Economic Report for the WHO Technical Expert Group Meeting on Intermittent Preventive Treatment of Malaria in Children

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Executive Summary

For Intermittent Preventive Treatment of Malaria in Children (IPTc) to be accepted and sustainable as a malaria control strategy it must be affordable and cost effective as well as safe and acceptable. Thus, several of the IPTc studies have included an economic component. These studies range from randomised controlled trials to operational research studies. In addition, modelling was used to supplement the information available from the trials and to provide predictions where the trials could not, for practical reasons, provide estimates. Both financial and economic costs associated with IPTc delivery have been investigated to help forecast how introducing the intervention may impact health budgets, and to help determine the cost effectiveness of IPTc compared to other malaria interventions.

In this report we present the costs and cost-effective of IPTc using three different drug regimens and various delivery strategies. Across all studies, the financial cost per IPTc course range from US$0.24 to US$3.44 and the economic cost per course from US$0.31 to US$3.44. These costs are within the range of the costs associated with delivering existing malaria control interventions. The cost effectiveness of the intervention was comparable, but marginally higher than other prevention strategies, however possibilities exist for reducing the costs of IPTc by scaling up and by incorporating delivery of IPTc with the delivery of other interventions such as the distribution of Vitamin A or Community and Home Management of Malaria. Supervision, training and remuneration of CHWs and IPTc drug delivery have been identified as the main cost components and key determinants to the success of the delivery strategy. There is scope for the costs associated with supervision and training to be reduced if IPTc is integrated into existing routine activities. Alternatively, in settings where supervision and training of CHWs is weak, IPTc may offer an opportunity to strengthen both these important aspects of service delivery which will offer benefits beyond reducing malaria morbidity and mortality.

1. Introduction

In addition to the devastating impact malaria can have on an individual's health, it also impacts the economic wellbeing of households, communities and nations. It is, therefore, incumbent on governments to *supply* and households to *demand* interventions that are known to successfully prevent and treat malaria. When deciding which interventions to select (both at the government and the household level) decisions have to be made about where to allocate limited funds and how best to use the resources of the health system.

Many issues are of critical concern when deciding where limited resources should be allocated. Two important considerations are the costs of an intervention and its 'value for money'. Costs are important because, in a context of limited finances and changing government and international commitments, there needs to be an accurate forecast of how an intervention will impact the health budget. Economic evaluations help to determine the relative efficiency of different choices and provide an explicit indication of how competing strategies compare in terms of their 'value for money'[1].

Recent trials have shown that Intermittent Preventive Treatment of Malaria in Children (IPTc) is a highly efficacious and effective intervention against uncomplicated and severe malaria [2]. Economic evaluations have been conducted alongside many of these studies to explore which drug combinations and delivery strategies are most cost effective. In this report, we summaries what has been published to date on the economics of IPTc and present for the first time the preliminary costing of a large scale IPTc delivery study in Senegal. We then compare the costs and cost effectiveness of IPTc to the costs and cost effectiveness of other malaria interventions. Finally we discuss the key issues associated with the delivery of IPTc.

2. Review of economic aspects of IPTc studies to date

For IPTc to be accepted and sustainable as a malaria control strategy it must be cost effective as well as safe and acceptable. Thus, several of the IPTc studies have included, or have an ongoing, economic component (Annex 1). These studies range from randomised controlled trials to operational research studies. Both financial and economic costs[1] associated with IPTc delivery have been or are being collected. The cost implications of different drug regimens have been studied in Hohoe, Ghana both from the perspective of the clinical trial and when modeled to reflect district wide implementation[3]. The costs of different delivery strategies have been studied in Basse, The Gambia and in Jasikan, Ghana [4,5] and the cost of IPTc when organised by the district health services has been studied in Tivaouane, Senegal [6]. Modeling was undertaken to predict the impact and cost-effectiveness where, for practical reasons, trials cannot be carried out; for many different settings and implementation characteristics and to capture the effects of severe episodes and deaths. The effects of different target age groups, seasonal or year-round delivery, transmission intensity, seasonality, proportion of malaria fevers treated and drug characteristics have been simulated[7].

