, in each health facility, consultation records were reviewed by the field workers to identify all consultations of children from study villages.

Laboratory methods: Capillary blood was used for diagnosis for this study. To obtain this, the participant's heel or thumb was wiped using a swab moisturized in 70% alcohol. A sterile lancet was used to make a prick on the participant’s thumb or heel and squeezed gently to obtain a large drop of blood. To ensure good staining and standardization of reporting, the blood sample was transferred from the participant to a sterile microscope slide using a bulb pipette. One drop was placed in the middle of the slide and another about 15mm to the right of the slide for both the thick and thin films. These films were prepared using a card showing illustrations of a thick and thin-film as a guide. The blood was then allowed to air dry by placing slides in a horizontal position. Thin

films were fixed by placing slide horizontally on a bench with a small drop of methyl alcohol such that the thick film did not get fixed in the process. The slides were stained using a 10% Giemsa solution for ten minutes. The stains from the slides were washed using running water and allowed to dry. One of the two slides from each participant was examined using x100 oil immersion microscopic lens and the other archived for confirmatory testing. A sample was considered negative only after 200 high power fields had been read. Parasite counts were converted to parasites per microliter (µl), assuming a white blood cell count of 8000 leukocytes per µl of blood. In instances where there were discrepancies in the findings in a slide between the two initial technicians (positive or negative or a 50% or more difference in parasite density), a senior microscopist read the slide and his reading was deemed to be the correct reading. Hemoglobin was measured using Hemocue ® (Hb 801 system)

Data management and Statistical analysis: Village registers that listed each child's record in the census were printed for health workers to record SMC administration and consultations for illness. All consultations for illness were recorded and the register checked for completeness during weekly supervision visits. Completed forms by trained personnel on the study were checked by field supervisors and data managers for consistency and accuracy before logging it out for data entry. All data collected were entered twice into a database using EpiData software. Again, automatic checks for consistency and range errors were done, and queries resolved before the dataset was locked for analysis. Other data management procedures such as taking the consent of the participants before participation in the research was also done. Effects of SMC on the prevalence of parasitemia, gametocyte carriage, mean hemoglobin concentration, and proportions of anemia (Hb < 110g/l) and severe anemia (Hb < 60g/l) were estimated from the survey at the end of the transmission season. The results were presented in tables and figures. Analyses were performed using Stata version 14 (Stata Corp, College Station, Texas). Descriptive statistics are presented for continuous variables.

Ethics approval and Community engagement: This study was conducted in full conformity with the current revision of the Declaration of Helsinki and with local regulatory requirements, to offer maximum protection to the subject. Members of the study team held community engagement meetings with community, administrative, and religious leaders to explain the aims and activities of the study. This was also done to seek community consent and to promote community ownership of the program. Staff then visited each household to explain the study in the local language, provided an information sheet, and sought signed consent from parents. Children whose parents consented were enrolled, and mothers/caregivers were issued with a unique identification card bearing the details and study number for each eligible child in their care. The cards were used to identify children if malaria was diagnosed and, for those in clusters randomized to receive SMC, to document SMC courses of treatment received. A data and safety monitoring board were convened to oversee the project and review data on tolerability and safety.

Study Results

Baseline characteristics: Seven hundred and thirty-one (731) children were recruited from the intervention district and 708 from the control district. Table 1 shows the background characteristics of the children recruited in both districts. Overall, 54.1% of participants were males and most of the children were aged 25–59 months (60.1%). The average weight of children at baseline in control district was 11.5 kg (95%CI 11.09, 11.90) and in the intervention district was 11.09kg ((95%CI 10.87, 11.32). Again, the average height (metres) among children at

baseline in the control in the district was 82.71 (95%CI 81.82, 83.61) and 86.93 (95%CI 86.05, 87.81) in the intervention district.

Table 1
Background socio-demographic characteristics of the study participants.

