Systematic assessment of factors affecting the delivery, access and use of interventions to control malaria in pregnancy in sub-Saharan Africa

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Progress with coverage of malaria prevention

Progress with achieving global and national coverage targets for malaria in pregnancy interventions over the past decade has been slow. In 2006, a year after the 2005 Abuja target of 60% coverage of malaria prevention interventions, only five countries had rolled out nationwide implementation following IPTp-SP policy adoption, namely Malawi (1993), Kenya (1998), Tanzania and Uganda (2000), and Zambia (2002) (Chapter 2), although about half of malaria endemic countries in sub-Saharan Africa (24 of 45) had adopted the policy [1]. DHS survey data on coverage for two doses of IPTp-SP was available for only two countries that had first made the policy change, Malawi (29%) and Kenya (4%). By 2011, DHS survey data on malaria in pregnancy indicators were available for many more countries, and average coverage in 2007 of IPTp-SP across 19 countries was 13.6%, and of ITN use the night before the survey across 32 countries was 17.0%, with lowest coverage in areas of highest transmission [2]. Only Zambia had reached national coverage of 60% or more with IPTp-SP, and at sub-national level 11 administrative (ADMIN1) regions had coverage of 60% or more, in Zambia, Senegal, Liberia, Ghana, and The Gambia. No country had reached 60% coverage for ITNs even though ITN policy adoption preceded IPTp-SP policy adoption by several years in almost all countries; the highest ITN coverage was reported in Rwanda (45.2%), Zanzibar (43.5%), and Madagascar (43.3%). At a sub-national level, ten ADMIN1 regions had ITN coverage of 60% or more, in Ethiopia, Madagascar, Senegal, and Zambia.

By 2010, Zambia and The Gambia were the only countries to have exceeded the 60% target for IPTp-SP and no country had reached the 2010 target of 80%, with average coverage of IPTp-SP across 27 countries of 21.5% and of ITNs across 37 countries of 38.8% (Chapter 3) [3]. Five countries had exceeded 60% coverage of ITNs (Benin, Mali, Madagascar, Niger and Rwanda), and none had achieved 80% coverage. A fall in coverage of more than 10% for IPTp-SP was observed in two countries and for ITNs in three countries. The fall in ITN use in Malawi may have been due to the later survey being done in the dry season [4], and in Equatorial Guinea to a shortfall in funding, however there were no obvious explanations for the dramatic fall in ITN use in The Gambia (from 45.0% to 26.1%) or IPTp-SP coverage in Senegal and Mozambique. Increases in coverage of both interventions was associated with higher per capita disbursement of malaria, and for IPTp-SP, a time interval of seven years or more between policy adoption and survey date.

While all but eight malaria endemic countries (Botswana, Burundi, Cape Verde, Djibouti, Eritrea, Ethiopia, Swaziland, and South Africa) had adopted IPTp-SP and all countries had adopted ITN policies by 2007, few countries are likely to meet the 2015 target of 100% coverage at the current rate unless radical improvements to programmes are made. The discrepancy between ANC coverage (approximately 75% of pregnant women attend ANC at least twice) and malaria intervention coverage identified in all three reviews [1-3] points to substantial missed opportunities to deliver IPTp-SP and ITNs at antenatal clinics.
Challenges to the delivery of malaria in pregnancy interventions

IPTp-SP. Of the two malaria in pregnancy prevention interventions, IPTp has been more problematic for national programmes to deliver. The first review of a limited number of available studies in 2006 (Chapter 2) identified a comprehensive list of challenges to the delivery of IPTp-SP experienced in the first five countries to adopt the policy, providing important lessons for countries about to embark on implementation. The main challenges concerned the policy change process at national level, which in Kenya took over seven years, and the translation of policy to the operational level i.e. delivery through antenatal care services. At the operational level, health worker confusion about the timing and spacing of the two doses, correct identification of trimesters, lack of awareness of drug policy, and the need for supervisory feedback were among the challenges identified, and the benefits of simplified messages and low cost job aids for health providers clearly described. Importantly, the review underscored, for the first time, that the assumption that high ANC attendance was sufficient to ensure high IPTp-SP coverage was misguided, and that in countries with low ANC coverage, alternative channels for delivering IPTp-SP may be needed to supplement delivery through routine ANC services. The review also called for a need to better document best practices and to develop simplified guidance to all countries and especially those about to embark on implementation.