While it is straightforward calculating the costs of IPTc, it is a little more complicated to decide on the most relevant effects to use as the denominator of the cost effectiveness ratio[2]. The effect that is measured as part of an economic evaluation is led by the clinical trial outcomes. A number of possible outcome measures were identified in the various IPTc trials. When possible an actual health gain was measured, i.e. cost per malaria case, death or DALY averted [3,4,7]. Where a health gain was not identified as part of the trial, the level of coverage was used as an intermediate measure [5,6]. As IPTc involves multiple doses and multiple courses, there are a number of potential outcome measures. To date, the primary outcome measure used in the economic evaluations has been the cost per child adherent to 'at least the first dose of each course'. This measure was seen as a fair representation of the intended aim of the intervention. There is an argument that a child who receives just the first dose of one course receives some protection and therefore the cost per course is a valid outcome measure. This applies particularly to IPTc regimens which employ sulphadoxine/pyrimethamine (SP) as, in areas where parasites remain sensitive to this antimalarial, a single dose will provide substantial protection and is

[1] Evaluation of *financial* costs of resources required to set-up and run the innovation in terms of the actual expenditures incurred (the price paid for the resources). Evaluation of *economic* costs captures the opportunity cost of all resources used to produce the innovation, whether or not they incur a financial cost. For example any donated or subsidised items used by the programme would need to be valued at market prices to estimate their economic cost.

[2] Cost effectiveness ration (CER)= $\frac{\text{intervention costs} - \text{baseline costs}}{\text{intervention effects} - \text{baseline effects}}$

recommended for IPT in pregnant women and infants. More discussion of this issue is provided in the section on the costings of the Senegal study (see below). Given the benefits of partial as well total adherence to IPTc, we show the unit costs of both in Table 1, i.e. 'the cost per course' and 'cost per child adherent to at least the first dose of each course' respectively. Table 1 also shows the difference between the financial costs and economic costs of delivering IPTc. While financial costs are important for planning budgets and indicating how much additional expenditure is needed, economist tend to focus on the economic costs of interventions as these show the full costs of all the resources used to deliver an intervention and allow more insightful comparisons between different interventions.

To make comparisons across studies easier all costs are inflated and presented as their US$2010 equivalent, unless otherwise stated[8]. Costs in this report may, therefore, vary slightly from those in the original publications.

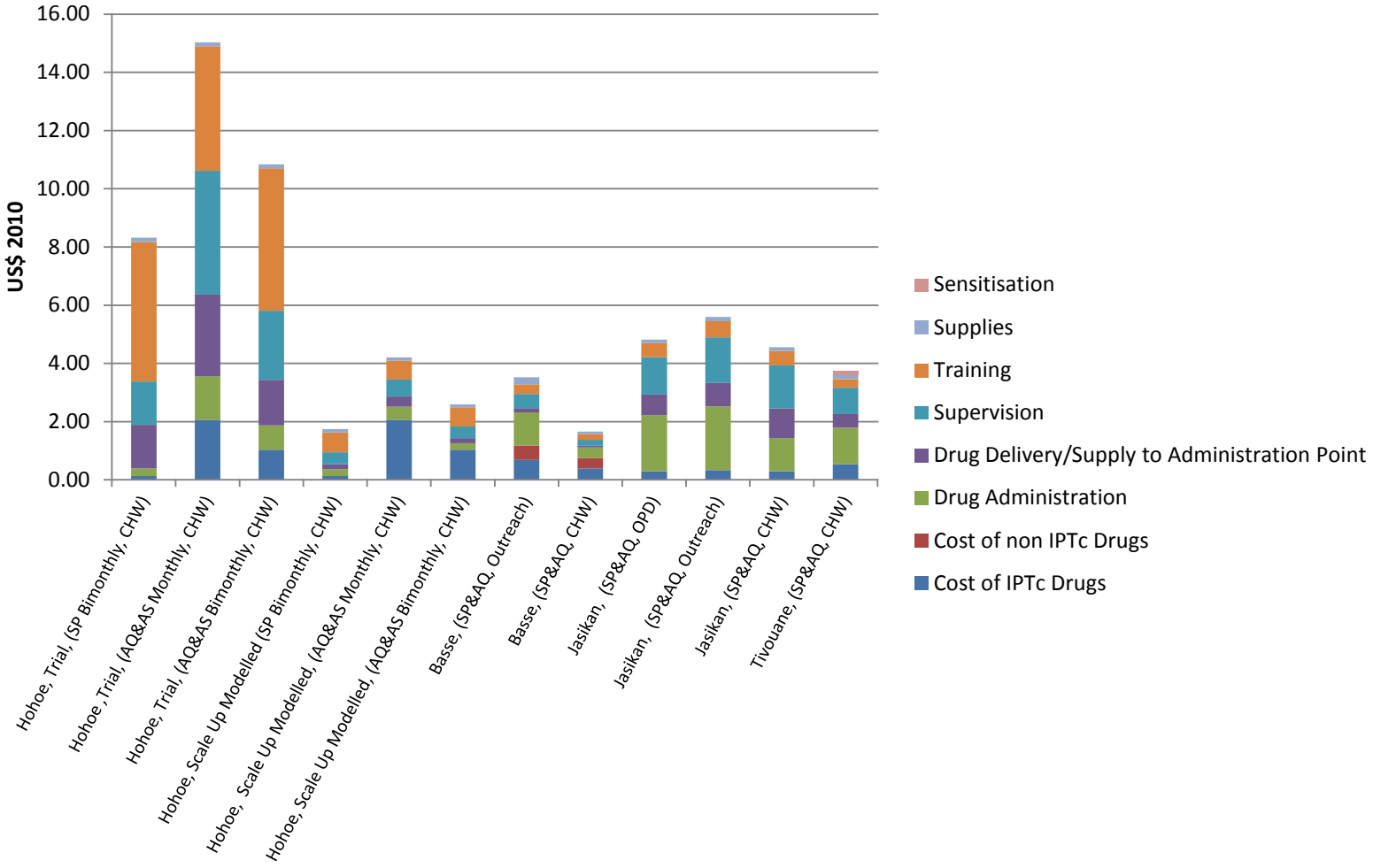
Table 1: Summary of Unit Cost of Delivering IPTc (US$ 2010)