Attributes		Control District (N = 708)		Intervention District (N = 731)	
	Category	n (%)	(95%CI)	n (%)	(95%CI)
Sex	Male	385(0.54)	(0.49, 0.59	393(0.54)	0.49, 0.59
	Female	323(0.46)	0.41, 0.51	338(0.46)	0.41, 0.51
Birth order	First	156(0.22)	0.15, 0.29	202(27.6)	0.24, 0.36
	Second	204(0.28)	0.22, 0.34	181(24.8)	0.19, 0.31
	Third	146(0.21)	0.14, 0.28	144(19.7)	0.13, 0.27
	four or more	202(0.30)	0.24, 0.36	204(0.28)	0.22, 0.34
Age groups	3- 6months	61(0.09)	0.07, 0.11	38(0.05)	0.04, 0.07
	6- 12months	106(0.15)	0.12, 0.18	60(0.08)	0.06, 0.10
	13–24 months	154(0.22)	0.19, 0.25	155(0.20)	0.17, 0.23
	25–59 months	387(0.55)	0.51, 0.59	478(0.65)	0.61, 0.68
Educational status of care giver	None	649(0.92)	0.90, 0.94	478(0.65)	0.61, 0.68
	Primary	34(0.05)	0.03, 0.07	196(0.27)	0.24, 0.30
	Secondary	17(0.02)	0.01, 0.03	39(0.05)	0.04, 0.07
	Tertiary	8(0.01)	0.01. 0.02	18(0.02)	0.01, 0.03
Temp. ≥ 37.5□C	Yes	10(0.014)	0.004, 0.020	30(0.04)	0.03, 0.06
Antimalaria Use in ≤ 2 weeks	Yes	3(0.004)	0.009, 0.012	26(0.04)	0.03, 0.06
IRS	Yes	651(0.92)	0.90, 0.94	720(0.98)	0.97, 0.99
ITN Use	Yes	493(0.70)	0.67, 0.73	727(0.99)	0.98, 1.00
Fever ≤ 2 weeks	Yes	27(0.04)	0.03, 0.06	40(0.06)	0.04, 0.08

Overall bed net use was almost universal in intervention district (99.5%) as against 69.5% in the control district. Though Indoor Residual Spraying against malaria was being used by both districts, 57(8.1%) of the participants in the control district have not had their house sprayed. For children reporting fever in the week before the survey, 27(3.8%) of children in control district reported having fever compared with 40 (5.5%) % of children in the intervention district. However, 30(4.1%) of children in intervention district compared with 10(1.1%) in the control

district had temperature ≥ 37.5□C at the time of the enrolment. The use of antimalarial two weeks before the survey was higher 26 (3.6%) in intervention district compared with 3(0.4%) in control district (Table 1).

Incidence rates of confirmed severe and uncomplicated malaria: A total of nine (9) cases of severe malaria were recorded in the two districts. There were three (3) cases in the intervention area and six (6) in the non-intervention area including one (1) death. The incidence rates of severe disease in the intervention district were 10 per 1000 person-years at risk as against 20 per 1000 person-years at risk in the control district with an adjusted rate ratio of intervention to control district of 0.52 giving protective effectiveness of 48% (p = 0.62) against malaria (Table 2). For clinically diagnosed malaria with any level of parasitemia, the incidence rates were 220 and 170 per 1000 person-years at risk for intervention and control respectively (Table 2). There was only one death in the study due to severe malaria and it occurred in the study control district.

Table 2
Impact of SMC on Episodes of clinical malaria

Outcomes	Intervention area		Control area		Unadjusted IRR	Adjusted IRR	PE (95% CI)	P-value
	n episodes (years at risk)	Incidence rate (95% CI)	n episodes years at risk	Incidence rate (95% CI)				
Malaria diagnosis with any asexual parasitaemia	55 (241.53)	0.22 (0.17–0.30)	42 (243.69)	0.17 (0.13–0.23)	1.29 (0.83–1.99)	1.25 (0.81–1.93)	-25	0.31
Malaria diagnosis with parasitaemia > = 5,000	46 (241.53)	0.19 (0.14–0.25)	31 (243.69)	0.12 (0.09–0.18)	1.48 (0.92–2.38)	1.42 (0.88–2.30)	-42	0.15
Severe Malaria	3 (307.2)	0.01	6 (285)	0.02	0.45	0.52 (0.04–7.04)	48	0.62

