ACCESS SMC

Achieving catalytic expansion of seasonal malaria chemoprevention in the Sahel

Evaluation of Seasonal Malaria Chemoprevention

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ACCESS-SMC is a UNITAID-funded project, led by Malaria Consortium in partnership with Catholic Relief Services, which is supporting National Malaria Control Programs to scale up access to seasonal malaria chemoprevention (SMC) to save children's lives across seven countries in the Sahel. By demonstrating the feasibility and impact of SMC at scale, ACCESS-SMC will promote the intervention's wider adoption.

For further information visit www.access-smc.org and www.unitaid.org

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Lay summary

Seasonal Malaria Chemoprevention is a new strategy for malaria control that is being introduced in West Africa. As with all public health programmes, it is important that SMC programmes are monitored, to ensure that the intervention is delivered effectively, reaching the children that need it, and that it remains safe and effective, and to measure the impact. In 2015 and 2016, seven countries (Burkina Faso, Chad, The Gambia, Guinea, Mali, Niger and Nigeria) will scale-up SMC, with funding from UNITAID, in a programme called ACCESS-SMC.

As part of this programme, comprehensive monitoring will be undertaken. A concern has been that SMC may lead to resistance to the drugs used, we will therefore monitor the efficacy of SMC treatments. SMC has been shown to be safe but as with all new interventions, safety monitoring needs to be maintained to check the drugs remain safe, this will be done by working to strengthen national safety monitoring systems. It is hoped that SMC, which has been highly effective in clinical trials, will have a substantial impact on child health, this will be monitored through surveillance at clinics and hospitals to assess the reduction in the number of cases of malaria.

The findings will help national control programmes to manage SMC programmes effectively, and will contribute to the evidence needed by policy makers to inform planning of SMC and other malaria control interventions.

Introduction

Seasonal Malaria Chemoprevention

Seasonal Malaria Chemoprevention (SMC) is a new strategy for the control of malaria in children involving monthly administration of sulfadoxine-pyrimethamine plus amodiaquine (SP+AQ) to prevent malaria. It is most suited to areas where malaria is highly seasonal, and transmission is intense, in such areas the majority of malaria cases, especially severe cases, occur in young children during three or four months of the year. The countries of Africa that meet these criteria, or include regions that meet these criteria, are mostly in the Sahel sub region and in this part of Africa both SP and AQ currently retain their efficacy against *P.falciparum*. SP+AQ provides a very high degree of protection for about 4 weeks, protection then wanes rapidly so to maintain protection treatments must be repeated every month.

The need to keep to strict timing means that delivery needs to be organised in the community through community health worker schemes, as part of community case management programmes or in mass campaigns. SMC was implemented in a large scale pilot in Senegal from 2008 to 2011. In 2012 WHO issued a policy recommendation that children 3-59months of age living in areas of highly seasonal malaria in the Sahel sub region should receive SMC.

SMC implementation started in August 2012 in MSF projects in Mali and Chad, and in 2013 SMC schemes started in Niger, Mali, Senegal, Togo and Nigeria, and in 2014 in The Gambia. In 2014 about 2.5million children received SMC in these eight countries funded by UNICEF, PMI/USAID, and other donors and national governments. In 2014 UNITAID announced funding of $67million to provide SMC for up to 8million children in 2015 and 2016 in seven countries (Burkina Faso, Chad, The Gambia, Guinea, Mali, Niger, and Nigeria). Due to a global shortage of quality-assured drugs for SMC in 2015, scale-up will be slower than expected with about 3 million children planned to be included in 2015. It is anticipated that manufacturing capacity will expand to meet demand in 2016.

Monitoring and evaluation of SMC programmes

It is important that SMC programmes are monitored to ensure that SMC is delivered successfully by national Malaria Control Programmes, reaching a high proportion of eligible children. Efficacy of SMC drugs need to be monitored to ensure local parasites remain sensitive to the drugs used, and pharmacovigilance systems should be strengthened to ensure drugs used remain safe and that adverse events that might be drug related are documented adequately. Changes in the malaria burden as SMC is introduced should be monitored to ensure it is having the expected impact. Costs of delivery, the acceptability of the strategy to communities and health staff, and in the longer term, the extent to which severe cases are delayed to older age groups, should also be monitored but are outside the scope of this protocol. This protocol describes the methods to be used to monitor the efficacy of SMC treatments, the safety of the drugs when used for SMC, the coverage of SMC, and the impact of SMC scale-up on the malaria burden, in the seven countries in the UNITAID programme, in 2015 and 2016.

Safety monitoring

There is now substantial evidence that SMC with SP+AQ is safe but nevertheless as with any new public health programme, it is important that effective safety monitoring should be maintained in areas where SMC is implemented. Current systems are known to be weak and will need to be strengthened, this will need to involve training programmes, for pharmacovigilance staff in the national PV centres and national malaria programmes, and inclusion of PV training in the training sessions for health staff involved inn delivery of SMC, to raise awareness of the importance of safety monitoring, and good coordination to ensure reporting forms are available and are collected each

month. Passive detection with a focus on the known side effects of SP and AQ will be used (Targetted Spontaneous Reporting). Stevens-Johnson syndrome has been observed in travellers using SP for prophylaxis, but the risk from routine use in African populations appears to be very low.

There has been no increase in incidence of Stevens Johnson syndrome reported since SP became widely used for IPT in pregnancy. An Institute of Medicine review [IoM, 2008] looked specifically at the safety of SP for IPTi and concluded that it was safe. A study in Malawi showed that the incidence of severe skin reactions in children from use of SP for malaria treatment is very low, only 2 events were recorded in over 300,000 treatments [Gimnig et al. 2006]. In a study of SMC safety conducted in Senegal 2008-2010, where over 750,000 SMC treatments were given, surveillance detected only one case of Steven Johnson syndrome and one of Lyell syndrome resident in the study area, both were associated with antibiotic intake and not with SMC drugs [NDiaye et al . 2015]. Since SMC has been introduced in national programmes, two cases of Stevens Johnson syndrome have been reported, both in Senegal, both girls aged 10 yrs. Amodiaquine has been associated with liver toxicity, neutropenia and other severe adverse events. WHO commissioned a review of the safety of amodiaquine (AQ) in 2002 [WHO 2003]. This review concluded that treatment with AQ was safe and AQ in combination with artesunate is now used widely as first line treatment for uncomplicated malaria. In the Senegal SMC effectiveness study, the occurrence of hepatic disease in children was uncommon, 48 cases were detected, only two of whom had received SMC and could potentially be associated with drug intake. One child developed an extra-pyramidal syndrome after SMC treatment which was probably associated with amodiaquine intake.

A review of 49 cases of extra-pyramidal syndrome associated with amodiaquine-artesunate treatment in Vigibase, the database of Individual Case Safety Reports maintained by WHO, suggests that there is an association with amodiaquine at recommended dosages [McEwen 2012]. Extra-pyramidal syndrome is an unpleasant but readily treatable condition, the incidence appears to be low but as it has not until recently been widely recognized as a potential side effect of amodiaquine treatment it may have been under-reported. Vomiting is the most common side effect of SMC drugs. The age pattern of vomiting in children who received SMC is consistent with a dose-related risk of vomiting [NDiaye et al 2015]. The overall rate of outpatient attendance with SMC-related vomiting in the Senegal study was low but higher rates have been reported from MSF projects in Niger [E Lasry, unpublished data]. It is not clear why some children are more likely to experience vomiting than others.
For effective pharmacovigilance, maintaining awareness of health staff is essential. In addition to passive reporting, since SMC delivery involves monthly contacts of families with health workers, an active check can be made each month for any severe adverse reactions. To document the incidence of mild and moderate adverse events, event cohort monitoring should be performed on a cohort of children.

Assessing coverage

Children in endemic areas should receive SMC every month for up to 4 months in the transmission season. A key indicator that should be reported is the percentage of children that receive all of their scheduled SMC treatments. Provided SMC doses are accurately recorded on a family-held record card, this can be done through household surveys using a similar methodology to that employed for vaccination coverage surveys, but will need to be supplemented by asking mothers about treatments.

By measuring impact through malaria surveillance, coverage with surveys, and efficacy of treatments with case-control studies, the impact, and the mechanism which brought it about, can in principle be demonstrated.

Measuring efficacy

A major concern for SMC is that its widespread deployment will lead to the selection of drug resistant parasites with progressive loss of efficacy. Thus, it is essential that any large scale SMC programme should incorporate a drug sensitivity monitoring component. This can be done through monitoring of molecular markers of resistance, in vivo testing (measuring parasite clearance when infected children are treated with SMC drugs), and using case-control studies. In vitro tests (using cultured parasites) could potentially be used but there are difficulties in using this method for SP and so this method has not been included in this protocol.

The presence of P. falciparum dihydrofolate reductase (pfdhfr) triple mutation (codon 108, 51 and 59) together with double P. falciparum dihydropteorate synthetase (pfdhps) mutations at codons 437 and 540 is associated with high levels of resistance to SP. In West Africa the mutation at codon 540 of the pfdhps is very rare and its presence is a useful single marker of quintuple mutation (triple pfdhfr plus double pfdhps). In addition to markers of resistance to SP, mutations at P. falciparum transporter (pfcrt) and P. falciparum multidrug resistance (pfmdr1) genes should be assessed to monitor SP+AQ efficacy in areas where SMC is implemented. Pfcrt mutant haplotype (CVIET) based on codon 72-76, which mediates high levels of resistance to chloroquine (CQ), has been linked with moderate resistance to AQ in Africa in the presence of particular haplotypes of Pfmdr1. These haplotypes have genetic mutations at codons 86, 184 and 1246 of pfmdr1, but the tyrosine substitution at position 1246 is rare in West Africa, and so its presence together with the CVIET allele of pfcrt is a good marker for AQ resistance [WHO 2013].

To monitor the prevalence of these markers in the circulating parasite population, parasites can be sampled from clinical malaria cases, or from the general population using community surveys, in adults and in children old enough for us to be confident they did not receive SMC. Sampling from malaria cases at the clinic is logistically much easier, and samples a larger biomass of parasites, but could potentially be biased in favour of individuals harbouring parasites resistant to first line treatments, and those with good access to health care or living near the clinic. In this study we will use both types of sampling, and compare the results, with a view to recommending the most suitable method for long-term monitoring. It will be necessary to sample children under 5 years of age, in addition to the older age groups, in order to check for evidence of selection in the treated age group. Because increasing resistance to SP and AQ might be expected over time independently of any pressure exerted by SMC it is important that, if possible, sampling should be done adjacent but outside the SMC areas, as well as where SMC is being deployed. Assessment of molecular markers in malaria cases who received SMC and cases in children who did not receive SMC allows the association of the markers with SMC failure to be assessed.

Although the frequency of molecular markers is a useful indicator, it is not known how a change in frequency of the markers may predict changes in efficacy. Therefore, in addition to monitoring molecular markers, direct measures of efficacy need to be made, using in vivo and case control studies. SP+AQ is no longer recommended for treatment of symptomatic malaria in Africa so conventional in vivo tests for drug sensitivity conducted in sick children can no longer be done with this drug combination. However, clearance of parasitaemia in infected children when they receive their first round of SMC treatment can be studied prospectively. The case control approach is a widely used method to measure efficacy of preventive interventions after they have been introduced at a national or regional scale, for example in the evaluation of the efficacy of new vaccines when introduced into national programmes. To use this method to measure SMC efficacy, confirmed malaria cases, and controls who do not have malaria, should be recruited concurrently, and the dates of the doses of SMC they received noted. For the method to be used it is essential that dates of SMC doses are accurately documented, so the method relies on good recording of SMC doses, with the date, on child health cards and in registers.

The efficacy monitoring covered by this protocol is intended a) to provide reassurance about sustained efficacy after two years of implementing SMC, b) to allow timely detection of any loss of efficacy if it occurs, c) to be able to understand factors associated with any loss of efficacy or development of resistance, and d) to establish a monitoring system that will continue to be used in the longer term to monitor SMC programmes. The findings will contribute to the evidence used to argue for continued support from communities, countries and donors. The sample size of the studies reflects the need to be able to detect resistance if it emerges, and to give enough precision to that if there is no evidence of resistance, we can demonstrate that there is no important reduction in efficacy, and no important increase in prevalence of the key markers.