The prolonged process of consensus development for IPTp-SP among stakeholders experienced in some East African countries was avoided in West Africa through a concerted action of the sub-regional network [5]. Nevertheless, the systematic review of 98 studies conducted between 1990 and 2013 (Chapter 4) suggest that important lessons from East Africa have failed to reach other countries in the Africa region, with many of the same mistakes at the operational level being repeated elsewhere. For example, the same barriers among health providers persist, such as confusion of the timing and dosing of IPTp-SP, lack of guidelines, lack of training and supervision, perceptions that women will not take SP on an empty stomach, and lack of water and cups. Health providers continue to blame pregnant women for low uptake of IPTp-SP, due to women’s late or infrequent ANC attendance, complaints of side effects from SP, and preferences for other antimalarials, and yet health providers themselves fail to give pregnant women accurate information about the drugs they provide. Some important additional constraints were identified, such as incompatibilities between provision of IPTp-SP and concurrent treatment of syphilis, anaemia, HIV, and malaria [6], or being referred to a laboratory for testing, which have to be overcome through provision of additional guidance. Inconsistent guidelines have the potential to cause confusion and lead to incorrect practices among health providers, contributing to low coverage of IPTp-SP and LLINs. A recent review of national malaria in pregnancy policies, guidelines, and training documents from across malaria and reproductive health programmes in five countries found that many documents were outdated and/or inconsistent, and failed to adhere to WHO policy [7]. Research suggests that implementing a three-dose IPTp-SP schedule achieves higher coverage of two doses [6,8,9] however, with the exception of Zambia, this has not borne out in national programmes.

ITNs. Comparatively fewer barriers to the delivery of ITNs at ANC were identified (Chapter 4), the main factors being insufficient stocks to meet demand or unavailability of vouchers. With the advent of universal coverage with ITNs, an ITN supply problem encountered in several countries has been the re-allocation of ITNs from routine delivery to meet shortfalls for national campaigns (Chapter 5). In a climate of limited funding commitments in the Global Fund to fight AIDS, TB and Malaria and other major donors, and an estimated shortfall of 70% of all LLIN needs for continuous distribution
systems (through ANC and EPI) [10], governments of endemic countries and their donors and implementing partners will need to balance the costs and benefits of ITNs to ensure the most cost effective strategies are utilised. In areas where transmission remains moderate-to-high, ITNs have the greatest benefits in pregnant women and young children, and coverage of these groups should be ensured.

**Case management.** Despite the widespread availability of ACTs for first line treatment of uncomplicated malaria, and the introduction in 2006 by WHO of the use of ACTs for treatment of malaria in the second and third trimesters of pregnancy, far less attention has been given to the availability and quality of case management of malaria in pregnancy. The systematic review identified only 37 studies undertaken in countries following the adoption by countries of the WHO 2006 policy, and the majority (30) of these were in Africa even though ACT use began much earlier in Asia (Chapter 9). The review identified important limitations in the implementation of the WHO policy, in particular a continued reliance on clinical diagnoses and poor adherence to treatment policy among health providers, especially in the first versus other trimesters. The low use of parasitological diagnosis will result in many women receiving unnecessary antimalarials in pregnancy, particularly in areas of high HIV prevalence where infected individuals have a high incidence of febrile illness [11]. Even where diagnostics are available, health providers have been reported to ignore negative test results and prescribe antimalarials where malaria is suspected [12]. These decisions may be based on a number of factors, such as patient demand, lack of trust in the accuracy of slide reading, or suspected insensitivity of RDTs to detect malaria in pregnancy. The sensitivity and specificity of RDTs to detect peripheral malaria in pregnancy is suboptimal because of haemodilution and placental sequestration of parasites [13].