Effect of SMC on asexual parasitemia: The proportion of children with parasites increased significantly from 9% (95% CI 7, 11) at baseline to 21% (95%CI 18, 24) at the end-line in the control district (P < 0.0001). In intervention district, however, the proportion of children carrying asexual parasites reduced significantly from 31% (95%CI 28, 36) to 12% (95%CI 10, 15), a difference of 19% (95%CI 15, 23) p < 0. 000.1. At baseline, the geometric mean trophozoite and gametocyte counts for intervention district were 1883 parasites/dl and 75 parasite/dl respectively. Both increased at the end-line to 3349 parasites /dl and 209 parasite/dl respectively. The number of children carrying gametocytes almost doubled (from 13 to 22) at the end of the SMC administration.

In the control district, the geometric mean trophozoite and gametocyte counts were 370 parasites/dl and 204 parasites/dl respectively at baseline and 1452 parasites /dl and 123 parasites/dl at endline. The geometric mean gametocyte count was lower than the baseline at four (4) count and 35 at endline.

Effect of SMC on Hemoglobin (Hb) levels: The mean Hb level of participants at baseline in the intervention area were 10.79 g/dl (95%CI 10.69, 10.88) and this increased to 11.18g/dl (95%CI 11.07, 11.31) at the end line. For the control area, the mean Hb levels of participants reduced from 10.77 g/dl at baseline to 10.53 g/dl at endline. For all participants present at the end line, there was a mean reduction in Hb levels of 0.24g/dl for participants at the control district and increase of 0.39g/dl for participants from the intervention district and both were significant ($p < 0.0001$).

The proportion of children with Hb < 11.0g/dl and Hb < 8.0g/dl at baseline was 55% (95%CI 51, 58) and 4% (95%CI 3, 5) respectively in the intervention district and they were similar to the respective proportions in the control district. At the end line, the proportion of children anemic with Hb less than 11.0g/dl and 8.0g/dl reduced to 39% (95%CI 35, 43) and 2% (95%CI 1,3) respectively and both were statistically significant ($P < 0.0001$). In the control district however, both proportions increased from 55–63% in those with Hb < 11/0g/dl and from 4–6% in those HB < 8g/dl and were also statistically significant ($P < 0.0001$).

Adverse events experienced by participants following SMC administration (Table 3): Of the 731 children recruited in the intervention district, 635(87%) received the second dose, while 587(80%) received the third dose. In the last round, 621(85%) took the intervention drug. Most participants received the intervention except those who had travelled or had taken prior malaria treatment. There was no severe adverse event. At least 11% of children experienced one adverse event or the other during each round of administration. Diarrhea, vomiting, and fever were the most experienced adverse events during the four rounds of SMC administration. Most of the adverse events were malaria-like symptoms and were mild to moderate and all resolved within the week. The frequencies of adverse events experienced are summarized in Table 3.

Discussion

Seasonal Malaria Chemoprevention (SMC) has been shown to be effective in the guinea savanna vegetation zones where there is intense malaria transmission in the very short rainy season (1–6). Several studies have demonstrated the efficacy of SMC under varying health systems and conditions (3, 6, 7). To help assess the feasibility and potential challenges of scaling up the SMC as a malaria control tool in northern Ghana, a pilot programme was proposed and implemented under the Ghanaian public health system. This is in line with global interest in ensuring how health system resources particularly in low resource settings like ours are used effectively. The study was therefore designed to determine how SMC as a malaria control tool could be operationally initiated and scale up in the vast impoverished northern Ghana in the most efficient and effective way.