Study Site	*Description* (IPTc drugs/ Delivery strategy)*	*Number of courses*	*Cost per course*		Child adherent to 'at least the first dose of each course'		*Source*
			Financial	*Economic*	*Financial*	*Economic*	
Hohoe, Ghana	SP Bimonthly, CHW	3	0.75	1.24	4.25** (1.27)	8.30 (1.74)	[3]
	AQ&AS Monthly, CHW	6	1.84	2.31	11.97 (3.66)	15.03 (4.20)	
	AQ&AS, Bimonthly, CHW	3	1.14	1.67	7.39 (2.11)	10.84 (2.60)	
Basse, Ghana	SP&AQ, CHW	3	0.24	0.31	1.25	1.66	[4]
	SP&AQ, Outreach	3	0.39	0.47	3.03	3.53	
Jasikan, Ghana	SP&AQ, CHW	4	2.41	3.14	3.39	4.56	[5]
	SP&AQ OPD	4	2.66	3.32	3.79	4.83	
	SP&AQ Outreach	4	2.81	3.44	4.54	5.60	
Tivaouane, Senegal	SP&AQ, CHW	3	NA	NA	2.65	3.73	[6]

* See Annex 1 for more details of trial characteristics
** Costs for Trial Conditions & modeling district wide implementation in parenthesis
CHW = Community Health Worker
OPD = Outpatient Department
NA= Not available

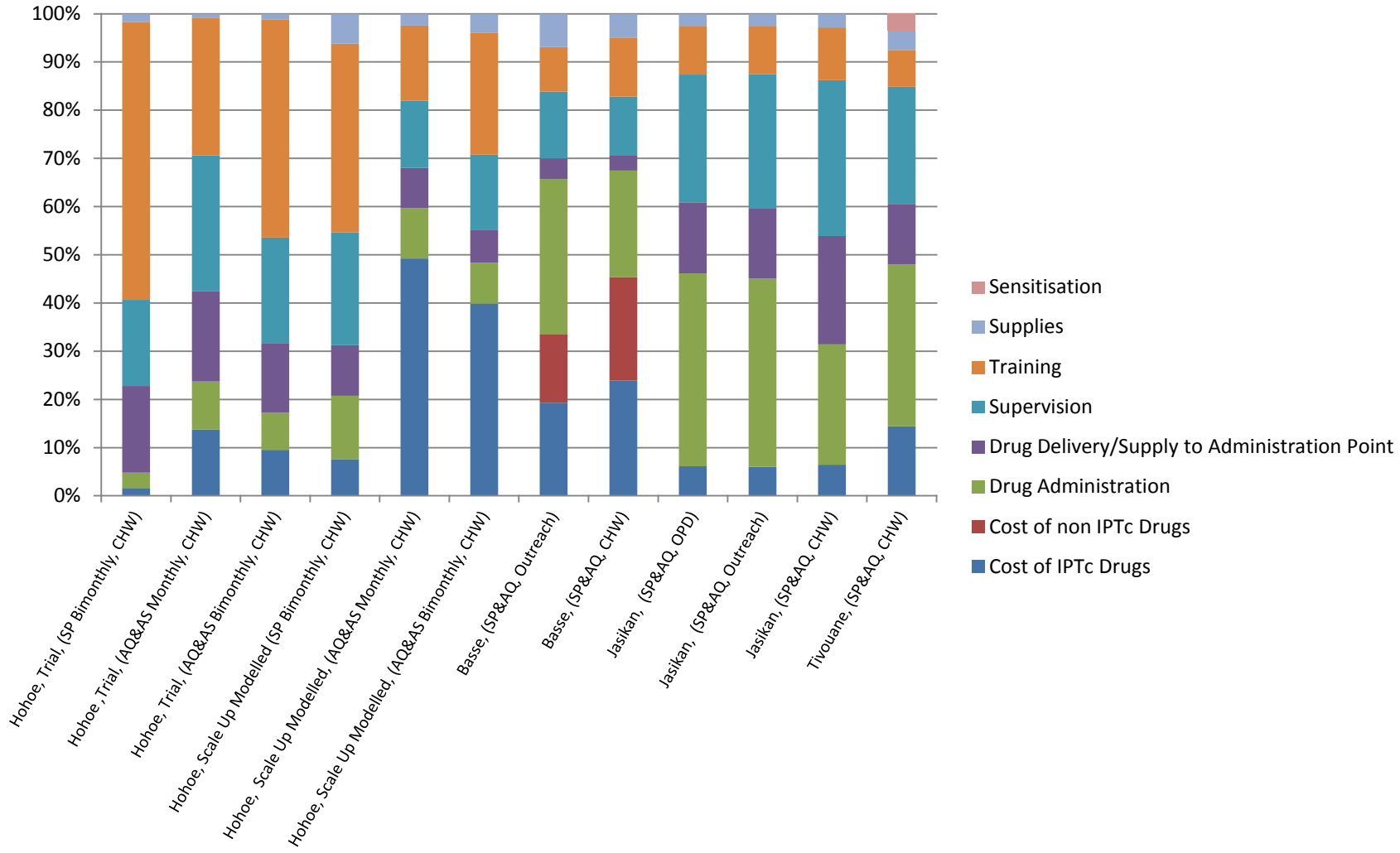
Figure 1 presents the costs broken down by cost categories by the economic per child who received at least the first dose of each course of IPTc for all the IPTc scenarios costed to date. Figure 2 presents these same costs by their percentage breakdowns.