In order to reduce the risk of resistance developing steps should be taken by SMC programmes, to ensure children receive SMC each month and adhere to the daily regimen, under-dosing should be avoided, and any breakthrough infections should be treated promptly with artemisinin combination therapy. The main risks of under-dosing occur when inadvertently including children older than 59 months, giving infant doses to older children, and when children receiving incomplete doses due to spitting out medication. Breakthrough malaria cases should be promptly treated with a drug regimen that does not include SP or AQ. Parasites carrying the CVIET haplotype of pfcrt and the 86Y allele of pfmdr1, associated with AQ resistance, may be more sensitive to artemisinins so prompt treatment of breakthrough infection with an ACT may impede selection for AQ resistance by SMC drugs. SMC will substantially reduce the need for first line treatment, reducing the scope for selection for resistance to first line drugs, but this advantage will be fully realised only if all suspected malaria cases are tested with an RDT. It is therefore especially important in SMC areas that health staff use RDTs to test children with suspected malaria. Monitoring should be done to document adherence to these good practice guidelines in the districts where SMC is implemented.

Impact

Measuring impact once an intervention has been introduced at a national level is difficult due to the variability in malaria incidence year to year, and the lack or poor quality of surveillance data from before intervention started and from control areas. However, in most countries SMC will be introduced in a phased manner, this allows surveillance (parasitological confirmation of malaria by RDT or microscopy at outpatient clinics and hospitals) to be established, so that areas that start SMC later can serve as controls in the early phase, providing more reliable estimates of impact. Routinely collected data on malaria cases at health facilities through national HMIS systems tends to be of variable quality, it will therefore be necessary to identify health facilities which can act as sentinel surveillance facilities, which are supported to document malaria cases carefully and where steps are taken to ensure adequate supplies of RDTs for malaria diagnosis, and of ACTs for treatment of malaria. These facilities can be visited on a regular basis to collect detailed information on incident malaria cases.

Deaths in hospital should be monitored, in addition the overall impact of the SMC programme in preventing child deaths can be monitored through surveys to measure all-cause child mortality, taking advantage of national surveys such as DHS surveys and malaria indicator surveys, where these are planned, with supplementary sampling as necessary in order to have adequate power to monitor changes in child survival in the areas where SMC is implemented. Several years of intervention may be needed to document an impact, and as many other factors may change during the same period, clear attribution to SMC may not be possible.

Study sites

Districts where SMC will be delivered through the ACCESS-SMC project, in 2015 or 2016, in Burkina Faso, Chad, The Gambia, Guinea, Mali, Niger and Nigeria (see maps in the Appendix).

Objectives

1. Measure the efficacy of SMC treatments in each year of the project
2. monitor the frequency of molecular markers of resistance to SMC drugs in the general population and in children under 5 years, in order to detect any important changes before and after two years of SMC
3. Measure the coverage of SMC treatments at the end of each year
4. Measure the impact of SMC on the incidence of outpatient malaria cases, malaria Inpatients, and child deaths
5. Monitor the safety of SMC through targeted spontaneous reporting and event cohort monitoring, to measure the incidence of adverse drug reactions and their association with SMC
6. Measure the efficacy of SMC drugs in clearing asymptomatic parasitaemia

Monitoring of molecular markers, measurement of coverage and impact, and safety monitoring, will be done in all countries. Case-control studies and clearance studies need not be done in all countries, and will be conducted depending on local capacity.

Methods

Case-control studies (Objective 1)

Efficacy of SMC treatments will be measured using the case control approach. Malaria cases, and controls who do not have malaria, will be recruited concurrently, and the dates of the doses of SMC they received noted. The efficacy of SMC can then be calculated as a function of the time since treatment using case-control analysis. It is essential that dates of SMC doses are accurately documented, and that malaria cases are parasitologically confirmed. Controls will be selected from the community, in the neighbourhood where the case lived at the time they had malaria. Trained fieldworkers will collect information about cases and controls, and make home visits to record bednet use and other household factors that may act as confounders. Microscopy will be used to confirm cases and to measure parasite density. Controls will be confirmed to be negative for *P.falciparum*, by RDT.

Study location and coordination: Outpatient clinics in SMC areas. In each country, two or more clinics may be required in order to be able to recruit about 250 cases in children under 5 years of age each year during the transmission season. A small team including a clinical coordinator, a laboratory technician to read blood films, and field workers, will coordinate the study in collaboration with the health centre staff.

Recruitment of cases: Recruitment of cases will start the same day, or shortly before, the first round of SMC delivery begins. Cases and controls should be children who were in the age range eligible for SMC, strictly this is children aged at least 3 months at the time of the most recent SMC round, and who were aged less than 5 years at the time of the first round of SMC that year. Where possible age should be verified from the date of birth on the child's heath card. Including children slightly outside

the range may be inevitable, and will not introduce a bias, provided their SMC status is accurately determined. Cases are defined as children attending clinic with a febrile illness, with no other obvious cause of the fever, whose parent or carer has given consent for them to participate, and confirmed to be positive for *P.falciparum* by microscopy (RDTs can have a high false-positive rate).

Measurement of exposures: The day the case is diagnosed, the family will be visited at home, to ask about adherence to SMC doses, to ask about bednet use and to check the child's sleeping place to inspect the net, and to ask about other household factors that may be associated with malaria. The date of the last SMC treatment (the date of the first daily dose administered by the community health workers) will be transcribed from the child's SMC card, if there is one, and the mother asked to confirm if the children received SMC and the date of the last treatment, and about adherence to each of the doses, and if the child vomited the medicine. Dates will be cross-checked against health centre records of the dates of SMC rounds. SMC registers will be consulted so that SMC doses can be verified by finding the child's entry in the register.

Recruitment of controls: The interviewer will then move at least two compounds away from the household of the case, to start to look for two suitable control children. Controls are defined as children aged 3-59 months, who do not have malaria. Field workers will keep a record of all potential controls considered and eligible children whose parent or carer consents to their participation, and who are not unwell, will be asked to give a finger-prick blood sample so that an RDT can be performed to confirm they do not have malaria infection. Dates of SMC doses and other information will be collected in exactly the same way as for cases.

Recruitment of cases and controls should start on the day of the first SMC cycle each year, and continue until 2 months after the last round of SMC the same year. The sample size required each year in each country is about 250 cases with two controls per case, to be able to estimate efficacy with adequate precision. In the analysis, case-control matched sets will be grouped according to the number of weeks since the treatment date, or smoothing methods will be used, in order to estimate SMC efficacy as a function of time since treatment. Comparison of efficacy profiles in the first and second year of SMC will be used to look for any evidence of loss of efficacy.

Laboratory methods: Slides, dried and stained with Giemsa, will be read independently by two microscopists. If there is a discrepancy, a third reading will be done and the median result taken as definitive. Blood spots will be taken onto filter paper (Whatman No3), dried and stored with desiccant, for later analysis of molecular markers of resistance. Used RDTs will also be stored so that they can be used to assess the utility of used RDTs for monitoring molecular markers.

Data management: Data will be captured using tablet PCs or PDAs.

Molecular markers surveys (Objective 2)

A survey will be conducted before the start of SMC, and again after two years of SMC, either in June 2015 and June 2017, or if timing is not possible for the first survey, in December 2015 and December 2017, to measure the prevalence of molecular markers associated with resistance to SMC drugs. The key markers to be monitored are the dhfr/dhps quintuple mutation, pfcrt76 and pfmdr1-86.

Each survey will include children eligible for SMC (3-59 months), and older children and adults aged 10 to 20 years, in order monitor trends of molecular markers in children who receive SMC and in the general population. The sample size is chosen to aim to yield at least 270 parasite positive samples in each age group, if the prevalence of parasitaemia is 15% and there is 10% overall non-response (missing samples or failed DNA extraction), 2200 in each age group will be needed.

Household sampling: The areas to be surveyed should not have received SMC at the time of sampling, but should be targeted for SMC the following transmission season. The aim is to sample before SMC and then to sample again after two years of SMC. It is advantageous if the same clusters can be sampled each time but it is not necessary to have complete geographical coverage of SMC areas. Where possible, it may be helpful for surveys to be done in the vicinity of sites used for monitoring therapeutic efficacy, as there will already be monitoring capacity in these sites. It is important to choose sites with a relatively high malaria burden to ensure that sufficient positive samples can be obtained, and then to sample representatively within the defined area, and sample from the same area again at the follow-up survey.

Clusters can be census enumeration areas, or villages, selected with probability proportional to estimated size (PPS). Within each selected cluster, households can be selected by simple random sampling using a list of households, but often such lists are not available or are out of date, and so area sampling based on a map of the cluster, may be used. If a census has been conducted recently enumeration areas may have been defined and can be used for the survey, and maps of the enumeration areas may be available. For PPS sampling, a list is prepared of all the clusters (all villages or enumeration areas in the SMC regions), this list is sorted geographically, a sampling interval determined, and a systematic sample chosen based on this interval using a random start value. Maps of the selected clusters are then required showing the location of residential areas. If maps are not available from the national government statistics department, they may have to be prepared in the field, they need not be highly accurate but need to show the main features (roads, mosque, school, river etc) and the main blocks of housing. Each map is then divided into segments such that a segment comprises an approximately constant population, drawn taking account of natural boundaries such as roads and pathways so that segments can be easily identified on the ground. It is advisable to have about 30-40 clusters. 40 clusters of 55 children will give a sample of 2200. Children 3-59mths form about 18% of the population, so if the population of the cluster (village or enumeration area) is N, we expect 0.18N children in the cluster and we should divide the cluster into S=1+INT(0.18N/55) segments. If there is 10% non-response this will give a total sample of 2000. The actual population may differ from available estimates, so to ensure that, approximately, the desired sample size is achieved, it may be useful to do a pilot in a small number of clusters to estimate the actual populations and if necessary, use this information to correct the estimated total population of each cluster. This method of sampling, referred to as compact segment sampling, is often used because while there is a potential increase in design effect due to homogeneity within segments, the simplicity of household selection in the field (every household in the segment is included) largely removes error and subjectivity in household selection in the field which can lead to bias.

The probability of inclusion for individuals in cluster i is: m x (Ni/ΣNj)*1/Si, where Ni is the total estimated population of the cluster, and Si the number of segments, and m the total number of clusters in the survey. Weighting in the analysis, using the inverse of this probability, will correct for any inaccuracies in estimated population size used for PPES selection.

Interview and sampling procedures: In each household, all children aged 3-59 months, and all persons 10-30 years, who are normally resident in the household (excluding temporary visitors) should be invited to participate, and call-back visits arranged to minimise non-response. For each of those who consent (in the case of children, whose parent/guardian consents), a short questionnaire will be completed to record personal identifiers and the age, date of birth, gender, date of interview,

residence location, and other details, and a finger-prick blood sample will be taken to make at least two blood spots onto filter paper (Watmann No 3).

Sampling older age groups: About 18% of the population are aged 3-59mths, and a similar percentage are aged 10-19yrs, so if we set the age range for the older age group at 10-19 years, we will get approximately the same number of children under 5 and of older individuals, in a house to house survey, if all are present in the household. As the older individuals are more likely to be away from the household, and because prevalence decreases with age, we will extend the age range to 30yrs.

Monitoring of molecular markers will also be done in the malaria cases recruited for the case-control studies. For each malaria case, two blood spots will be taken onto filter paper which will be kept, for analysis of molecular markers. The date of diagnosis, dates of SMC dose received, residence location, age and gender should be recorded. Dates of SMC should be checked against the child's SMC card, if available, and confirmed by asking the carer. This will permit analysis of markers in relation to the time since treatment.