In general, efficacy is the utility of a given intervention under controlled conditions, whereas the efficacy of SMC is not in dispute for SMC to be effective in the Ghana health system means that the intervention should have a meaningful effect on the population in our local settings. The efficacy of the SMC intervention is well documented in many trials but its meaningful effect on patients in different health systems is sometimes varied (1–6) and for the health system conditions in Ghana was unknown. The success of SMC introduction into Ghana health system depends on a complex interplay of factors including the local community dynamics, drug acceptability, climate conditions, malaria transmission dynamics and population distribution. The leadership of the National Malaria Control Programme in Ghana, decided to use two regional health administrations in northern Ghana to pilot SMC as a malaria control tool and employed an independent evaluator to document the

outcome of the pilot. This was to test how different stakeholders could work together for an effective and efficient introduction of the seasonal malaria chemoprevention in Ghana.

From the study results, the overall study retention rate was very satisfactory ranging from about 87% after the first dose to about 85% in the fourth and last dose. This is very impressive and consistent with previous SMC studies (3). High participant retention in research is important as it serves as a proxy of how effective a programme will be if it is fully scale up in normal conditions. High dropouts in programme interventions can engender staff apathy, increase implementation costs and longer duration of implementation among others. In addition to the above findings, the information available indicated that the staff numbers were optimal for the scaleup and, parents were very cooperative and appreciative of the intervention. This shows the potential acceptance and possible public health impact seasonal malaria chemoprevention will have in these settings. It also shows the successes the introduction of SMC could have and missed opportunities if not introduced. These are further supported by the reported adverse events which were mild and consistent with routine malaria symptoms ranging from ten percent to fifteen percent.

Furthermore, how the SMC when scaled up could operationally impact on malaria infections, severe malaria and malaria mortality within the existing health system of northern Ghana was also revealed. The results showed a trend towards a good impact on the disease outcomes. Though the number of severe outcomes captured in this study was low, the number in the control area was more than double that of the intervention area. While the difference was not statistically significant probably due to the small numbers and the sample size, as a pilot study this gives an indication how effective the SMC intervention could be in our settings when the actual programme is implemented and scaled up. Moreover the rate of 10 per 1000 child years at risk is about double the rate of 5 per 1000 child years in Mali (7) and this could improve with a bigger sample size. There was a significant increase in the proportion of children carrying parasites in the control area between the baseline and end-line surveys compared to the intervention area. The study further demonstrated that SMC implementation was effective in reducing the proportion of children with asexual parasitemia during the high transmission season. The proportion of children carrying asexual parasites at baseline reduced substantially at the end line survey in the intervention district, though geometric mean counts of trophozoites at both baseline and end line in the intervention area were significantly higher than the control area, the intensity of transmission being relatively high in the intervention area. However, in this evaluation, the proportion of gametocytemia increased in both districts and the increase at the end line was much higher in the non-intervention group. This suggests that the drug combination may not be effective in killing the sexual forms of the parasite responsible for malaria transmission.

This notwithstanding, at the end of the transmission season, moderate anemia was reduced by about fifty percent in the intervention arm which was consistent with earlier studies (3–8). This was in contrast with an increased proportion of about 25% in the non-intervention area. A similar effect was documented with mild anemia. This is noteworthy because despite the high intensity of malaria infection in the intervention area, children were protected against anemia. Moreover, children were able to build up their hemoglobin levels as clinical and subclinical malaria parasitemia is reduced. SMC therefore even without iron supplementation would be a good tool for the prevention of anemia due to malaria in these children.

The safety and tolerability of SMC in the intervention area were good. There were no serious adverse events reported and there was no report of stopping subsequent administrations due to safety of the drugs. Diarrhea

and vomiting were the dominant adverse drug reactions, but they were mostly self-limiting. At least eleven percent of children taking the SMC medications at a time experienced adverse drug reactions and this is much higher than reported in other studies. The level of adverse drug reactions reported in this study is thus acceptable especially as they were all self-limiting and none resolved with sequelae. The study has been limited by the sample size and number of study sites.

In conclusion, this SMC pilot study provided substantial protection against anemia and malaria parasite carriage in children in the Northern Sahelian belt of Ghana in addition to the other control measures like IRS and ITN use. The choice of Amodiaquine and sulfadoxine-pyrimethamine is safe and tolerable among children in this region. Our findings support the proposal to scale up the implementation of SMC to the other two regions of northern Ghana.