Figure 1: Unit Cost (economic) per child receiving at least the first dose of IPTc each course



NOTE: Hohoe Trial Setting: Cost per child receiving at least one course. District Wide: Cost per child receiving at least one course assuming a district size of 33,000 children

Figure 2: Percentage Breakdown of IPTc Delivery Costs by Cost Category based on Figure 1 Unit Costs



Costs and Cost Effectiveness of Different IPTc Drug Regimens

In the Hohoe study where up to 6 courses of treatment were given, the economic costs per child who received at least the first dose of each course of IPTc showed that, as expected, SP bimonthly, at US$8.30, was the cheapest to deliver, followed by AQ+AS bimonthly at US$10.84 and then by AQ+AS monthly at US$15.03[3]. Training, supervision and drug delivery (in terms of the personnel and transport needed to deliver the IPTc drugs to the CHW ahead of their monthly IPTc drug administration) accounted for approximately 20-30% each of total unit costs (Figure 2). During the intervention period, AS + AQ monthly was the most cost effective drug regimen at US$68.64 (62.50, 75.71, CI 95%) per malaria case averted based on intervention costs only. The costs of scaling up the intervention to 33,000 children, i.e. to district level, were modelled and under these conditions the cost per child enrolled fell considerably compared to costs under trial conditions as did the cost per malaria case averted. Based on intervention costs only, IPTc using SP was US$28.59 (20.23, 42.65 CI 95%) per malaria case averted, US$22.60 (20.59, 24.88 CI 95%) using AS+AQ monthly and US$60.37 (36.87, 115.02 CI 95%) using AS+AQ bimonthly. This reduction in cost occurred because semi-fixed costs, such as training and drug delivery, benefited from economies of scale and fixed costs such as incentives to CHW and health facility staff were spread over a larger number of children per CHW or staff member delivering IPTc. The economic evaluation of the Hohoe project did not take into account the potential savings that might have been achieved from preventing cases of severe malaria or death as these were not end-points of this trial.

If IPTc were to be implemented routinely, additional benefits such as increased efficiency and lower costs of delivery could be achieved by integrating IPTc with other current successful health interventions aimed at the same populations; what economists term 'economies of scope'. For example, if delivery was combined with other non-IPTc activities such as Vitamin A campaigns or home management of malaria (HMM) a fall in the costs of IPTc delivery would be likely together with a potential increase in IPTc access and coverage [9,10].

The combination of SP+AQ used in several other studies of IPTc is likely to be more cost effective that the figures obtained during the study in Hohoe because of the lower costs of SP than AS and similar or higher levels of protective efficacy. The Hohoe study was not powered to detect an impact on hospital admissions or mortality. However, subsequent larger studies of IPTc with SP+AQ conducted in Burkina Faso and Mali have shown a substantial reduction in hospital admissions with malaria in children who received IPTc [11,12]. Based on intervention costs alone IPTc may appear costly, however, once the savings to the health system and to households are included IPTc appears more favourable. The cost savings would have been more pronounced had there been more of an impact on severe episodes as has been observed in larger studies conducted in Burkina Faso and Mali.