Laboratory methods: Filter papers should be used for blood sampling, which is a WHO recommendation for filter paper collection, including patients in clinics. At least one spot from each sample will be retained for analysis. Standardisation of laboratory methods will be important, and a standard protocol will be proposed for sites to follow. In addition, a second spot from each sample will be sent to LSHTM for quality control purposes to ensure the reliability of results from all countries. Details of laboratory methods will be specified in an SOP.

Human genetic markers associated with adverse reactions to amodiaquine and to SP have been identified, however the prevalence of these markers in SMC areas is not well known. Consent forms will include a request for permission to use the blood samples to look for these markers, this may be helpful in interpreting the pattern of incidence of adverse events.

Coverage surveys (Objective 3)

One month after the last SMC cycle in 2015, and after the last cycle in 2016, a household survey will be undertaken to record the dates of SMC doses received that year. The survey will be done shortly after the last CMS cycle in order to minimise the time interval for recall. A two-stage cluster sample survey will be used to provide estimates of the proportion of eligible children who received 0,1,2,3 or 4 SMC treatments, representative of the areas where SMC is implemented.

Study populations: SMC is aimed at children aged 3 to 59 months old. Children who receive SMC at the first cycle of the year, but have their 5th birthday before the last SMC cycle, should continue to receive SMC that year, but will not be eligible next year. Therefore, in the survey, eligible children are defined as those who are aged at least 4 months at the time of the survey (hence would have been at least 3 months old when the 4th SMC cycle took place), and are aged less than 5 yrs and 4 months. However, it is possible that older children are receiving SMC and it will be useful to capture this. Therefore, in the survey, all children aged less than 7 years at the time of the survey will be included, and the date of birth and age carefully noted to allow estimates of coverage in the target age range to be made. The sample size will be increased to ensure the target number in the eligible age range is obtained.

Care should be taken to obtain the correct date of birth, this should be noted from the child's health card, where this is not available, the child's age should be recorded as accurately as possible using an

event calendar, and referring to children in the compound of similar age whose date of birth is known.

SMC doses: Dates of SMC doses will be recorded from the child's SMC card. In countries where administration of SMC doses was recorded electronically, a hand-held device will be used to read the QR code on the child's card. The mother or carer should also be asked about receipt of SMC doses to cross-check the information on the card and to provide information about doses where the card has been lost. A short questionnaire, including reasons for missed SMC cycles, and adherence to the supervised and home doses, occurrence of fever in the child in the last 2 weeks and any treatment seeking for that fever, and the use of bednets by the child, will be completed. Where possible, a cross-check on SMC dates should be made from the SMC register.

Sampling for the coverage survey: From a list of all communities (villages or census enumeration areas) in the areas that received SMC, about 60 communities will be selected with PPES. In each selected community, a sample of an approximately constant number of households will be made from village lists or using area sampling. All eligible children resident in the household at the time of the survey should be included. If any children are away or the parent is not present to interview, a call-back visit should be arranged before documenting a non-response for that child or household.

Sample size: About 10 children per community are required for a sample size of 600 this will give good precision on the overall estimates of coverage while permitting reasonable precision on sub-regional estimates. To allow for the fact that children up to 7 yrs of age will be surveyed, the sample size is increased to 14 per cluster (total 60x14=840). In vaccination coverage surveys in the Gambia, the rate of homogeneity (roh) for DPT3 was about 0.2, this gives a design effect of Deff=1+(b-1).roh=2.8 for a cluster size b=10. A survey of 600 then corresponds to a sample size of 600/2.8=214 if we were to use simple random sampling and this would give, if the coverage was 70%, a margin of error (95% confidence interval) of +/-6%, if the coverage was 50%, +/-7%. And for sub-regional estimates, if we divide the area into three with 200 sampled in each of these three areas, the precision would be 50% +/-12% or 70% +/-11%. For estimating coverage in the out-of-range children (>5yr and 7<yrs), if we have about 4 of these per cluster, a total of 60x4=240, we would have a margin of error of +/-8% if the coverage was 20%.

Data management: Data will be captured using PDAs.

Malaria sentinel surveillance (Objective 4)

Settings: Health facilities (outpatient clinics and hospitals) located in the areas targetted to receive SMC through the ACCESS-SMC programme starting in 2015 and 2016, and adjacent areas not targeted for SMC, will be selected as sentinel surveillance sites, in order to monitor changes in the incidence of malaria as SMC is introduced.

Selection of surveillance clinics: Where possible, outpatient clinics will be selected with probability proportional to the estimated size of the catchment population. A list of all clinics in and adjacent to SMC areas will be required, with their catchment population. PPS sampling is then used by specifying a sampling interval and random start, after putting the list into an approximate geographical order to give an implicit geographical stratification. The selection should then be checked with respect to geographical coverage, malaria cases and malaria incidence rates from HMIS data to ensure the sample is representative. PPS sampling improves the precision of the estimate when the outcome is associated with population size.

Methods: Each facility will be visited to explain the project, and where necessary to provide training on malaria diagnosis and record keeping. Health facility staff will be asked and trained to keep accurate records for all inpatients (i.e. all ages) tested for malaria at the health facility and their test result, throughout the year. In addition, for any patients aged under 5 years with a positive test for malaria, the date of the most recent dose of SMC will be recorded.

Data collection: Every two to three months, each facility will be visited to collect data on all cases that were tested for malaria and all that were treated for malaria. For all cases (of any age, child and adult) tested for malaria, and any cases treated for malaria without a test, details of date of consultation, age, gender, residence location, symptoms, whether a test was performed and the result, and the treatment given, will be captured from the clinic register into a database on a tablet PC. For the positive cases in children under 5, the date of the most recent SMC dose will also be captured. The latter, combined with estimates of SMC coverage from the coverage surveys, will permit a crude estimate of the efficacy of SMC to be made using the screening method. In hospitals included in the sentinel surveillance, similar procedures will be followed. For all inpatients (children and adults) with a positive test for malaria, the same information as for outpatients will be collected, and in addition, the date of admission, date of discharge (or date of death if they died in hospital), and the final outcome (died or discharged), and for children under 5, the date of the most recent SMC dose.

Quality control: After capturing the data to the tablet PC, an independent tally of the total cases in the register for the reporting period, should be done as a cross-check, and supervisory visits made to cross-check accuracy of data entry.

A sample of used positive and negative RDTs will be collected, for extraction of parasite DNA from the blood in the RDT cassette and analysis by PCR, so that we can determine the sensitivity and specificity of RDTs.

N.B.: Malaria cases may be treated at community level by community health workers in malaria community case management schemes (CCM) such as PECADOM. If there are areas with CCM within the catchment of the sentinel surveillance outpatient clinics, the details of the cases treated in these schemes should be captured by visiting the villages involved or by arranging with the health facility that records are submitted to the health facility by the community health workers on a regular basis.

Historical data: At the first visit to each sentinel facility, the data on cases tested or treated for malaria, as described above, should be captured from the registers for the previous two years, if available.

Assessment of impact: Impact will be estimated from the difference in incidence with and without SMC and with SMC, using comparisons between SMC and control areas, and data on incidence before and after SMC implementation. Data on the incidence in older age groups will be used to help control for effects of year to year variation.

Pharmacovigilance: (Objective 5)

Context: The incidence of severe adverse events to SMC drugs has been very low but when SMC is implemented on a very large scale severer adverse drug reactions will occur and they should be properly managed and documented. A better understanding of associated predisposing factors may allow such events to be avoided in future. When severe events occur, communities need to be reassured that safety is being properly monitored and children with side effects are adequately

cared for. National pharmacovigilance systems are weak and SMC is an opportunity to strengthen them.

Methods: Three approaches will be used to detect adverse reactions to SMC drugs:

1. Targeted spontaneous reporting at health facilities, enhanced through a system of SMC reminders to health staff, with a focus on severe skin reactions (Stevens-Johnson syndrome), liver injury, and extra-pyramidal syndrome.

2. Active follow-up, when community health workers visit to administer the next monthly treatment. Before administering the next treatment the health workers will check there has been no very serious side effect last time. It will be important not to with-hold SMC from children because of mild or moderate side effects reported from the previous administration, since mild and moderate side effects are common but severe reactions are extremely rare so any such policy would result in a large number of children being excluded from SMC and therefore at increased risk of malaria.

3. As part of supervisory spot-checks performed in SMC areas after each SMC cycle to check acceptability of the intervention and adherence to home doses, questions about side effects will be asked, in order to document the incidence of mild adverse events which if common could become important.

Training: Training in the recognition of drug adverse reactions, clinical care of patients, and how to investigate and document the event, will be organised for district medical officers and for nurses as part of training sessions in SMC delivery. The training will emphasise that all medicines including traditional medicines taken in the 2 weeks prior to the event will be documented with the name of the medicine, dosage, and timing of intake, and any other predisposing factors such as concurrent illness, noted. A job aid for health workers has been developed (see Appendix).

Community health workers who deliver SMC will be trained to ask if the child had any severe illness since the previous SMC treatment, this will be marked in the SMC register to be followed up by the nurse and the family advised to take the child to the clinic. Only reports consistent with a severe allergy to SP or AQ (severe skin rash or yellow eyes), would lead to SMC being withheld, but the family would be advised to take the child to the clinic immediately if symptoms recur.

Some adverse reactions can be detected only through laboratory tests of liver function enzymes and blood counts. Laboratory capacity in terms of staff training and availability reagents will be reviewed and recommendations made to the ministry of Health but strengthening lab capacity is outside the scope of this project.
Pharmacovigilance reporting forms will be made available at all health facilities in SMC areas before the start of SMC and additional forms distributed with the SMC drugs. A database of names and phone numbers of the head of each health facility in the SMC areas will be compiled, and automated SMC messages sent to each number shortly before each SMC cycle, to thank and remind about pharmacovigilance, and 10 days after each cycle, to remind to submit a report. Each facility involved in SMC delivery will be asked to submit a report on SMC delivery each month, this will include a checklist for reporting adverse drug reactions that were seen.

Any suspected case of Stevens Johnson syndrome will be referred immediately to the nearest hospital. All severe events will be reported immediately to the district medical officer. All serious adverse events will be reported within 15 days to the regulatory authority.

All completed pharmacovigilance reporting forms will be collected after each monthly cycle, entered into a database before being forwarded to the regulatory authority. A review panel will assess each event for severity and relatedness to SMC drugs, and will be responsible for monitoring that any children with severe adverse reactions were provided with appropriate clinical care.
Regional hospital laboratories will be visited to make an assessment of capacity to perform assays that may be required in the investigation of adverse drug reactions including liver function tests and whole blood counts, and availability of reagents.

Referrals: To track children referred to hospital, a unique ID (patient initials, date, age, gender, and the name of the health facility) will be generated on the reporting form at the clinic where the case was first seen, and entered on the referral form.

Data management: Pharmacovigilance forms should be entered into Vigiflow by the national PV centre, who also assess imputability, and then submit to the Uppsala Monitoring Centre. Due to the expected volume of forms, an Access database will be established in each country so that forms can be entered by the research group, and the forms then forwarded to the national centre who will enter severe cases to Vigiflow and perfom imputability assessment before submitting to Uppsala. The non-severe cases will be exported in a standard PV format from the Access database and submitted to the national PV centre.

Genetic risk factors: It is not known why some children are at greater risk of adverse drug reactions, but genetic factors may be important. Variants in the CYP2C8 gene are associated with a reduced rate of metabolism of amodiaquine to its active antimalarial metabolite, N-desethylamodiaquine [Li Xue-Qing et al. 2002]. Therefore people with these gene variants who eliminate amodiaquine more slowly than normal, especially homozygotes, may be at increased risk of adverse events related to amodiaquine. Parikh et al.[2007], in a study of patients treated with amodiaquine-artesunate, found that heterozygotes and homozygotes for the CYP2C8*2 genotype were more likely to report abdominal pain compared to those with the wild-type, but there was no association with vomiting or other adverse events, and no evidence that treatment efficacy was impaired. The CYP2C8*3 variant, associated with more marked reduction in AQ metabolism, is uncommon in Africa [Gil 2012]. The frequency of the CYP2C8*2 allele has been estimated to be 0.115 in Burkina faso [Parikh et al 2007] and 0.168 and 0.179 in Ghana [Rower et al 2005, Adjei et al 2008, Kudzi et al 2009], with homozygote frequencies of 1%-3%. Stevens-Johnson syndrome is strongly associated with the human leukocyte antigen (HLA) genes HLA-B*1502 and HLA-B*5801 in Chinese, and HLA-A*3101 but not HLA-B*1502 in Caucasians and Japanese [Chung et al 2004,2010; Genin et al 2011; Shi et al 2012]. A genome-wide association study on a sample of 424 European cases and 1,881 controls found 6 SNPs located in the HLA region were risk factors with odds ratios in the range 1.53-1.74 [Genin et al. 2011].