The administration of ACTs in the first trimester, reported in Ghana, CAR and Nigeria, poses potential safety concerns due to insufficient safety data in early pregnancy [14,15] and, while population-based studies on the Thai-Burmese border showed no toxic effects of artemisinin use in early pregnancy [16], WHO recommends that ACTs should only be used in early pregnancy if this is the only treatment available. Studies by the Malaria in Pregnancy Consortium to develop pharmacovigilance systems to monitor prospectively the safety of antimalarials in pregnancy in resource-poor settings will be important to provide much needed data [17]. The continued use of drugs that are no longer efficacious nor recommended in national treatment policies, such as SP (recommended for IPTp use only) in Ghana and Nigeria, and chloroquine (due to high levels of resistance [18]) in Nigeria [19], is of concern, and the use of artemisinin monotherapies is a threat for the development of artemisinin resistance in the Africa region, as occurred in parts of Asia [20,21].

A major challenge for improving practices for the diagnosis and treatment of malaria in pregnancy is the wide range of providers administering antimalarials to pregnant women in the community. A recent cluster randomised trial to evaluate whether RDTs should be introduced into drug shops in Uganda illustrates the complexities of achieving a detailed evaluation without inadvertently influencing prescribing behaviour [22]. Ministries of Health need to incorporate private sector providers into national training and policy dissemination activities. In addition, licensing systems to regulate which antimalarials are sold at the community level through formal drug sellers and pharmacies are also needed. As the structure and characteristics of antimalarial distribution chains vary across countries, efforts aiming to improve access to quality treatment through the private sector will require a good local understanding of these chains [23]. Countries continuing to use
chloroquine or artemisinin monotherapies should consider proactively withdrawing these drugs from importation and circulation, as done in Malawi [24] and Kenya [25].

**Women’s access to and use of malaria in pregnancy interventions**

**Systematic Reviews.** From the perspective of pregnant women, many of the barriers to receipt of IPTp-SP related to their lack of knowledge about IPTp-SP, its benefits, dosing schedule, perceptions of drug safety, concerns that SP could not be taken without food, fear or prior experience of side effects, and negative media coverage of SP (Chapter 4). In the absence of knowledge, women are required to place considerable trust in health providers to provide interventions that are safe and beneficial, and yet health providers are often rude and treat women with a lack of respect. Evidence from seven studies that health providers often fail to offer IPTp-SP also means that unless women are informed about which services to receive and when, they are ill equipped to ask for them. Cost was a second major barrier to receiving both doses of IPTp-SP due to fees for ANC registration on repeat visits, penalties imposed by health providers for coming to ANC late, or for purchasing SP and water.

Barriers to pregnant women’s use of ITNs related to the inconvenience and discomfort of using them, and lack of support from their husbands or their community (Chapter 4). The second major category of barriers was access due to the direct and indirect costs of accessing ITNs, lack of availability of ITNs or ITN vouchers at ANC, with urban versus rural residence an important factor affecting access.

Up to three-quarters of women report malaria illness during pregnancy, with a high proportion of these women (>85%) seeking treatment (Chapter 9). Low knowledge of treatment options, drug safety and efficacy, and cost affected treatment choices, and consequent reliance on self-medication or traditional remedies was common. Socio-cultural factors also affect women’s access to treatment, such as not wishing to disclose their pregnancy, needing their husband’s consent, and other factors at the household level that restrict a woman’s autonomy to seek care [26,27]. The review identified important limitations in the implementation of the WHO policy; there is an apparent disconnect between the WHO policy and women’s beliefs and practices. Importantly, pregnant women do not uniformly seek care within a formal health facility and when they do, they may not access appropriate diagnosis and care due to the limitations among health provider practices or inadequate resources, or because they cannot afford to pay for the services.