Costs and Cost Effectiveness of Different IPTc Delivery Strategies

In both the studies conducted in Basse, The Gambia, and in Jasikan, Ghana, IPTc delivery by community health workers (CHWs) was found to be more effective (in terms of higher coverage) and less costly than delivery by those employed in the formal health system [4,5]. In Jasikan, the cost per child who took at least the first dose of all 3 IPTc courses was US$4.56 when the intervention was delivered by a CHW, US$4.83 when delivered via outreach and US$5.60 when delivered in an outpatient department, with supervision the largest cost component. In Basse, the economic costs of a fully adherent child who received all 3 doses of IPTc with SP+AQ were US$1.66 and US$3.53 when delivery was achieved via CHWs and outreach /routine trekking teams respectively. The largest component of total costs associated with delivery by reproductive and child health trekking teams was the cost of administering IPTc. This is because the trekking teams are skilled health care workers and so were paid substantially more for their time than the CHWs who received a monthly incentive payment of approximately US$11.10 (US$2010). Non-IPTc drugs (for example anti-malarials for treatment and paracetemol) contributed 22% of the total economic costs of delivery via CHWs compared to only 14% for the RCH trekking teams.

None of the caretakers (n=390) interviewed in Basse during the study reported direct costs associated with receiving IPTc, such as travel costs, and only one caretaker reported a loss in earnings while accessing IPTc.

For ethical reasons, no placebo group was included in the Basse study so it was not possible to compare the cost-effectiveness of these two strategies to current practice. However, net cost-effectiveness was calculated by subtracting resources saved from the total programme compared to the relevant outcome measure. In terms of cost-effectiveness, this incremental analysis shows that the CHW strategy is both more effective and less costly than delivery of IPTc via RCH trekking team. Comparing delivery by CHWs to delivery by RCH trekking team highlighted three positive incremental effects - a reduction in the number of malaria episodes averted, an improvement in the number of fully adherent children and an improvement in the number of children who received at least one dose. The CHW strategy was also less costly in both economic and financial terms resulting in an incremental saving of US$ 883 and US$ 1260, respectively. This indicates that, in The Gambia, CHWs is the most appropriate delivery route for IPTc.

Tivaouane, Senegal could be considered the most operational of the studies reported so far as it was left to the District Medical Officer to organise the delivery of IPTc and its associated costs using a lump sum of money provided by the research team. At this site, the a cost of receiving at least the first dose of each of

the 3 courses of SP+AQ was US$ 3.73 per child. The largest component of the cost of IPTc was the cost of drug administration by CHWs, this was driven by the amount of incentive they received.

Modelling the Cost Effectiveness of IPTc

Modelling was used to supplement the information available from the trials and to provide predictions where the trials could not, for practical reasons, provide estimates such as for many different settings or for severe outcomes. A comprehensive individual-based model [13]which had been fitted to data from sites across sub-Saharan Africa and subsequently validated against trials of IPTc was used to simulate the epidemiological impact and cost-effectiveness of IPTi and IPTc [7]. Setting, drug or implementation characteristics were varied. Costs were based on a summary of all available costings of IPTc [3,4,5]. The approach adopted followed previous work on modelling the cost-effectiveness of malaria vaccines [14,15] and followed standard practices [16]. The primary outcomes were the number of DALYs averted and cost per DALY averted. The predictions covered a period of ten years from the start of the IPTc programme.

Simulations were run to investigate the effects of the different target age groups, seasonal or year-round delivery, transmission intensity, seasonality, treatment coverage and drug characteristics. IPTc was cost-effective, defined using the threshold suggested by the World Bank of US2009 $223 per DALY, in nearly all the simulated scenarios. The number of DALYs averted by IPTc was driven mainly by the predicted effect on deaths. Cost-effectiveness was predicted to decrease with low transmission, badly timed seasonal delivery in a seasonal setting, short-acting and more expensive drugs, high frequencies of drug resistance and high levels of treatment of malaria fevers. The number of DALYs averted was predicted to decrease if a target five-year age-band for IPTc was shifted from children under 5 years into older ages, except at very low transmission intensities.

3. Financial costs of delivering IPTc to children under ten years of age at scale in Senegal

Background

In this section we present the recently calculated, and therefore as yet unpublished, financial costs of delivering IPTc at scale in Senegal. The aim of the Senegalese study is to evaluate the safety, cost effectiveness and public health impact of seasonal IPT in children with SP+AQ when delivered by district health staff. The study design is described in the paper on safety of IPTc [17]. In brief, the 54 rural health posts in four districts (Bambey, Mbour, Fatick and Niakhar) were randomized to start implementation of IPTc in 2008 (9 health posts), 2009 (18 health post), 2010 (18 health posts), or, pending interim analysis of effectiveness, in 2011 (9 health posts). In 2008, children aged 3-60 months at the time of the first round of treatment were included, in 2009 the age range was increased to include children up to the age of 120 months. A census of the study area was carried out in March-May 2008. In August 2008, all households were revisited to give each mother/carer a card bearing an ID number for the household, for the mother/carer, and for each child in her care, with space for IPT, Vitamin A and mebendazole doses to be recorded. Health facilities were provided with blank forms to be issued to first-time mothers at their first contact with health staff after delivery. From September 2008, rounds of household visits were initiated to record changes in household occupancy.