To better understand geographical variation in the risk of adverse reactions to SMC drugs, consent for blood sampling in the surveys of molecular markers of P.falciparum resistance, will include permission for human genetic testing to determine the frequency of the markers associated with reactions to AQ an SP. For cases of Stevens-Johnson syndrome and cases of extra-pyramidal syndrome, when cases are notified, the patient and their family will be visited, to ask if blood sample can be kept for genetic analysis. For some cases it will be routine to take a blood sample and we will ask consent to keep a portion for DNA extraction, and will ask some questions about predisposing factors. If samples are not taken, the patient will be visited at home after the episode has resolved, to ask further questions about potential predisposing factors and to take a blood sample for genetic analysis.

Ethics and consent processes

Meetings with community leaders, administrative staff and health staff will be held in communities where the surveys and case control studies will be conducted to explain the aims and the procedures involved. For surveys and for case controls studies, signed consent will be sought after trained projct staff have explained the objectives and procedures of the study, using information sheets in French explained in the local language by the field worker, in the presence of a witness who will sign to confirm the information was correctly explained, if the participant (or their parent in the chase of children), cannot read. Blood sampling will be done by staff trained to take finger prick samples safely with a minimum of discomfort. Steps will be taken to ensure confidentiality of personal information by removing identifiers linked to names and addresses from computer databases. All samples, including those for genetic testing, will be anonymised. The protocol will be submitted to the ethics committee in each country and to the LSHTM ethics committee. Permission will be sought from the appropriate authority in each country for permission to ship samples to the UK.

Monitoring and quality assurance

A monitor will be appointed who will visit each site at least once per year to check that the trial is being conducted according to the study protocol, that appropriate ethical procedures are in place and s/he will examine a random selection of clinical and laboratory records during each visit. Quality control procedures will be developed in each site including supervisory checks on data recording by field staff and manual checks on accuracy of data entry.

Statistical analysis plan

A statistical analysis plan will be prepared and submitted to the advisory committee for approval before the end of the first year of data collection. Coverage, and prevalence of molecular markers, will be estimated using a ratio estimator with confidence intervals calculated using a standard error taking account of the cluster sampling design, using survey commands in Stata. Analysis of impact will be done using random effects Poisson regression to estimate changes in incidence of malaria associated with SMC. For case-control studies, smoothed estimates of the rate ratio as a function of time since SMC dose will be estimated using splines or fractional polynomial models.

Stakeholder engagement and dissemination plans

The *Université Cheikh Anta Diop* (UCAD), as member of the WARN-SMC group, will keep WARN informed about project progress through the regular meetings of the WARN-SMC group, always sharing with the partnership the official minutes of all meetings as well as email-based updates on the project. Data on adverse events will be made available promptly to a regional Safety Advisory Committee which will be convened, which will advise on pharmacovigilance and will consider notifications of events as they are reported. This committee will report to the WHO Safety of Medicines Advisory Committee. Reports will be shared with PNLP managers and national PV centres and WHO Global Malaria Programme on a regular basis. Results on drug resistance will be shared with WWARN and with PNLP managers, and WHO, as soon as they become available. Updates will be prepared in collaboration with project partners, to be presented at annual WARN meetings. Findings will be prepared for publication following a publication plan which will be agreed with partners during the first year of the project. Media press releases aimed at the general public internationally and locally will be prepared in collaboration with Speak Up Africa.

Roles of investigators and collaborators

In each country, the PI will be responsible for the day to day coordination of activities. Regular meetings will be held with PNLP, PV and MC or CRS staff, to ensure activities are well coordinated. LSHTM will be responsible for developing the protocol, and for overall project coordination. UCAD and TDR will contribute to project coordination, supervision and communication. UCAD will be responsible for site quality control monitoring. Data management and quality control will be the responsibility of the investigators in each country, data centralisation in a master database will be the responsibility of LSHTM.

Data management, governance and sharing

A data governance plan will be developed among the project partners, and a data sharing plan for making datasets available in the public domain will be developed. It is intended to make the data available through a public data repository shortly after the completion of the project.

Project sponsor and project management

This project is a collaborative project between the National Malaria Control Programmes in each of the 7 countries, the research institutions, the National Pharmacovigilance Centres, and the ACCESS-SMC country offices of Malaria Consortium and CRS, the UCAD, WHO/TDR and LSHTM. The project is funded by UNITAID. LSHTM are responsible for developing the protocol and scientific coordination. UCAD and TDR will contribute to project coordination and communication. Independent advisory committees on drug resistance monitoring, and on safety, will provide oversight and their approval of the protocol will be obtained. These committees will hold teleconferencing or face-face meeting annually to monitor progress and advise on the technical aspects of the study. The project management group will include the country PIs, LSHTM, UCAD and TDR, in collaboration with Malaria Consortium and CRS. A full time monitor, and a coordinator, will be appointed.

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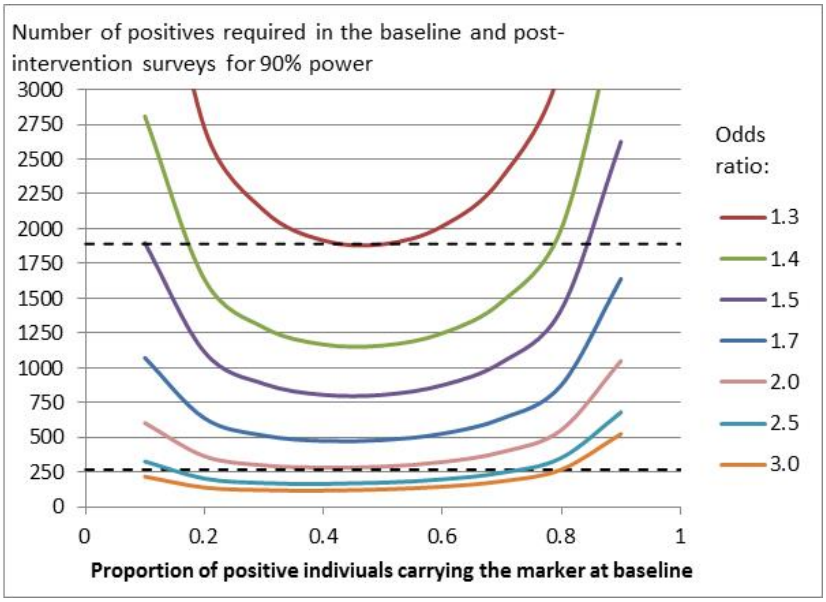
Appendixes

Timeline of key activities

		SMC cycles	Protocol	Budget	Ethics	Molecular markers survey	Case-control study	Safety monitoring	Coverage survey	Malaria sentinel surveillance
2015	March		X	X						
	April				Submit					
	May					Preparation		Training		Preparation
	June				Approval	Field work	Preparation	Preparation		Baseline
	July	SMC					X	X		X
	August	SMC					X	X		X
	September	SMC					X	X		X
	October	SMC					X	X	Preparation	X
	November							X	Field work	X
	December							X		X
2016	January							X		X
	February							X		X
	March							X		X
	April							X		X
	May							X		X
	June							X		X
	July	SMC					X	X		X
	August	SMC					X	X		X
	September	SMC					X	X		X
	October	SMC					X	X	Preparation	X
	November							X	Field work	X
2017	December							X		X
	January							X		X
	February							X		X
	March							X		X
	April							X		X
	May					Preparation		X		X
	June					Field work		X		X
	July									
	August									

Sample size calculations for surveys

The aim is to be able to estimate changes in prevalence of markers of resistance, with enough precision to provide reassurance here has been no important increase, if that is the case, while having adequate power to detect changes if they occur. A design effect needs to be allowed for both for clinic cases (which are clustered by clinic), and survey estimates. A design effect of 2 has been assumed for these calculations. The figure below shows the sample size (no. of parasite positive individuals) required for 90% power (using a 5% significance level) to detect a change in prevalence of the marker among parasite positive individuals, if the true change post-intervention is as indicated, assuming a design effect of 2. The dashed lines, corresponding to 270 positive individuals in each country (lower line) i.e. 7x270=1890 in a pooled analysis of 7 countries (upper line), show that with this number we would have 90% power to detect an odds ratio of at 1.4 or more in a pooled analysis and of 2.5 or more in each country. 270 was chosen here as this corresponds to the minimum number it may be feasible to obtain in a survey of manageable size (corresponding to the number that would be obtained in a survey of 2200, if the prevalence is towards the lower end of the expected range, 15%, and loss to follow-up is 10%).



To estimate the sample size required for surveys, we have to make an assumption about the prevalence of parasitaemia in the groups surveyed. The table below shows the number to include in the survey in order to obtain 270 positives, in relation to the prevalence of parasitaemia:

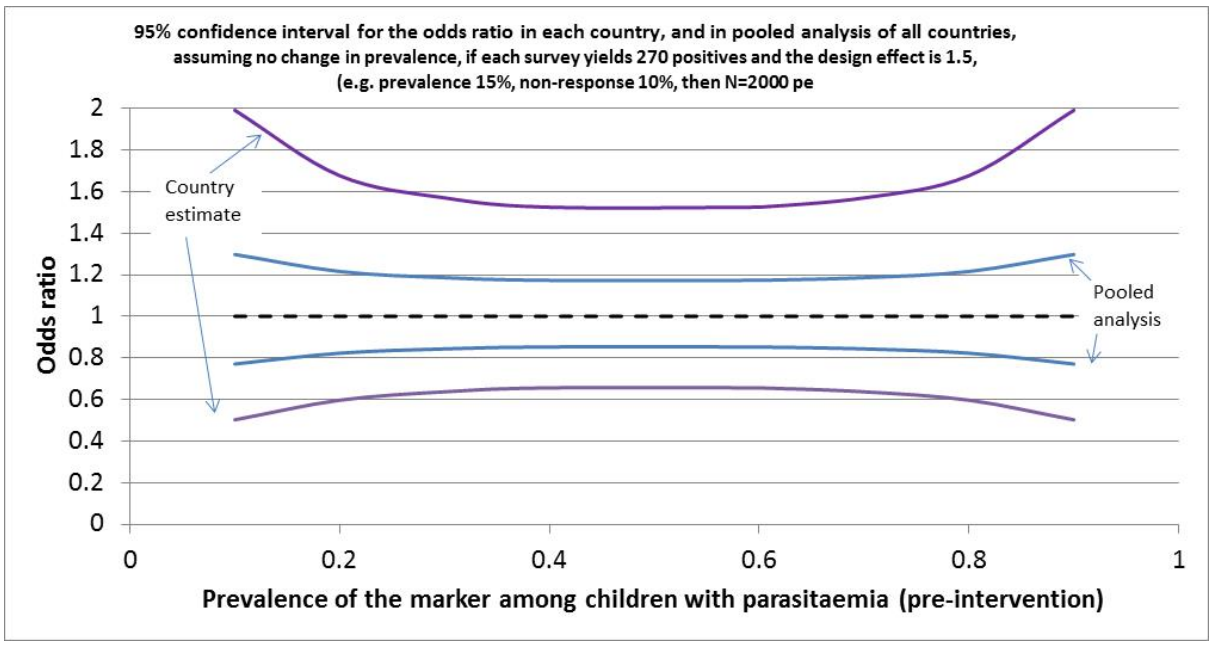
Prevalence of parasitaemia	Proportion of non-response	No. of positives required	Sample size
0.1	0.1	270	3000
0.15	0.1	270	2000
0.2	0.1	270	1500
0.25	0.1	270	1200
0.3	0.1	270	1000
0.35	0.1	270	857
0.4	0.1	270	750

It is better to be conservative when predicting the prevalence of parasitaemia in order to avoid doing surveys which are too small. The table below shows estimates of the prevalence of parasitaemia from SMC studies, to guide this decision:

			End of transmission season				Before season
			<5yrs		5-9yrs		<5yrs
Source:	**Year**	**Country**	**SMC**	**Control**	**SMC**	**control**	
I Zongo (PhD thesis)	2009	Burkina	0.12	0.36			.40
JL Ndiaye (unpub)	2011	Saraya	0.057	0.18	0.058	0.25	
Dicko et al (2010)	2008	Mali	0.072	0.132			
Dicko et al (2011)	2009	Mali		0.15			
Cisse et al (2010)	2009	Senegal	0.05				
Bojang et al (2010)	2006	Gambia	0.03				
Bojang et al (2010)	2008	Gambia	0.03				<1%
Konate et al (2010)	2008	Burkina	0.114	0.415			
Konate et al (2011)	2009	Burkina		0.4			
		Range:	3% to 12%	13% to 42%			

Most of these estimates in this table are for children sampled at the end of the transmission season. Prevalence at the start of the season, and in older age groups, is likely to be somewhat lower.