Table: Frequencies of Reported Adverse Event by Participants per Treatment Round

Adverse events	*Number per Treatment Round*				
	One (N=731)	*Two (N=635)*	*Three (N=587)*	*Four (N=621)*	*Total*
Vomiting	*33*	*27*	*33*	*51*	*144*
Fever	*7*	*19*	*32*	*27*	*85*
Diarrhea	*26*	*25*	*7*	*12*	*70*
Weakness	*11*	*7*	*3*	*3*	*24*
Abdominal pains	*0*	*5*	*0*	*0*	*5*
Cough	*0*	*14*	*0*	*5*	*19*
Rashes	*0*	*9*	*4*	*0*	*13*
Others	*6*	*3*	*13*	*14*	*36*
Total	*83*	*109*	*92*	*112*	*396*

Declarations

Ethics approval and consent to participate: The study was approved by the Institutional Review Board of the Navrongo Health Research Centre and the Ghana Health Service Ethics Review Committee before study implementation. All amendments were to be approved by the ethics boards before implementation, as appropriate. In addition, all participants provided parental informed consent before study enrolment and participation.

Consent for publication: All authors approved the final version of the manuscript and the corresponding author has the permission of all authors to publish this manuscript

Availability of data and materials: The datasets during and/or analysed during the current study available from the corresponding author on reasonable request

Competing interests: The authors declare that they have no competing interests

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Authors' contributions:

Conceived and designed the project: POA, NAA, KM, ARO

Experimentation and data collection: POA, NAN, DA, NP, SD, YS, CM, JA, JAW, WO, ARO

Review and intellectual input: POA, NAN, KM, DA, NP, SD, YS, CM, JA, JAW, WO, ARO