The population served by each health post (2008 estimates) ranges from 1,772 to 42,374 with a median of 8,400. The number of children aged 0-120 months ranges from 592 to 16363 (median 2694), and the number of those aged 0-59 months ranges from 309 to 9020 (median 1420) per health post. Each health post is usually staffed by 4 people - a full-time nurse, an assistant (Agent Sante Communautaire), a community health worker responsible for taking payments, and a midwife or birth attendant. The study area also has 72 cases de sante (health huts), smaller facilities staffed part-time by one community health volunteer who has received a short period of training. Vitamin A is delivered to children aged 6 months to 5 years twice per year (usually around June and December) by community health workers (CHWs, or 'relais') who visit each household. Children aged 1-5 years are also treated with mebendazole during these visits. In Bambey district, from 2006-2009, azithromycin treatment was delivered to all age groups above 6 months except pregnant women, once per year during the period of November to December for control of trachoma. About 59% of 12-23 month old children are fully vaccinated. In 2010, detailed data on costs of delivery of IPTc were collected in order to estimate the incremental financial and economic costs of implementing IPTc at scale. All 46 health facilities that delivered IPTc in 2010 were included (45 health posts and one mission health centre which contributed to IPT delivery).

Both financial and economic costs were collected as part of the study, however, this report presents only the incremental financial costs of implementing IPTc. The final report, which will be submitted for publication in a peer-reviewed journal, will include the full incremental economic costs of implementing IPTc. These financial costs are an indication of the additional funding that districts would need to implement IPTc in future in the same manner. The analysis of economic costs, which is in preparation, will assess the value of the additional resources used to implement IPTc, including those which did not incur a financial cost, such as the time required of the district health team, health post staff, and CHWs. The opportunity cost for households to participate in IPTc is being explored through qualitative work, but is expected to be low as IPTc is delivered door-to-door.

Methods

Delivery strategy

A series of consultations were held with district health staff to identify the most appropriate method of delivery, the approach adopted was similar to that used for Vitamin A, using community health workers paid a daily rate to deliver house to house. Before the main study, a pilot study in three health posts in 2006 and 2007, showed that high coverage could be achieved, and there was good compliance with both the IPT doses supervised by the CHW and the doses of amodiaquine taken unsupervised. In 2008 project staff provided training and supervision for IPT delivery, these inputs were gradually reduced and in 2010 were primarily organised by the district health teams. Drugs for IPT were provided to the district health centre each month, which then organised distribution to health posts. Administration started on the same date in each health post, the 5 day period at the middle of each month was chosen taking into account public holidays, and other health activities of district staff. Training workshops for nurses and CHWs were organised by the district medical officers and community sensitization and local mobilisation were organised by the district communication officer. In September 2010, each health post was provided with a printed register for each village in their catchment area, listing eligible children. CHWs, who worked in pairs, were assigned by the nurse a circuit of villages to visit over a 5 day period in September, October and November, they visited house to house to administer the first dose of IPT each month, all children aged 3-120 months who were normally resident in the village were eligible, those not listed in the register being added to the list. Breakable dispersible AQ and SP tablets were used, mixed with water provide by the household, with dosage determined by age group. Successful treatment, refusal or vomitting was noted in the register and the date of treatment recorded on the mother's DSS card, and the mother was given amodiaquine tablets to give to the child on each of the next two days. At end of each day, the CHWs reported to the health post the number of children seen, drugs remaining, and checked the register for

any children who had been missed, and the nurse then issued CHWs with drugs for the next day. Health posts had supervisory visits each month during IPT administration from either the district public health officer, the district medical officer, or the project's district supervisor.

Head nurses had considerable autonomy in deciding how to manage IPTc administration at their health post. Some had experience of organising IPT in previous years - of the 46 health posts, 18 were administering IPTc for the first time, 19 were in their second year of administration, and 9 were in their third year of administration. In most cases, they trained CHWs over the course of several hours on the day before administration in September, but did not repeat this full training in October and November.

Each head nurse received a lump sum payment to cover CHW incentives based on the estimated number of CHWs needed and the estimated number of days work it would take the CHWs to cover the IPTc target population of each health post. Each head nurse was responsible for organising the hire of CHWs, the number of days they were hired for, and their payment. Some nurses chose to divide the lump sum by the number of CHWs aligned to their health post and pay CHWs a fixed amount as an incentive, while others paid on a daily rate. Further analysis of how payment schemes impacted delivery is being conducted.