The figure below shows the 95% confidence interval that would be obtained on the odds ratio for the change in frequency of markers after two years, among parasite positive individuals, if surveys in each country yield 270 positives, and there has been no change in the prevalence of markers:



SMC monitoring survey: Information sheet (children) Dated 24 May 2015, V1.

Name of research institution

Your child is being invited to take part in a research study. To help you decide if your child can participate, we will explain why we are doing the study, and what it will involve. If there is anything that you do not understand, ask for it to be explained until you are satisfied. Take time to decide whether or not you wish to take part.

1. **Why is this study being done?**

Seasonal Malaria Chemoprevention (SMC), where children are given drug treatment each month to prevent malaria, is being introduced for children in this area. The drugs are very effective against the parasites that cause malaria, but in other parts of Africa some malaria parasites are resistant to these drugs. The National Malaria Control Programme and <research institution> are doing this survey to make sure that none of these resistant malaria parasites have come to this area. We will also test the blood of each child in the survey to check that the drugs used for SMC can work well. The information from this survey will help the malaria control programme ensure SMC remains effective.

2. **Why has my child been chosen?**

We are including children who received SMC or may receive SMC in the future. We need about 2000 children in the survey and have selected certain villages to participate.

3. **Does my child have to take part? What happens if I change my mind?**

You do not have to let your child take part. If you decide they can take part, you are still free to stop their involvement whenever you wish without having to justify it, this won't affect their normal health care. If you decide to join the study, you will need to sign or thumbprint a consent form saying you agree to be in the study. You will receive a copy of this.

4. **What does this study involve?**

If you agree for your child to participate:

we will ask to take a sample of blood from the finger,
we will ask some questions about your child's age, date of birth, any recent illness and travel, the family's ethnicity, and we will ask to see where they slept last night to inspect the bednet if there is one.

5. **Expenses and payments**

There will be no payment for participation.

6. **What are the risks or disadvantages of participation?**

The finger prick can cause discomfort but is safe and will be done by staff who are trained to do it safely with a minimum of discomfort.

7. **What are the benefits of participation?**

If your child is unwell, we will test for malaria and if the test is are positive we will treat them for malaria as the nurse would do in the clinic or refer them to the clinic where they will be treated for malaria free of charge.

8. **What will happen to the samples taken in this study?**

We will put two spots of blood onto absorbent paper to be analysed to test any parasites present in the blood to see if they are the type that are resistant to SMC drugs. We will also keep the blood sample to test if the SMC medicines can work well.

Some people have characteristics in their blood that make the medicines work less well. These characteristics (called genes) are inherited from one's parents (in the same way that children resemble their parents because of other inherited characteristics). We will use these samples to find out how many people have these characteristics.

These tests may be done at a later time by our collaborators outside this country so we will send them part of your child's blood sample. Your child's name will not be linked to the sample so no-one will know the name of the person that gave the sample. We would also want to keep some of the leftover sample for further tests in the future when we understand more about the parasites.

9. **How will your personal records remain confidential and who will have access to them?**

The personal information we collect about your child will be kept private, the only people who will be allowed to see the information will be the study investigators.

10. **Who is organising and funding the research**

The study is being organised by <research institution> in collaboration with the National Malaria Control Programme, the London School of Hygiene&Tropical Medicine, the Malaria Consortium and the Catholic Relief Services. The work is funded by UNITAID as part of the SMC programme.

11. **Who has approved the study?**

The study has been approved by the ethics committee in <country>.

Do you have any questions now? If you have any questions later about the study you may contact <Name and contact details of the principal investigator>.

SMC monitoring survey: Information sheet (adults) Dated 24 May 2015, V1.

Name of research institution

You are being invited to take part in a research study. To help you decide to participate, we will explain why we are doing the study, and what it will involve. If there is anything that you do not understand, ask for it to be explained until you are satisfied. Take time to decide whether or not you wish to take part.

1. Why is this study being done?

Seasonal Malaria Chemoprevention (SMC), where children are given drug treatment each month to prevent malaria, is being introduced for children in this area. The drugs are very effective against the parasites that cause malaria, but in other parts of Africa some malaria parasites are resistant to these drugs. The National Malaria Control Programme and <research institution> are doing this survey to make sure that none of these resistant malaria parasites have come to this area. The information from this survey will help the malaria control programme ensure SMC remains effective.

2. Why have I been chosen?

We are including adults living in areas where SMC will be used. Although SMC is for children, adults harbour the parasites and can transmit them to mosquitoes. We need about 1500 adults in the survey and have selected certain villages to participate.

3. Do I have to take part? What happens if I change my mind?

You do not have to take part. If you decide to take part, you are still free to stop whenever you wish without having to justify it, this won't affect your normal health care. If you decide to join the study, you will need to sign or thumbprint a consent form saying you agree to be in the study. You will receive a copy of this.

4. What does this study involve?

If you agree to participate:

we will ask to take a sample of blood from the finger,
we will ask some questions about your age, date of birth, any recent illness and travel.

5. Expenses and payments

There will be no payment for participation.

6. What are the risks or disadvantages of participation?

The finger prick can cause discomfort but is safe and will be done by staff who are trained to do it safely with a minimum of discomfort.

7. What are the benefits of participation?

If you are unwell, we will test for malaria and if the test is are positive we will treat you for malaria as the nurse would do in the clinic or refer you to the clinic where you will be treated for malaria free of charge.

8. What will happen to the samples taken in this study?

We will put two spots of blood onto absorbent paper to be analysed to test any parasites present in the blood to see if they are the type that are resistant to SMC drugs.

9. How will your personal records remain confidential and who will have access to them?

The personal information we collect about you will be kept private, the only people who will be allowed to see the information will be the study investigators.

10. Who is organising and funding the research

The study is being organised by <research institution> in collaboration with the National Malaria Control Programme, the London School of Hygiene&Tropical Medicine, the Malaria Consortium and the Catholic Relief Services. The work is funded by UNITAID as part of the SMC programme.

11. Who has approved the study?

The study has been approved by the ethics committee in <country>.

Do you have any questions now? If you have any questions later about the study you may contact <Name and contact details of the principal investigator>.

Consent Form (children)

Study title: SMC monitoring survey
Name of Principal Investigator:

Child's name:_____ Participant No. |__|__|__|__|

Tick as appropriate :

I have had the information (dated 25/5/15) explained to me by the study team: ☐
I understand that participation is voluntary: ☐
I have been able to ask questions about this study: ☐
I agree for data about my child to be used by the investigators: ☐
I agree for my child to take part in this study: ☐

I agree to further research on my child's samples as described in the information sheet: ☐ **Yes** ☐ **No**

Name of Parent/guardian *(printed)*	Signature/Thumbprint	Date

Name of Person taking consent	Signature	Date

The participant is unable to read the information sheet. As a witness, I confirm that all the information about the study was given and the participant consented to taking part:

Name of Impartial Witness *(if required)*	Signature	Date

Assent Form (children)

Study title: SMC monitoring survey
Name of Principal Investigator:

Participant No. |__|__|__|__|

The information about the survey has explained to me. I understand I do not have to take part.

I agree to take part in this study: ☐ **Yes** ☐ **No**

Name of child *(printed)*	Signature/Thumbprint	Date

Name of Person taking assent	Signature	Date

Consent Form (adults)

Study title: SMC monitoring survey
Name of Principal Investigator:

Participant No. |__|__|__|__|

Tick as appropriate :

I have had the information (dated 25/5/15) explained to me by the study team: ☐
I understand that participation is voluntary: ☐
I have been able to ask questions about this study: ☐
I agree for data about me to be used by the investigators: ☐
I agree to take part in this study: ☐

Name of Participant *(printed)*	Signature/Thumbprint	Date

Name of Person taking consent	Signature	Date

The participant is unable to read the information sheet. As a witness, I confirm that all the information about the study was given and the participant consented to taking part:

Name of Impartial Witness *(if required)*	Signature	Date

SMC case-control study. Information sheet (cases) Dated 24 May 2015, V1.

Name of research institution

Your child is being invited to take part in a research study. To help you decide if your child can participate, we will explain why we are doing the study, and what it will involve. If there is anything that you do not understand, ask for it to be explained until you are satisfied. Take time to decide whether or not you wish to take part.

1. Why is this study being done?

Seasonal Malaria Chemoprevention (SMC), where children are given drug treatment each month to prevent malaria, is being introduced for children in this area. The National Malaria Control Programme and <research institution> are doing this study to check that SMC is working properly.

Children with malaria, and children from the neighbourhood who do not have malaria, will be visited at home to ask about any SMC treatments they had. This will allow us to understand how well SMC is protecting children. The information from this survey will help the malaria control programme ensure SMC remains effective.

2. Why has my child been chosen?

Your child is being treated for malaria. We would like to keep a sample of blood to test the malaria parasites to make sure they are not resistant to SMC drugs, and visit you at home to ask about any SMC treatments. We are including children who have malaria in this clinic. We need about 200 children and have chosen this health centre to do the study.

3. Does my child have to take part? What happens if I change my mind?

You do not have to let your child take part. If you decide they can take part, you are still free to stop their involvement whenever you wish without having to justify it, this won't affect their normal health care. If you decide to join the study, you will need to sign or thumbprint a consent form saying you agree to be in the study. You will receive a copy of this.

4. What does this study involve?

If you agree for your child to participate:

- we will keep a sample of blood to test the malaria parasites to make sure they ae not resistant to SMC drugs,
- we will ask you some questions about your child (their age, date of birth), and your address
- we will visit you at home to ask about any SMC treatments, any recent travel, and we will ask to see where the child slept last night to inspect the bednet if there is one.

5. Expenses and payments

There will be no payment for participation.

6. What are the risks or disadvantages of participation?

The finger prick can cause discomfort but is safe and will be done by staff who are trained to do it safely with a minimum of discomfort. The home visit will be done at a time convenient to you and will take about 30 minutes.

7. What are the benefits of participation?

During the home visit the fieldworker will explain about SMC and how you can protect your family from malaria.

8. What will happen to the samples taken in this study?

We will put two spots of blood onto absorbent paper to be analysed to test any parasites present in the blood to see if they are the type that are resistant to SMC drugs. These tests may be done at a later time by our collaborators outside this country so we will send them part of your child's blood sample. Your child's name will not be linked to the sample so no-one will know the name of the person that gave the sample.

9. How will your personal records remain confidential and who will have access to them?

The personal information we collect about your child will be kept private, the only people who will be allowed to see the information will be the study investigators.