**Field based studies.** The effectiveness analyses of household survey data from recently pregnant women in Kenya (Chapter 6) [28] and Mali (Chapter 7) [29] were useful in identifying programmatic deficiencies and critical points in the delivery of IPTp-SP and ITNs in ANC where missed opportunities occurred. The cumulative effectiveness of receiving two doses of IPTp-SP by DOT in an eligible gestational age and using an ITN obtained from ANC was low in both countries and lowest in Mali; 13.5% and 5.8% in Kenya and Mali respectively. ITN use among pregnant women last night was higher in Mali than in Kenya (92.6% vs 80.2%), with about three-quarters of nets sourced from ANC in both countries.

In Kenya, pregnant women’s ANC clinic attendance was not the primary cause of low uptake of the second dose of IPTp-SP since a high proportion of women who received the first dose of IPTp-SP made a return visit to ANC (89.6%). Only about half of women attending ANC received either the first or second dose of IPTp-SP, suggesting health providers were responsible for low effectiveness of
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IPTp-SP delivery. Where IPTp-SP was given however, adherence to DOT was more successful but still less than the national target of 80%, with about three-quarters of women who received either dose of IPTp-SP reporting they had received it by DOT. In Mali, while receipt of the first dose of IPTp-SP was effective receipt of the second dose was poor, and conversely, the practice of giving IPTp-SP by DOT was poor for the first dose (33.0%) but high for the second dose (80.0%). Of concern was the finding that women reported receiving the first dose of IPTp-SP in their first trimester of pregnancy. Women in both countries reported that they were not informed a second dose was necessary or they had not been offered it, which is consistent with findings from other studies (Chapter 4).

As with DHS surveys, these findings rely on self-reported data, and cannot be considered conclusive on the practice of IPTp-SP provision by health providers. In Kenya, concordance between reported and documented information on women’s ANC cards was fair for receipts of two doses of IPTp-SP (Kappa score (K) 0.399) and use of an ITN obtained from ANC (K 0.26), though relatively few ANC cards were available. Concordance between reported and documented data in Mali was better, with good concordance for timing of first ANC visit (K 0.6945) and receipt of two doses of IPT-SP (K 0.682). The report by women that they received IPTp-SP in their first trimester appears to be supported by the confusion among health providers, reported in a parallel, qualitative, study in health facilities within the same district in Mali, that women of less than one month gestation rather than the first trimester should not be given SP [30]. The lower effectiveness of IPTp-SP in Mali may have been exacerbated by the narrower eligibility period for administering IPTp-SP in the national policy, between 4-8 months gestation vs 4-9 months in the WHO policy. Indeed, health providers in the parallel study in Mali demonstrated considerable misinterpretation of the guidelines, some of whom considered the 8th month to be exclusive, narrowing the eligibility to 4-7 months, and that the first dose should be denied unless women could make two scheduled visits before the end of her pregnancy [30]. Women’s report of low receipt of IPTp-SP by DOT is supported by the health facility study which used observations of ANC staff and pregnant women interactions in ANC undertaken in parallel to the household survey in Mali, with 0% and 34.3% (95% CI 10.5, 69.8) provision of IPTp-SP by DOT observed in district and community-level health facilities respectively [31]. The main reason for poor adherence to DOT given by the majority of ANC staff interviewed was that IPTp-SP should not be given to pregnant women on an empty stomach in case of side effects [30]. Women in the focus group discussions linked the vomiting associated with SP with taking the drug when hungry, and said that they had been advised by the district hospital to eat before taking SP (Chapter 8). The lower adherence to DOT for the first dose of IPTp-SP compared to the second dose found in the effectiveness analysis may be due to women learning to eat before taking SP or possibly due to higher tolerance in later pregnancy with the cessation of pregnancy-related nausea [32].

Women’s perceptions of antenatal care from focus group discussions in both countries were generally positive, key motivating factors being a desire to maintain a healthy pregnancy and preventing problems at delivery, however there were a number of barriers mitigating access and uptake of malaria in pregnancy interventions (Chapter 8). Many of the key barriers were related to ANC access, such as the quality of the interaction with health providers, perceptions of provider skills and experiences of malpractice, drug availability and the cost of services, consistent with findings from the systematic reviews (Chapter 4 and 9) and with other studies not specific to malaria [27]. Regarding malaria treatment specifically, a major finding was women’s lack of information on the safety, efficacy and side effects of antimalarial use in pregnancy, with a heavy reliance on trained health providers to prescribe safe and effective regimens. Cost, stock-outs at health facilities, and
inconvenience however caused women to buy drugs locally from shops, or to resort to traditional remedies, consistent findings in the systematic review on case management (Chapter 9). The perception that SP was no longer effective for treatment of malaria might also deter women from actively seeking IPTp-SP.