This study takes a provider perspective. The focus is on costs of implementation at the district-level and below. Costs incurred only at national level, such as those associated with meetings amongst national-level representatives, are not included. Nearly all the costs of implementation from the district level and below were considered to be recurrent, meaning that they would have to be repeated for each year of implementation. The only capital costs (resources that last over a year) associated with IPTc implementation were those of the research team vehicles, which were used in a few instances to support the distribution of IPTc drugs and supervision.

The costs of research activities were generally excluded from the analysis. However, in two cases, costs associated with research activities were very likely to have contributed directly to the success of the administration and so they have been included and are described in detail. While all costs of the demographic surveillance system (DSS) set up to support the trial were excluded, some of the DSS fieldworkers and supervisors provided supervisory support on the administration days in September and October and transported some of the drugs; the costs of their time and of drivers and vehicles for these implementation activities have, therefore, been included under supervision and supply chain, respectively. In addition, health staff at post, district, and regional levels received incentives for participation in the research. These incentives were paid over the 12 months of the year and were intended to support participation in research activities such as morbidity surveillance. While it is not

anticipated that such incentives would be paid if IPTc were implemented outside a study context, these incentives may have contributed to more assiduous implementation of IPTc, and so they are also presented as a separate cost category.

Data collection

Tools were developed to collect data on costs and resource use at four levels: the project, the district, the health post, and the CHW. The project-level budget tool captured data on the total quantity and unit costs of drugs and supplies purchased centrally, incentive payments, cash transfers to districts and prefectures for fuel costs, the number and cost of some of the meetings and training session,; resource use associated with the delivery of drugs and supplies, and the number of days' supervision and associated costs of DSS fieldworkers and supervisors.

At the district, health post, and CHW levels, questionnaires were developed, introduced to all district medical officers, head nurses, and CHWs at the IPTc planning meetings before IPTc administration began, and refined to incorporate their feedback. Data were collected from all four districts and all 46 health posts following each round of administration in September, October, and November. District and health post questionnaires covered similar areas so that data could be triangulated: time spent and incentive payments received by staff for supervising administration of IPTc; resource use and costs of transport for the delivery of drugs and supplies and of personnel, meetings and training sessions, sensitization activities, and recording of all drugs and supplies received, bought, and used (or wasted) over the course of administration. Both questionnaires collected data on the number of years of experience of implementing IPTc for the facility and for the particular district medical officer or head nurse so as to explore determinants of resource use and efficiency. In addition, the health post questionnaire collected detailed data on the number and composition of CHW teams, the incentives paid to them, and the number of children who received treatment from each relais team.

The CHW questionnaire was administered to a representative, systematic sample of CHWs each month. The CHW questionnaire collected basic demographic information, data on the CHW's experience in administering IPTc, the number of days worked, training and per diems received that month, the type of transport used, who paid for it, and the cost, the villages covered on each day of administration, and any other costs associated with IPTc.

Data analysis

Coverage levels were estimated based on routinely collected activity data as well as a cross-sectional household survey conducted in December 2010.

Costs were summarized according to the categories presented in Table 2. These categories were established to ensure comparability with previous studies of IPTc [3,4] and to reflect the key IPTc cost centres. Costs are presented as the total incremental financial cost for administration in the 46 health posts in both the local currency, the West African Franc (XOF), and in United States Dollars (USUS) based on the average 2010 exchange rate (1 USUS = 495 XOF). While previous papers have tended to focus on the cost per fully adherent child (i.e. per child receiving three doses of IPTc), this study presents the incremental financial cost of IPTc per course administered. Each course of IPTc protects a child from malaria for approximately one month. Thus, children who receive only one or two courses of IPTc derive important benefits, which would not be taken into account if only fully adherent children were considered. Furthermore, given the highly mobile nature of populations both in the study area and in other areas where IPTc is likely to be of benefit, children may have missed doses because they were away from the area and, therefore either not exposed to malaria or potentially able to receive IPTc elsewhere if it was available more widely. Additional data on resource use and unit costs of key cost drivers are also presented.

Future analyses will consider the economic costs of implementation and will disaggregate findings by such variables as the number of years of experience at the health post in delivering IPTc.