10. Who is organising and funding the research

The study is being organised by <research institution> in collaboration with the National Malaria Control Programme, the London School of Hygiene&Tropical Medicine, the Malaria Consortium and the Catholic Relief Services. The work is funded by UNITAID as part of the SMC programme.

11. Who has approved the study?

The study has been approved by the ethics committee in <country>.

Do you have any questions now? If you have any questions later about the study you may contact <Name and contact details of the principal investigator>.

SMC case-control study. Information sheet (controls) Dated 24 May 2015, V1.

Name of research institution

Your child is being invited to take part in a research study. To help you decide if your child can participate, we will explain why we are doing the study, and what it will involve. If there is anything that you do not understand, ask for it to be explained until you are satisfied. Take time to decide whether or not you wish to take part.

1. Why is this study being done?

Seasonal Malaria Chemoprevention (SMC), where children are given drug treatment each month to prevent malaria, is being introduced for children in this area. The National Malaria Control Programme and <research institution> are doing this study to check that SMC is working properly.

Children with malaria, and children from the neighbourhood who do not have malaria, will be visited at home to ask about any SMC treatments they had. This will allow us to understand how well SMC is protecting children. The information from this survey will help the malaria control programme ensure SMC remains effective.

2. Why has my child been chosen?

We are including well children under 5 years of age living near the <> health centre. We need about 400 children and have chosen this health centre to do the study.

3. Does my child have to take part? What happens if I change my mind?

You do not have to let your child take part. If you decide they can take part, you are still free to stop their involvement whenever you wish without having to justify it, this won't affect their health care. If you decide to join the study, you will need to sign or thumbprint a consent form saying you agree to be in the study. You will receive a copy of this.

4. What does this study involve?

If you agree for your child to participate:

- we will take a sample of blood from the finger to test for malaria parasites using a rapid test. If the test is positive they will be treated for malaria but we will not need to ask further questions.
- if the test is negative, we will ask you some questions about your child: their age, date of birth, any SMC treatments, any recent travel, and we will ask to see where the child slept last night to inspect the bednet if there is one.

5. Expenses and payments

There will be no payment for participation.

6. What are the risks or disadvantages of participation?

The finger prick can cause discomfort but is safe and will be done by staff who are trained to do it safely with a minimum of discomfort. The visit will take about 30 minutes. If your child has malaria they will be treated with the same medicine (ACT) used in health posts to treat malaria, it is safe and effective, as with all medicines it can cause mild side effects in some people, more severe side effects are very rare.

7. What are the benefits of participation?

Your child will be tested for malaria and if positive they will be treated for malaria free of any charge. During the visit the fieldworker will explain about SMC and how you can protect your family from malaria.

8. What will happen to the samples taken in this study?

We will put two spots of blood onto absorbent paper to be analysed to test any parasites present in the blood to see if they are the type that are resistant to SMC drugs. These tests may be done at a later time by our collaborators outside this country so we will send them part of your child's blood sample. Your child's name will not be linked to the sample so no-one will know the name of the person that gave the sample.

9. How will your personal records remain confidential and who will have access to them?

The personal information we collect about your child will be kept private, the only people who will be allowed to see the information will be the study investigators.

10. Who is organising and funding the research

The study is being organised by <research institution> in collaboration with the National Malaria Control Programme, the London School of Hygiene&Tropical Medicine, the Malaria Consortium and the Catholic Relief Services. The work is funded by UNITAID as part of the SMC programme.

11. Who has approved the study?

The study has been approved by the ethics committee in <country>.

Do you have any questions now? If you have any questions later about the study you may contact <Name and contact details of the principal investigator>.

Consent Form

Study title: SMC case-control study
Name of Principal Investigator:

Child's name:_____ Participant No. |__|__|__|__|

Tick as appropriate :

I have had the information (dated 25/5/15) explained to me by the study team: ☐
I understand that participation is voluntary: ☐
I have been able to ask questions about this study: ☐
I agree for data about my child to be used by the investigators: ☐
I agree for my child to take part in this study: ☐

Name of Parent/guardian *(printed)*	Signature/Thumbprint	Date
Name of Person taking consent	Signature	Date

The participant is unable to read the information sheet. As a witness, I confirm that all the information about the study was given and the participant consented to taking part:

Name of Impartial Witness *(if required)*	Signature	Date

SMC coverage survey: Information sheet Dated 24 May 2015, V1.

<Name of research institution>

Your child is being invited to take part in a research study. To help you decide if your child can participate, we will explain why we are doing the study, and what it will involve. If there is anything that you do not understand, ask for it to be explained until you are satisfied. Take time to decide whether or not you wish to take part.

1. Why is this study being done?

Seasonal Malaria Chemoprevention has been introduced in this area. Each child should receive treatment each month for four months during the rainy season to protect them from malaria. The National Malaria Control Programme and <research institution> are doing this survey to find out how many children did not receive SMC and the reasons.

2. Why has my child been chosen?

We are including children who should have received SMC this year. We need about 800 children in the survey and have selected certain villages to participate.

3. Does my child have to take part? What happens if I change my mind?

You do not have to take part. If you decide to take part, you are still free to stop whenever you wish without having to justify it, this won't affect your family's health care or entitlement to SMC in any way.

4. What does this study involve?

If you agree to participate we will ask to see your child's SMC card, we will ask you about any SMC treatments, reasons for any missed doses, about any recent illnesses your child had, and some other questions about your household.

5. Expenses and payments

There will be no payment for participation.

6. What are the risks or disadvantages of participation?

The visit will take about 15 minutes to go through the questions.

7. What are the benefits of participation?

The fieldworker will explain about SMC and how you can protect your family from malaria.

8. How will your personal records remain confidential and who will have access to them?

The personal information we collect about your child will be kept private, the only people who will be allowed to see the information will be the study investigators.

9. Who is organising and funding the research

The study is being organised by <research institution> in collaboration with the National Malaria Control Programme, the London School of Hygiene&Tropical Medicine, the Malaria Consortium and the Catholic Relief Services. The work is funded by UNITAID as part of the SMC programme.

10. Who has approved the study?

The study has been approved by the ethics committee in <country>.

Do you have any questions now? If you have any questions later about the study you may contact: <Name and contact details of the principal investigator>.

Consent Form

Study title: SMC coverage survey
Name of Principal Investigator:

Child's name:_____ Participant No. |__|__|__|__|

Tick as appropriate :

I have had the information (dated 25/5/15) explained to me by the study team: ☐
I understand that participation is voluntary: ☐
I have been able to ask questions about this study: ☐
I agree for data about my child to be used by the investigators: ☐
I agree to take part in this study: ☐

Name of Parent/guardian *(printed)*	Signature/Thumbprint	Date

Name of Person taking consent	Signature	Date

SMC pharmacovigilance study: Information sheet Dated 24 May 2015, V1.

Name of research institution

Your child is being invited to take part in a research study. To help you decide if your child can participate, we will explain why we are doing the study, and what it will involve. If there is anything that you do not understand, ask for it to be explained until you are satisfied. Take time to decide whether or not you wish to take part.

1. Why is this study being done?

Seasonal Malaria Chemoprevention (SMC) is a new strategy for malaria control where children are treated once a month for up to 4 months of the rainy season to protect them from malaria. SMC I svery effective and is being used widely in West Africa. The drugs used for SMC are known to be safe but they can, very rarely, cause severe side effects in some children. This study is being done to better understand why some children experience bad side effects to these drugs, in order to avoid such events in future.

2. Why has my child been chosen?

Your child's recent illness may have been caused, or partly caused, by SMC drugs. We are including children who experienced side effects from SMC in this study to learn more about why some children are affected.

3. Does my child have to take part? What happens if I change my mind?

You do not have to let your child take part. If you decide they can take part, you are still free to stop their involvement whenever you wish without having to justify it, this won't affect their normal health care. If you decide to join the study, you will need to sign or thumbprint a consent form saying you agree to be in the study. You will receive a copy of this.

4. What does this study involve?

If you agree for your child to participate:

we will ask to take a sample of blood from the finger, if one has not already been taken
we will ask to keep this blood sample for analysis
we will some questions about your child's age, date of birth, previous illnesses, medications that your child may hav taken recently, and the family's ethnicity

5. Expenses and payments

There will be no payment for participation in this study.

6. What are the risks or disadvantages of participation?

The finger prick can cause discomfort but is safe and will be done by staff who are trained to do it safely with a minimum of discomfort.

7. What are the benefits of participation?

This study will help us understand better why your child became unwell. Your child should avoid SMC medications in future but the information we obtain may help us avoid such side effects in other children in the future. We will reimburse any costs of participation for example costs of attending the clinic if this is required.

8. What will happen to the samples taken in this study?

We will put two spots of blood onto absorbent paper, to be analysed to find out how the SMC medicines reacted in your child. Some people have characteristics in their blood that make the medicines work less well or cause side effects. These characteristics (called genes) are inherited from one's parents (in the same way that children resemble their parents because of other inherited characteristics). We will use these samples to find out if children who had side effects have these characteristics. Some tests may be done at a later time by our collaborators outside this country so we will send them part of your child's blood sample. Your child's name will not be linked to the sample so no-one will know the name of the person that gave the sample. We would also want to keep some of the leftover sample for further tests in the future when we understand more about the drugs.

9. How will your personal records remain confidential and who will have access to them?

The personal information we collect about your child will be kept private, the only people who will be allowed to see the information will be the study investigators.

10. Who is organising and funding the research

The study is being organised by <research institution> in collaboration with the National Malaria Control Programme, the London School of Hygiene&Tropical Medicine, the Malaria Consortium and the Catholic Relief Services. The work is funded by UNITAID as part of the SMC programme.

11. Who has approved the study?

The study has been approved by the ethics committee in <country>.

Do you have any questions now? If you have any questions later about the study you may contact <Name and contact details of the principal investigator>.

Consent Form

Study title: SMC pharmacovigilance study
Name of Principal Investigator:

Child's name:_____ Participant No. |__|__|__|__|

Tick as appropriate :

I have had the information (dated 25/5/15) explained to me by the study team: ☐
I understand that participation is voluntary: ☐
I have been able to ask questions about this study: ☐
I agree for data about my child to be used by the investigators: ☐
I agree for my child to take part in this study: ☐

I agree to further research on my child's samples as described in the information sheet: ☐ **Yes** ☐ **No**

Name of Parent/guardian *(printed)*	Signature/Thumbprint	Date

Name of Person taking consent	Signature	Date

The participant is unable to read the information sheet. As a witness, I confirm that all the information about the study was given and the participant consented to taking part:

Name of Impartial Witness *(if required)*	Signature	Date

Adverse drug reactions

Safety monitoring for SMC: Guide to the rare severe side-effects of SMC drugs

Condition	Description	Actions
Stevens-Johnson syndrome (severe skin rash) 	Painful red or purplish rash that spreads and blisters. Then the top layer of the affected skin dies and sheds. May begin with flu-like symptoms.	Notify. Medical emergency that requires hospitalization. Avoid all sulfa-containing drugs in future.
Hepatotoxicity (jaundice) 	Signs of liver injury include yellow eyes, dark coloured urine, with loss of appetite, nausea, vomiting or abdominal pain, or weakness.	Notify. Confirm with lab tests for liver function if possible. Refer to hospital.
Extra-pyramidal syndrome (neurological disorder)	Involuntary muscle movements in the face and neck. May include lip smacking, tongue movements, blinking, and head or finger spasms. The patient may have difficulty moving the arms and legs, and slur their words.	Notify. Avoid AQ in future. Refer to hospital.
Repeated vomiting 	Repeated vomiting can start hours after drug intake, and in severe cases can persist for several days with vomiting several times per day.	Eligible for SMC in the next round, but advise the family to bring the child to clinic if symptoms recur.

- Severe adverse reactions to SMC drugs are very rare.
- Cases of conditions marked "Notify" should be reported immediately to Dr._____ at this number: Tel. _____
- For all suspected side effects, mild or severe, a Pharmacovigilance Form should be completed.
- When completing the Pharmacovigilance Form, record when the symptoms started, and ask about ALL medications including traditional medicines the child has received in the last 2 weeks.