**Determinants of access.** Women’s access to ANC is influenced by economic and societal factors that reduce care-seeking, access to information and health care services, such as gender discrimination, low levels of education, few income-earning opportunities and other societal factors affecting women’s empowerment [27]. It was therefore interesting that the determinants of IPTp-SP and ITNs uptake were not the same, as illustrated by the meta-analyses (Chapters 3 and 4) and the field studies (Chapters 6 and 7), and predictors showed regional variations. The determinants of IPTp-SP coverage in the meta-analyses were education, knowledge about malaria/IPTp (also in Kenya, Chapter 6), socio-economic status, parity, maternal age, and number and timing of ANC visits (also in Kenya, Chapter 6), with lower IPTp coverage among the poorest, uneducated women and, in some countries, rural women. The inequitable distribution of IPTp-SP has been reported previously [33], and while inequity in access to ANC may contribute to this effect, the barrier studies show that some determinants are specific to IPTp, such as having to pay for SP or water for DOT and lack of information given by health providers about the benefits, safety and side effects of IPTp-SP. Predictors of receiving IPTp-SP by DOT in Kenya (Chapter 6) were low socio-economic status, experiencing no previous side effects to SP, and a high malaria knowledge score, and in Mali (Chapter 7) being unmarried and living >5km from health facility.

ITN coverage was lower among women who had no education, less malaria knowledge, single, adolescent or primigravid women, unemployed women, and rural women (Chapters 3 and 4). Alternative strategies may be needed to reach adolescent women with ITNs especially given the higher risk of poor pregnancy outcomes in this group [34,35] and poor intra-household access due to low social position [36].

**Strategies to improve delivery**

Despite a large body of evidence on the barriers to delivering malaria prevention interventions to pregnant women, and particularly IPTp-SP, the systematic review identified relatively few studies which explored the impact of interventions to improve delivery, access or use (20/98 studies) (Chapter 4). The majority of the intervention studies were demand-side interventions (19/20) illustrating a dearth of research on interventions to address supply-side factors at ANC which contribute to slow progress with IPTp and ITN uptake. Only one intervention study was identified for improving provider case management practices specifically for malaria in pregnancy (Chapter 9). The two supply-side intervention studies, for IPTp-SP [37] and case management [38], involved training of health providers.

The reviews have been used to categorise the barriers to the delivery of malaria in pregnancy interventions at the different levels of the health system in order to facilitate the design of appropriate, targeted interventions. Many barriers to the delivery of IPTp and ITNs reflect broader weaknesses in the health system or socio-cultural settings, requiring medium to long term strategies, however some were specific to MiP interventions and provide some short to medium term opportunities as outlined below.
**Simplify and streamline IPTp policy.** The updated 2012 WHO policy recommendation of giving a dose of IPTp-SP at every ANC visit (and at least month apart) [39] provides an opportunity for countries to realign national policies and guidelines across the malaria and reproductive health departments. The new schedule is better aligned with the new Focused Antenatal Care (FANC) Training Manual from the WHO AFRO Regional Office, which recommends four ANC visits during the second and third trimesters in addition to a booking visit in the first trimester to promote early entry into care [40]. It is anticipated these adjustments to IPTp-SP and ANC schedules will reduce earlier confusion about the optimal timing of the two-dose regimen and increase the number of doses women receive [41]. The dissemination of the new policy guidance to health providers should make use of the policy brief which provides information on the safety and efficacy of the new regimen and practical advice on how to give IPTp-SP in the context of treatment for HIV, malaria and anaemia [40].