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Figures

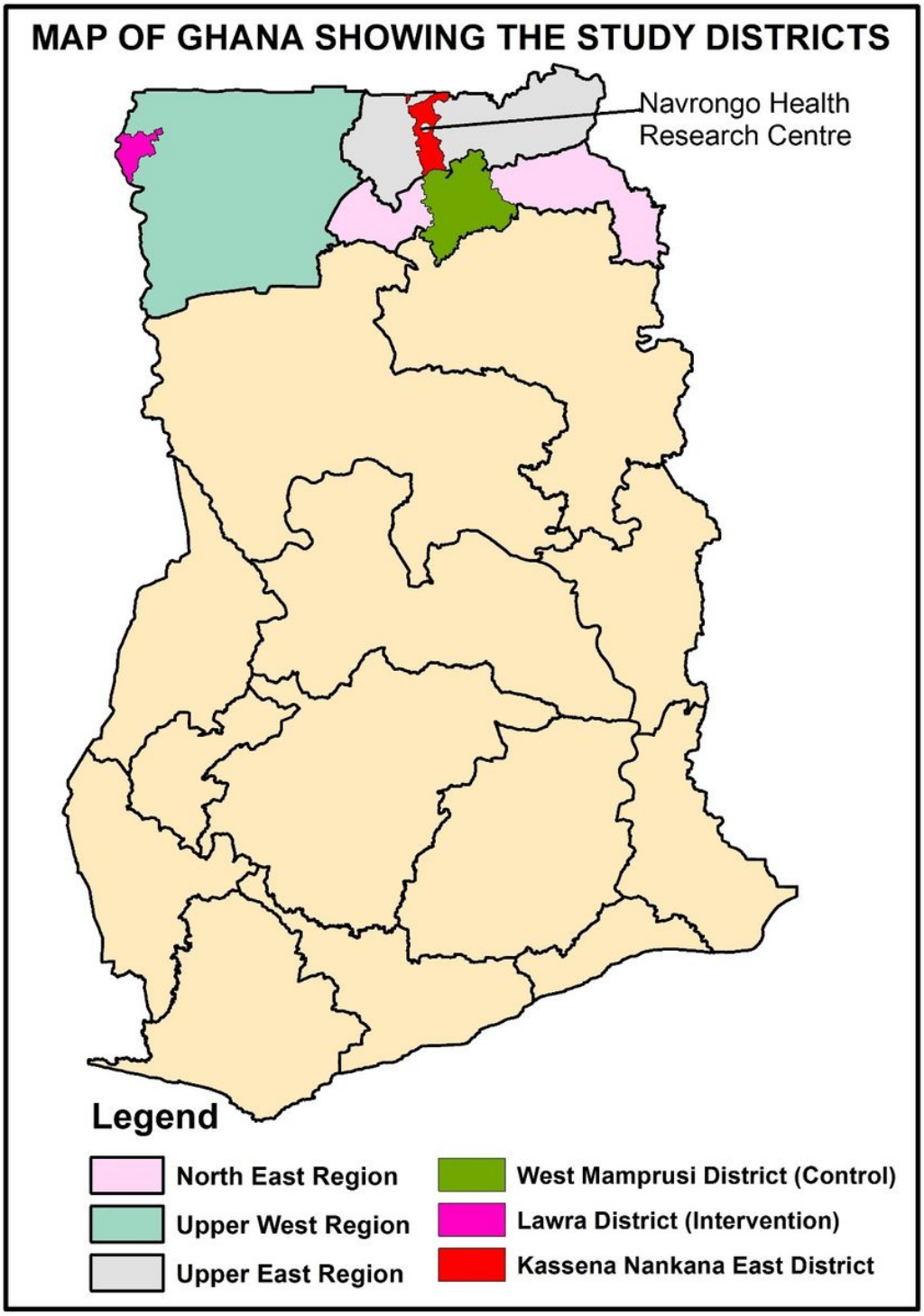

Figure 1

Map of Ghana showing the regions and districts of the intervention and control areas and that of the Navrongo Health Research centre.

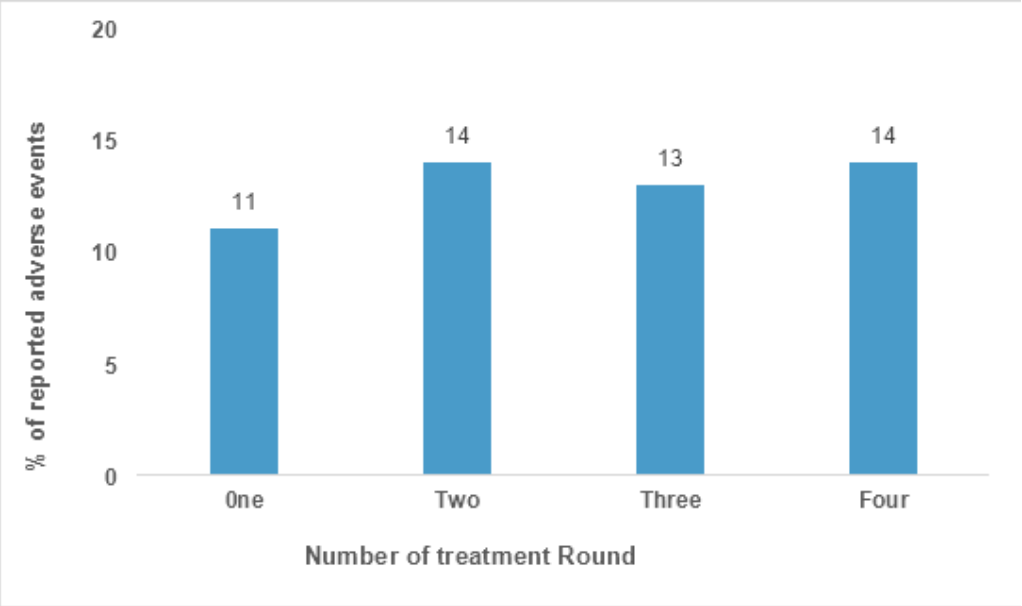

Figure 2

Percentage of children experiencing at least one adverse event per treatment round