Safety monitoring for SMC: Guide to the rare severe side-effects of SMC drugs

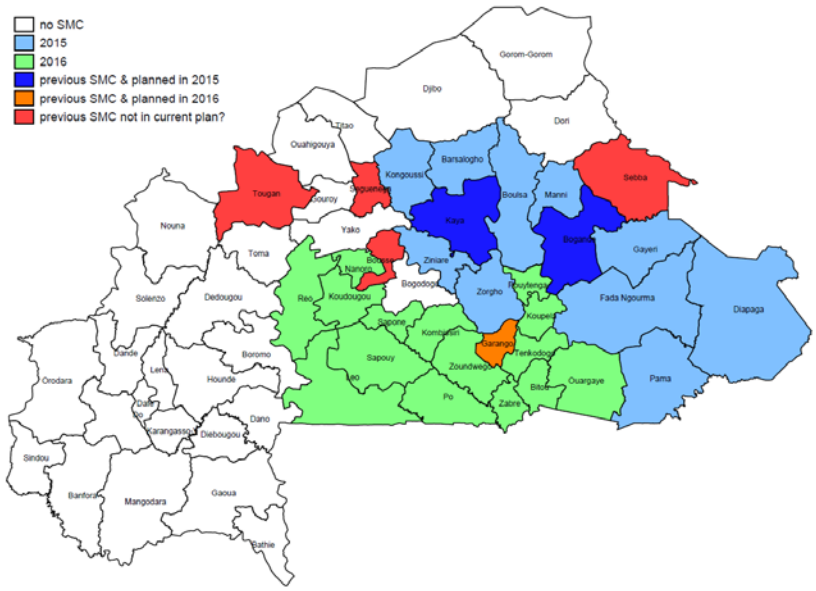
- Mild symptoms commonly reported include rash, itching, fever, headache, drowsiness, diarrhoea.
- In case of fever, always test to confirm if malaria with RDT or microscopy.
- Most side effects will appear within the first week after taking the drugs, but if a child is unwell at any time they should come to the health facility
- Very rarely, medicines can cause anaphylactic shock, a severe allergic reaction that occurs quickly. This is a medical emergency and requires immediate hospitalisation. If this occurs, SP+AQ should be never be given in the future.
- Some rare side effects affecting the blood (agranulocytosis, thrombocytopenia, and aplastic anaemia) can be detected only using laboratory tests. If diagnosed SP + AQ should be avoided in the future.

Adverse reactions that are detected using laboratory investigation:		
Agranulocytosis (low white blood cell count) **Occurs when the white cell count (neutrophils) is low (<750/mm³). It can turn minor infections in more serious ones.**	Symptoms include sudden fever, chills, a sore throat, and weakness in the limbs. The mouth and gums may be sore, mouth ulcers can develop, and gums might begin to bleed.	Notify. Diagnosis requires a white cell count. Antibiotics or antifungal drugs may be given to treat any infections. Avoid AQ in future.

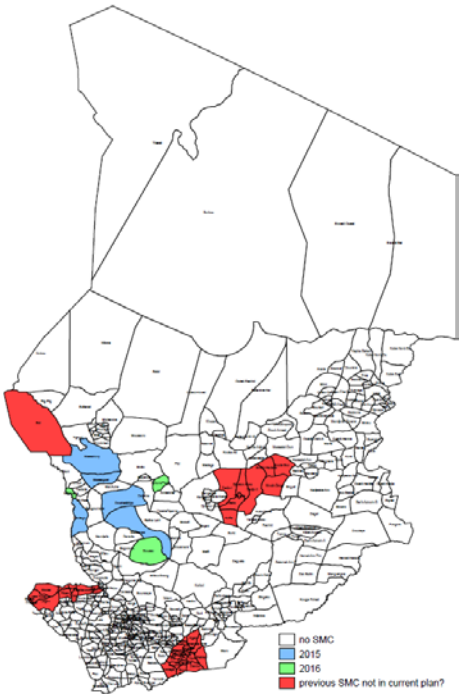
Picture credits: Prof JLNDiaye, Universite Cheikh Ant Diop, Dakar
https://www.flickr.com/photos/27849635@N05/2735492595 CDC/Dr. Thomas F. Sellers/Emory University
Malaria Consortium 2012

Maps showing areas where SMC will be implemented in 2015 and 2016

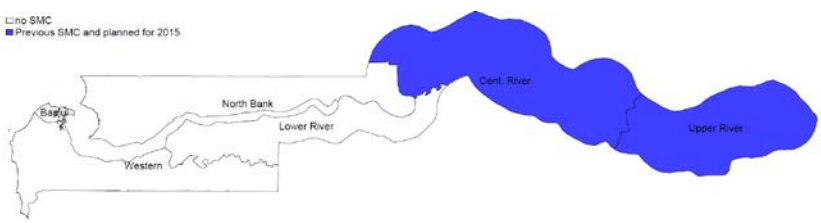
Burkina Faso



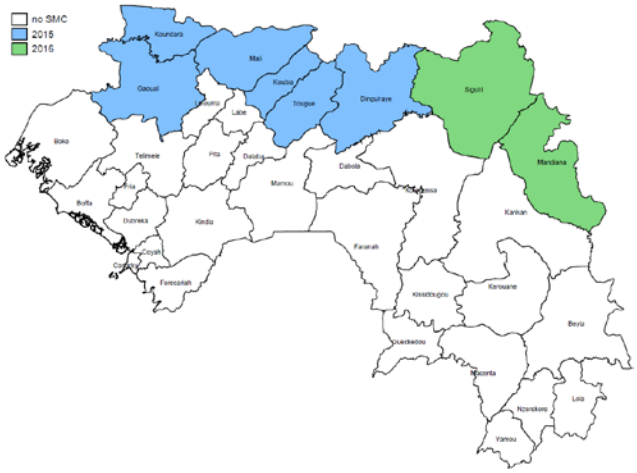
Chad



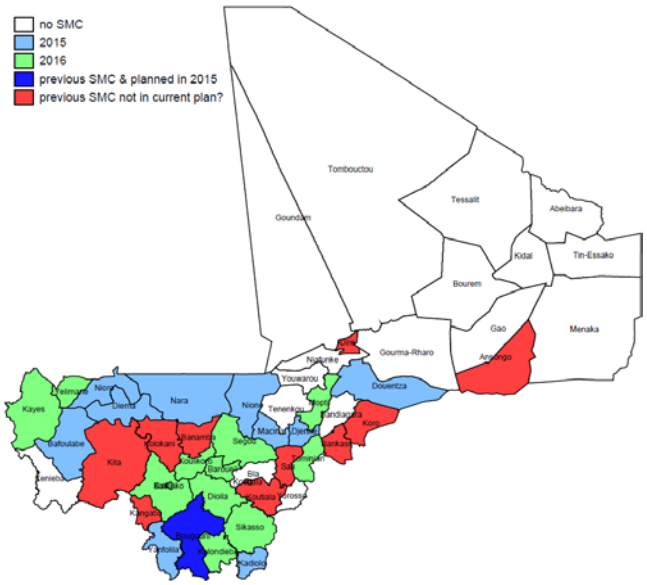
The Gambia



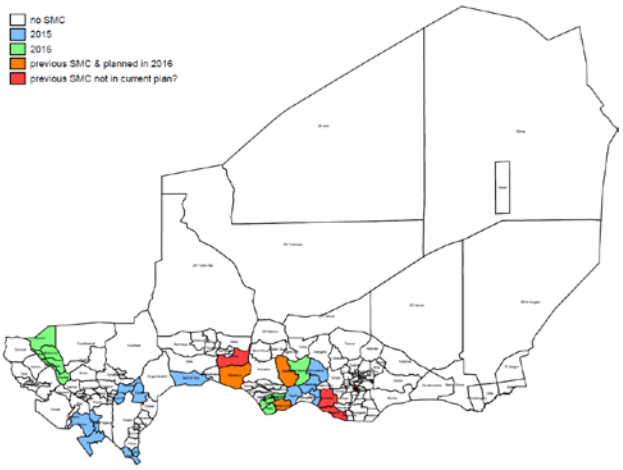
Guinea



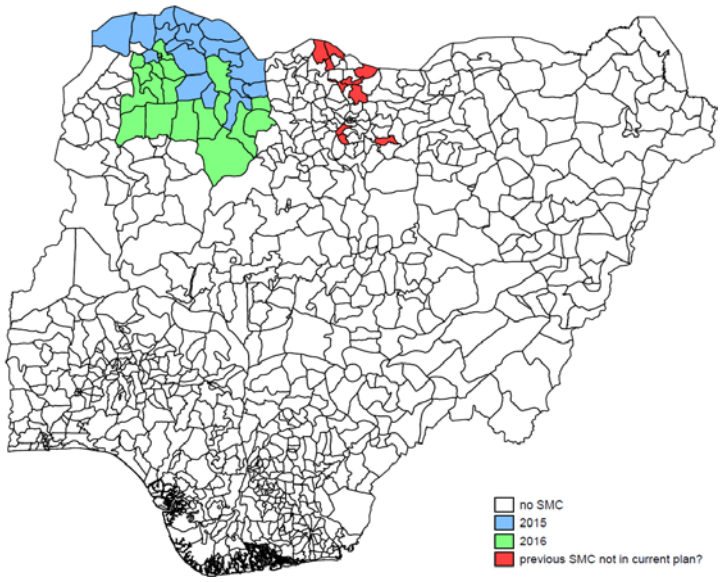
Mali



Niger



Nigeria



SMC case-control study forms

Malaria Case

Health centre: _____ District _____ Initials of nurse _____

Name of child _____ _____ Name of mother _____ _____

dd mmm yyyy
Age|__| yrs |__|__| months Date of Birth |__|__| |__|__|__| |__|__|__|__|

Village _____ Head of household _____ _____

---

dd mmm yyyy
Today's date |__|__| |__|__|__| |__|__|__|__| Axillary temperature |__|__|.|__|^{o}C

RDT performed |__| 1=Y 0=N RDT result |__| 1=Positive 0=Negative

Blood film |__|1=Y 0=N Result:|__|1=Positive 0=Negative Parasite density|__|__|__|__|__|__|/µL

SMC doses: <*check the child's SMC record card, and ask the mother/carer about the doses received. If possible also check in the SMC register*>

SMC record card seen |__|1=Yes 0=No Child found in the SMC register |__| 1=Yes 0=No

dd mmm yyyy
Has the child received SMC this year |__|Y/N Date of last treatment: |__|__| |__|__|__| |__|__|__|__|

First dose administered by the Health Worker |__| Yes/No |__| 1=Swallowed 2=spat or vomited 3=refused

Dose given at home on the second day |__| Yes/No |__| 1=Swallowed 2=spat or vomited 3=refused

Dose given at home on the third day |__| Yes/No |__| 1=Swallowed 2=spat or vomited 3=refused

---

Home visit: <*Ask to see where the child sleeps*>

Did the child sleep under a bednet last night? |__|Y/N Type of net: |__| 1=LLIN 2=other

About the mother or carer of the child:

Highest level of formal education |__| 1=None 2=Koranic 3=Primary 4=Secondary 5=College

<Enter the name and village of this case on two control forms. Move at least two compounds away from the home of the case, and look for control children aged 3-59 months. Each control child should come from a different household>

Controls

Name of case _____ _____ Village of case _____

Name of child _____ _____ Name of Mother _____ _____

dd mmm yyyy
Age|__| yrs |__|__| months Date of Birth |__|__| |__|__|__| |__|__|__|__|

Village _____ Head of household _____ _____

---

dd mmm yyyy
Today's date |__|__| |__|__|__| |__|__|__|__| Axillary temperature |__|__|.|__|°C

RDT performed |__| 1=Y 0=N RDT result |__| 1=Positive 0=Negative

If Positive: referred for treatment |__|1=Yes 0=No

If Negative: enrolled as a control |__| 1=Yes 0=No

SMC doses: <*check the child's SMC record card, and ask the mother/carer about the doses received. If possible also check in the SMC register*>