**Coherent programme planning.** Fragmentation across different programmes, including malaria, has meant that many important interventions delivered during pregnancy or the postnatal period are vertically oriented and ‘owned’ and funded by different management units within Ministries of Health and technical agencies. At the service provider level, this fragmentation has resulted in competition for resources between programmes and has rendered ANC what has been described as a programmatic ‘no-man’s land’, a relatively neglected service delivery channel [42]. More coherent planning between malaria, curative and reproductive health departments is needed, including joint budget planning and joint efforts to track progress and improve quality of services provided through ANC [43].

**Data for decision making at the level of implementation.** The systematic reviews and field-based studies demonstrate that the barriers to delivery of interventions vary at the sub-national level, such that improvements at district and facility levels will require decentralised data for decision making and accountability. The current interest in development of evaluation methodologies for large scale programmes [44,45] is not yet reflected in the development of improved monitoring methods, and criteria for assessing the quality and performance of health information systems have been poorly defined [46]. The core indicators recommended by WHO to guide national programmes [47] while useful for strategic development at the national level [48], have limited usefulness at the facility level. Similarly, health facility assessments to determine quality of services against a set of standard performance indicators, such as the Service Provision Assessment (SPA) surveys, are neither designed nor powered to identify problems at the local/district level, because they were designed to be undertaken at the national level to guide overall national strategic investments. Cross validation between the tools used in the household surveys (Chapters 6 and 7) and facility surveys [30,31] will be used to direct a significant downsizing to formulate second generation, streamlined tools for intermittent, more rapid surveys applicable in a range of contexts. A further study to explore the use of enhanced routine Health Management Information System data to support systems effectiveness analyses is also ongoing.

**Earmarked funding.** In addition to securing earmarked funding for procurement of SP and LLINs delivered through ANC, with donors forecasting budget commitments well in advance of procurement, mobile phone technologies could be used to improve stock control and supply chain management for better forecasting of supply needs. National governments and donor and technical agencies need to develop coherent funding strategies for increasing investment in strengthening the ANC platform [49].
Strategies to improve access and use

Of 20 intervention studies on malaria prevention, five were demand-side interventions to increase coverage with IPTp-SP and 14 were delivery strategies to increase ITN access, ownership and use (Chapter 4). Community-based distribution of IPTp-SP was found to increase IPTp-SP coverage in four studies however there was a concurrent decrease in women’s attendance at ANC in two studies, leaving pregnant women without other essential antenatal care services. Community-based promotion of IPTp-SP through delivery at ANC in Burkina Faso on the other hand not only increased coverage of IPTp-SP but had the additional benefit of more women attending ANC earlier and making two or more ANC visits [50]. While 13 studies were identified that evaluated the effectiveness of alternative delivery strategies to increase ITN coverage among pregnant women, the study objectives and designs were heterogeneous; hence, it was not possible to draw generalisable conclusions. Nevertheless, ANC services appear to be an important source of free ITNs for pregnant women in rural areas, a finding supported in a review of best practices of ITN programmes in sub-Saharan Eastern Africa [51] (Chapters 4 and 5). No intervention studies to improve pregnant women’s access and adherence to malaria case management policy were identified (Chapter 9).

Efforts to improve women’s access to all antenatal care services, including IPTp-SP and ITNs, would benefit from a review of ANC fee structures [27] as well as a review of fees for antimalarials and partner drugs for the treatment of malaria in pregnancy. Access to quality antenatal services is a rights-based issue, hence pregnant women need to be educated and informed of their rights to free antenatal care so they become empowered to demand the services available, and to counteract independent decision making by health staff at ANC, preferably through national media channels. National communication initiatives need to be support by targeted promotional campaigns and community engagement initiatives coordinated by health facilities to increase ANC utilisation among high-risk populations of pregnant women according to local settings (e.g. rural, poor, adolescent women) and for defaulter-tracing, as used in HIV programmes [52]. Pregnant women urgently need access to information on which antimalarials are safe to use at different stages in pregnancy so that they can make informed choices, and is particularly pertinent given the wide-scale non-rational use of antimalarials by health providers (Chapter 9).

Methodological observations

DHS surveys. The failure of DHS surveys to record the gestation when pregnant women receive IPTp-SP results in an overestimate of coverage, as noted in Mali (43.4% vs 38.9% for two doses in all trimesters and 4-8 months, respectively), or administration by DOT (96.7% vs 25.5% for the second dose without and with DOT, respectively) (Chapter 6) [29]. Conversely, the lack of information on whether or not women are taking cotrimoxazole, or have been treated for acute malarial episodes, will underestimate coverage of IPTp-SP in areas of high HIV prevalence (Chapter 7) [28].

Systematic reviews. The systematic review of barrier studies were far more informative than the meta-analysis of determinants for identifying areas for making programme improvements. However, the integration of findings from the barrier studies and determinants, and of barriers and intervention studies, was useful and contributed robustness to findings. The synthesis of findings from the barrier studies with the intervention studies was instructive in identifying gaps in studies to evaluate relevant and targeted interventions to mitigate barriers.
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**Household surveys and FGDs.** There are limited methods for assessing systems effectiveness for the delivery of interventions as part of other antenatal care services at the district level. The use of household data to assess delivery effectiveness may be a useful approach where individual participant data from household surveys are available. Household surveys are however expensive to implement and are unlikely to be a cost-effective method for assessing systems effectiveness in isolation, although alternative sampling strategies would reduce cost [53] or hybrid methods which combine small household surveys with facility based assessments [54]. The additional benefit of household surveys is that they measure access in the community, and are useful in identifying risk groups of women who do not attend ANC at all, or who attend infrequently, and can be used to explore the predictors of IPTp and ITNs uptake and adherence to antimalarial regimens. The health facility surveys provided observations [31] and contextual information [30] on the actual practices of health providers, and provided evidence for some of the practices reported by women. The qualitative data from focus groups discussions with pregnant women and other members of the community provided important explanatory data about why certain practices occurred, and will be useful for Ministries of Health in Kenya and Mali to inform the design tailored communication interventions and other strategies to improve uptake of IPTp-Sp, ITNs and case management.

**Translation of research findings into practice**

The consistency of the findings from the two sequential reviews in 2006 and 2013 (Chapters 2 and 4) and the interim review in 2011, points to the failure of research findings from individual studies on the delivery, access and uptake of IPTp-SP informing and being translated into programmatic improvements, highlighting the need for improved dissemination of research findings to Ministries of Health, technical agencies, and funding partners. Furthermore, more than half of the studies in the systematic review (Chapter 4) were conducted in countries in East and Southern Africa, and yet Malawi, Kenya, Tanzania and Uganda, among the earliest countries to implement IPTp-SP and ITNs, have yet to achieve 60% coverage with either intervention.

The findings from the systematic reviews (Chapters 4 and 9) and from the field studies in Kenya and Mali (Chapters 6,7 and 8) have contributed concrete evidence for the development of a policy brief for programme managers that accompanied the recent WHO IPTp policy update, in terms of appropriate messaging to simplify the guidance specifically on the timing, frequency, and safety of taking SP on an empty stomach and by DOT [40]. The findings have also been incorporated into a Roll Back Malaria Partnership Progress and Impact series report in an effort to disseminate findings to Ministries of Health, technical agencies, and funding partners [55].