SMC record card seen |__|1=Yes 0=No Child found in the SMC register |__| 1=Yes 0=No

dd mmm yyyy
Has the child received SMC this year |__|Y/N Date of last treatment: |__|__| |__|__|__| |__|__|__|__|

First dose administered by the Health Worker |__| Yes/No |__| 1=Swallowed 2=spat or vomited 3=refused

Dose given at home on the second day |__| Yes/No |__| 1=Swallowed 2=spat or vomited 3=refused

Dose given at home on the third day |__| Yes/No |__| 1=Swallowed 2=spat or vomited 3=refused

---

<*Ask to see where the child sleeps*>

Did the child sleep under a bednet last night? |__|Y/N Type of net: |__| 1=LLIN 2=other

About the mother or carer of the child:

Highest level of formal education |__| 1=None 2=Koranic 3=Primary 4=Secondary 5=College

SMC Survey for monitoring markers of drug resistance

Met etiquette ici

Date |DD_|_MMM_|_2015_|

District |_____| Health post name | _____|

Village/quartier |_____|

Nom chef menage |_____|

Participant Name |_____| Gender |__|

Date of birth |_____| Age |__|__| yrs |__|__| mths

Participant seen |__| Y/N and gave consent |__| Y/N

Temperature |__|__|.|__|°C Fever |__| Y/N If Yes -> RDTperformed ?|__|Y/N
Result|__|1/0

Blood sample obtained |__| Y/N Smear |__| Y/N Filter paper |__| Y/N

Ethnic group of mother _____ Ethnic group of father _____

L'enquêté a-t-il dormi sous moustiquaire la nuit dernière ? |__| Oui /Non

Demander à voir là où dort l'enquêté d'habitude et inspecter la moustiquaire.
A propos de la moustiquaire :

A t elle été traitée au moins 1 fois lors les 12 derniers mois? |__| Y/N
Si Non :
n'importe quel type |__| Y/N Moustiquaire imprégné |__| Y/N Milda |__|
1-Olyset Net; 2- Parmanet ;
3-Dawaplus ;4-Iconelife ;
5- autres_____
Peut-elle être bordée sous le matelas? |__| Y/N Est-elle intacte (<5 trous) |__|Y/N
Depuis combien de temps votre ménage possède-t-il cette moustq? |_|_|Ans |_|_| Mois

---

When was the last time they were ill and went to a health worker? |__|
1 – in the last week ; 2-in the last month ;
3 –in this year 2012 ; 4 – not in this year
Did they have a finger prick ? |__|Y/N Did they get malaria treatment?|__|Y/N

Have they spent a night away from home in the last 2 weeks? |__|Y/N

Name of field worker |_____|

Coverage survey

Prénom et nom de l'enfant : **Date de naissance ou âge de l'enfant:** **Sexe : 1❑ M 2❑ F**

Numéro ID de l'enfant : /_____/ **Prénom et nom de la mère :**

Nom de l'enquêteur : **Date de la visite : /___/_____/_____/** **Village :**

_____

L'enfant est-il présent ? 1❑ Oui 2❑ Non Si Non, Motif absence :…… Lieu :…….

Nb d'années dans le village ? |___| Années Ou de mois |___| Mois

L'enfant est-il résident ? 1❑ Oui 2❑ Non (vécu 6 mois ou intention de rester pendant au moins six mois)

Prénom et Nom de celle (ou celui) qui s'occupe de l'enfant _____ _____ Sexe |___| M/F Âge |___|___| années

Quelle est la relation avec l'enfant? |___|

1=Mère, 2=Père, 3=Sœur, 4=Grand-mère, 5=Tante, 6=Autre: _____

Statut matrimonial : 1❑ Marié(e) 2❑ Célibataire 3❑ Veuve 4❑ Divorcée

Cette personne a t elle été à l'école coranique ? 1❑ Oui 2❑ Non si oui, combien d'années d'école au total? |____|____| Années

Cette personne a t elle été à l'école française? 1❑ Oui 2❑ Non si oui, combien d'années d'école au total? |___|___| Années ou Niveau d'étude /_____/

Connaissances sur le paludisme

Comment attrape t-on le paludisme? (Plusieurs réponses possibles) 1❑ Le vent 2❑ La pluie 3❑ Les moustiques 4 ❑ les saletés 5❑ Les esprits 9❑ Autres à préciser : …….

Quels sont les signes du paludisme? (Plusieurs réponses possibles) 1 ❑ Les maux de tête 2 ❑ Les frissons et les sueurs 3❑ Les Vomissements 4❑ La toux 5 ❑ Le corps chaud

9❑ Autres à préciser : ……..……

Peut – on mourir du paludisme? 1❑ Oui 2❑ Non 3 ❑ Nsp

Avez-vous entendu parler du TPI ? 1❑ Oui 2❑ Non

Si Oui, à quelle occasion ? 1❑ Au centre de santé 2❑ A la radio 3❑ A la télévision 4. Par votre voisin 9❑ Autres à préciser : ……

A quoi sert-il ? 1❑ Protège contre le paludisme 2❑ Protège contre les moustiques 3❑ Baisse la fièvre 4❑ Je ne sais pas 9❑Autres à préciser :…….

Les médicaments du TPI, peuvent-ils donner des réactions secondaires aux enfants? 1❑ Oui 2❑ Non

Si oui, lesquels ? : 1❑ Fièvre/corps chaud 2❑ Diarrhée 3 ❑ Eruption cutanée 4 ❑ Vomissement 5 ❑Perte de l'appétit 6 ❑ Jaunisse 7 ❑ Toux 8 ❑ Prurit

9❑Autres à préciser :……

Votre enfant a-t-il été malade ces deux dernières semaines ? |___| Oui /Non /NSP si oui a-t-il pris un traitement|___| Oui /Non /NSP

si oui où l'a-t-il pris 1, 2, 3, 4, 5, 6, 7, 8,9,

1 : à la maison 2 : case de santé 3 : poste de santé 4 : centre de santé 5 : hôpital 6 : boutique 7 : pharmacie 8 : marché hebdomadaire 9 : guérisseur

Un guérisseur a-t-il vu votre enfant ces 6 derniers mois ? 1❑ Oui 2❑ Non Si Oui, Pourquoi : ……

Moustiquaires

L'enfant dort-il d'habitude sous une moustiquaire ? |___| Oui /Non/NSP, quelle est la dernière fois qu'il a dormi sous moustiquaire : jours |___| semaines |___| Mois |___| JAMAIS |___|

Pendant la saison des pluies dors t-il sous moustiquaire : Toutes les nuits |___| la plupart des nuits |___| quelques nuits |___| jamais |___|

L'enfant a-t-il dormi sous moustiquaire la nuit dernière ? |___| Oui /Non/Nsp

Demander à voir là où dort l'enfant *d'habitude et inspecter la moustiquaire*

A propos de la moustiquaire

D'où provient-elle? Achetée |___| Etat |___| ONG |___| Si oui lequel _____

Cette moustiquaire a t elle été traitée au moins 1 fois lors les 12 derniers mois? |___| Oui/ Non/ Nsp

Si Non : Moustiquaire de n'importe quel type ? |___| Oui /Non/Nsp Moustiquaire imprégné ? |___| Oui /Non/Nsp Milda ? |___| Oui /Non/Nsp

Peut-elle être bordée sous le matelas? |__| Oui /Non Est-elle intacte (<5 trous) |__| Oui/Non

Autres médicaments reçus :

Votre enfant a-t-il reçu cette année les capsules rouges et bleues données tous les 6 mois |___| Oui /Non (vit A)

A-t-il reçu cette année les comprimés blancs donnés tous les 6 mois |___| Oui /Non (mebendazole)

L'ASC/DSDom qui travaille dans le village et traite votre enfant, reçoit-il un appui de la part des villageois ? 1❑ Oui 2❑ Non 3 ❑ Nsp

Si oui, quelle forme d'appui ? 1❑ Aide aux travaux champêtres 2❑ aide financière ❑ autres à préciser :……. Si non, pourquoi ?……

L'enfant était-il présent lors de l'administration du TPI au mois de novembre? 1❑ Oui 2❑ Non Si Non motif : /_____/

A- t-il été nécessaire de recueillir l'aval d'une tierce personne avant administration du TPI à l'enfant ? 1❑ Oui 2❑ Non

Si Oui, qui est cette personne? 1❑ Mère 2❑ Père 3❑ Sœur 4❑ Grand-mère 5❑ Tante 6❑ Autre à préciser :……..…

Quelle est l'action des comprimés que votre enfant a pris au mois de novembre? 1❑ Protègent contre le paludisme 2❑ Protègent contre les moustiques 3❑ Baissent la fièvre 4❑ Je ne sais pas 9❑Autres à préciser :……..

Si (1❑ Protège contre le paludisme), pendant combien de temps ? jours |___| semaines |___| Mois |___|

la protection qu'elle confère est elle totale? 1❑ Oui 2❑ Non

L'enfant est il allé à l'école en octobre et novembre 2011 ? 1❑ Oui 2❑ Non **si Oui, a-t-il manqué une classe à cause de l'administration de médicaments ?** 1❑ Oui 2❑ Non

Si non à la question précédente, **est ce que l'ASC/Dsdom a administré les médicaments en dehors des heures de classe** 1❑ Oui 2❑ Non

Carte TPI vue ? 1❑ Oui 2❑ Non **Si Non, une carte TPI lui a-t-elle été délivrée ?** 1❑ Oui 2❑ Non 3❑ Nsp

Mentionnez (et vérifier aussi sur la carte) si les traitements TPI ont été reçus chaque mois et si cela n'a pas été le cas, demandez la raison

Mois	Traitement	
Juliet	1❑ Oui 2❑ Non 3❑ Nsp	si non, précisez la raison |__| 1, 2, 3, 4, 5, 6, 7, 8
Août	1❑ Oui 2❑ Non 3❑ Nsp	si non, précisez la raison |__| 1, 2, 3, 4, 5, 6, 7, 8
Septembre	1❑ Oui 2❑ Non 3❑ Nsp	si non, précisez la raison |__| 1, 2, 3, 4, 5, 6, 7, 8
Octobre	1❑ Oui 2❑ Non 3❑ Nsp	si non, précisez la raison |__| 1, 2, 3, 4, 5, 6, 7, 8
Novembre	1❑ Oui 2❑ Non 3❑ Nsp	si non, précisez la raison |__| 1, 2, 3, 4, 5, 6, 7, 8

1=enfant absent mais dans le village, 2=enfant en voyage, 3= Enfant présent mais mère ou tutrice absente, 4=enfant trop malade 5=réaction adverse lors de la précédente administration 6=enfant trop jeune, 7=refus des parents, 9=autre, spécifiez

Si les parents avaient refusé : spécifier la raison du refus_____

Lors de la dernière administration de médicaments (Novembre) avez-vous eu des problèmes pour donner la 2ème ou 3ème dose à votre enfant ? 1❑ Oui 2❑ Non

Si Oui, spécifier la raison : 1❑ oubli 2❑ l'enfant avait refusé 9❑ Autres spécifier : ……

Si non L'enfant a-t-il: ***(cochez la réponse)***	2ème dose	3ème dose
Bien avalé le médicament ?	|__| Oui/Non/Nsp	|__| Oui/Non/Nsp
Avalé le médicament mais l'a aussitôt rendu?	|__| Oui/Non/Nsp	|__| Oui/Non/Nsp

Votre enfant avait eu-il eu une réaction secondaire à la prise de médicaments ? 1❑ Oui 2❑ Non 3❑ Nsp si Oui, décrivez la……..

Pourquoi faut-il donner le TPI sur 3 jours ? 1❑ Protection totale 2❑ recommandation de l'ASC 3❑ Nsp 9❑ Autres à préciser :……..

Etes-vous prêts à accepter que votre enfant prenne le TPI l'année prochaine ? 1❑ Oui 2❑ Non 3❑ Nsp Si Non, pourquoi ……