**Future Research**

Given the very low coverage of the previous two-dose IPTp-SP regimen, the question remains whether the updated WHO guidelines recommending a dose of IPTp-SP at every scheduled ANC visit will improve the uptake of IPTp-SP. It will be important to evaluate whether the 2012 WHO policy update on IPTp-SP leads to an improvement in uptake of IPTp-SP. The continued effectiveness of IPTp-SP in the context of increasing resistance to SP, particularly in East and Southern Africa, will need to be monitored using methodologies recently developed by the MiP Consortium.
The challenges to delivering two relatively simple malaria prevention interventions, and IPTp-SP in particular, also raises important questions about the feasibility of delivering the next generation of interventions to prevent malaria in pregnancy, which will contain more expensive and complicated regimens than two doses of IPTp-SP [56,57] or more complicated strategies requiring the administration of an RDT and three-day treatment regimens for RDT-positive cases. The new regimens are not as well tolerated as SP [58] and screen and treat strategies do not have the benefit of controlling infections missed by diagnostic tests. Research on user acceptance and adherence to longer treatment regimens, such as dihydroartemisinin-piperaquine, and strategies that are likely to replace IPTp-SP, such as intermittent screening and treatment [59,60], will be crucial. Research on provider proficiency and adherence to diagnostic malaria tests is also needed [61,62], in addition to evaluating strategies that streamline integrated point of care testing for malaria, HIV, syphilis and anaemia at ANC. Strategies which deliver ITNs to adolescents, as a vulnerable group and also in order to protect pregnancies from as early in the first trimester as possible, such as through adolescent-friendly services that deliver STD control, are needed [34,63].

Comparatively less research has been undertaken on the case management of malaria in pregnancy, and this represents a critical research gap due to emerging evidence of the use of artemisinins in the first trimester, use of artemisinin monotherapies, the continued use of inefficacious drugs such as chloroquine and SP for treatment, and the practice of clinical diagnosis. Systematic assessment of the extent of substandard case management practices at the national scale are required, together with implementation research to evaluate strategies to improve health provider performance. These might include a combination of interventions used for non-pregnant adults and children, such as: capacity development of health professionals [12], SMS messages to drug shop staff on appropriate treatment regimens for pregnant women; providing RDTs to shop staff [64]; improved availability of RDTs for health providers plus a comprehensive training package with unambiguous guidelines [65]; interventions that address negotiation of health worker-patient relationships and encourage self-reflection of practice; feedback systems for results of quality control of RDTs; and RDT augmentation such as a technical and/or clinical troubleshooting resource. Community-based interventions to evaluate and improve pregnant women’s adherence to multiple day regimens are also needed, paying attention to the impact of study procedures on adherence outcomes [66].

Conclusions

Malaria in pregnancy is an important public health problem for maternal and neonatal health programmes. Despite the availability of highly cost-effective prevention interventions that should be relatively straight forward to deliver, coverage is unacceptably low and there is a dearth of studies reviewing the quality and access to case management. Countries have some significant opportunities to improve the quality of delivery of current interventions as identified in the thesis. The ongoing dissemination of the updated WHO IPTp-SP policy to countries, and from national to sub-national levels, provides an important opportunity for programmes to improve the quality of service delivery at ANC and to launch targeted communication campaigns for pregnant women around IPTp-SP, the safety of antimalarials in pregnancy, and the importance of malaria prevention and prompt and appropriate case management. It will be important for Ministries of Health to evaluate whether the revised policy indeed leads to an improvement in uptake of IPTp-SP, as anticipated, and to work with research partners to monitor the continued effectiveness of IPTp-SP in the context of increasing resistance to SP, particularly in East and Southern Africa.
Evidence from the feasibility and acceptability studies of the new generation of interventions, will be important components of the evidence dossiers provided to the WHO and Governments of malaria endemic countries. Countries will also need guidance on the threshold at which current strategies should be replaced with new strategies, which will be based on multiple determinants requiring information on SP resistance, transmission intensity and cost-effectiveness. These factors, and the local availability of data, will vary substantially across countries in sub-Saharan Africa and also at sub-national level, requiring more sophisticated surveillance data and decision making processes at country level to enable tailored approaches. The move away from a one-size-fits-all to tailor-made approaches will place an additional burden on countries, many of which will require multiple strategies in single country, including countries such as Kenya and Mali both of which have malaria transmission patterns across a very wide epidemiological spectrum. The malaria elimination agenda has introduced competition for scarce resources and brings the risk of diverting funding away from vulnerable or high risk groups, as noted with the delivery of ITNs. As transmission decreases, in populations in rapid transition from high exposure to low exposure, the proportion of individuals with enough acquired immunity to harbour asymptomatic infections, including pregnant women, may remain substantial making the case for continued attention to this high risk group.
References


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