Table 2. Description of cost categories

COST CATEGORY	DESCRIPTION
1. IPTc Drugs	*This reflects the cost of sulphadoxine-pyrimethamine (SP) and amodiaquine (AQ) actually used or wasted during IPTc administration. Unit costs reflect the cost of the drugs themselves and the costs of importation to the Port of Dakar.*
2. Drug Transport/ Supply Chain	*This reflects the cost of transporting drugs from Dakar to the districts (via a local storage site) by the research team, and from the districts to the health posts by district and health post staff. When research team drivers were used, their daily wage rate has been included.*
3. Drug Administration (CHWs)	*This includes the cost of payments of per diems to and transport for CHWs to come to the health post, retrieve drugs and registers, administer drugs to children, and return to the health post to return their reports and remaining drugs on each day of the administration. Transport costs paid by the CHW and not reimbursed by the health facility have been excluded.*
4. Supervision	*This reflects the cost of incentive payments to a head nurse, assistant, and in some cases trainee at each health post; to each district health management team, region, and prefecture to supervise the implementation of IPTc and to manage any side effects or refusals; and the costs of any transport used for this supervision. The pro-rata costs of wages and transport for the demographic surveillance system (DSS) supervisors and fieldworkers have also been included for the days on which they helped districts to supervise the administration.*
5. Training of CHWs	*CHWs attended a single day of training at their health post before administration in September. The payment of per diems, as well as the costs of any food or supplies provided or used during the training and any transport paid for by the health post and the district are included. The costs of the head nurse's incentive payments are included under "supervision".*
6. Training of head nurses	*Head nurses travelled to their district health centre for a single day of training before administration in September. Costs include the per diems paid to the head nurses, the costs of their transport, and the costs of any food or supplies provided. The District Health Mangement Teams, who led the training, did not receive any per diems specifically for the training.*
7. Evaluation & planning meetings	*Prior to the training, head nurses attended one or more evaluation and planning meetings at their district during which they evaluated results of the IPTc implementation in 2009 and outlined plans and budgets for implementation of IPTc in 2010. Costs include per diems, transport, and any food or materials provided specifically for the meetings. Meetings were held for head nurses at district level and for district managers in Dakar and at one of the districts.*
8. Sensitisation	*Both districts and health posts arranged activities to promote awareness of IPTc within the community, such as travelling caravans, radio announcements, and community meetings. The costs of meetings with regional or local authorities are also included.*
9. Drugs for side effects	*Health posts were provided with a small stock of drugs and medical supplies with which to manage potential adverse events. The amount provided to health posts was costed regardless of the amount used, as these supplies would need to be provided again in future. In addition, head nurses were reimbursed the cost of treating children whose parents reported side effects, in cases where the head nurse used medications other than those provided.*
10. Supplies	*All supplies used in the administration were costed. These included hats, t-shirts, and polo shirts with IPTc sensitization messages and the MoH logo; registers of children and other monitoring tools; phone cards, etc. provided to them. In addition, health posts also purchased some supplies themselves, such as pencils and erasers, to complement those provided by the district; these costs have also been included.*
11. Research participation incentives	*Regional medical officers, district medical officers, and head nurses all received quarterly incentive payments throughout the year to support research activities such as morbidity surveillance. The entire value of these payments over 12 months to the 3 regions, 4 districts, and 45 health posts that implemented IPTc in 2010 are included, as they are likely to have contributed to more assiduous implementation of IPTc in September, October, and November. It is not expected that this level of incentive payment would be repeated outside a research context.*

RESULTS

The head nurse in each of the 46 health posts was interviewed after each round of IPT, completed questionnaires were also collected from 405 CHWs, reflecting 48% of the average of 822 CHWs who administered IPTc each month, and district level expenditures were collected from each district each month. A total of 471,282 documented courses of treatment were administered by CHWs working in pairs, delivering IPT to on average 90 children per day (Table 3). Health posts employed from 4 to 68 CHWs and delivery each month took from 2 to 5 days (Table 4). High coverage was achieved with about 90% of eligible children treated each month. In total, it cost $233,714 to administer IPTc to a population of 175,000 children under 10 years of age in 4 districts of Senegal over one malaria season, achieving an average monthly coverage of 90% (Table 3) at a cost of $0.50 per course (Table 5).

Table 3. Estimated coverage and total number of course administered

			District			
		TOTAL	Mbour	Bambey	Fatick	Niakhar
Estimated coverage	Sept	88%	78%	94%	80%	87%
	Oct	90%	80%	96%	79%	91%
	Nov	91%	79%	98%	79%	95%
Courses administered	Sept	154,013	34,401	74,047	22551	23,014
	Oct	157,602	35,310	76,018	22219	24,055
	Nov	159,667	35,000	77,292	22405	24,970
	Total	471,282	104,711	227,357	67175	72,039

* Coverage estimated as the number of courses delivered divided by the estimated population eligible to receive IPT, from the DSS.

The main cost drivers in this study were the costs of the drugs (representing 24% of non-research costs, Table 5) and the incentives paid to CHWs (44%). Incentives paid to nurses and district staff may have contributed to the success of delivery and such incentives are not normally provided for programme, although these form a relatively small proportion of total costs.

The incentives paid to CHWs in this project (Table 6) were similar to those paid by the National Malaria Control Programme for community health activities, somewhat less than is paid by some NGOs, but somewhat higher than is paid for delivery of Vitamin A. Vitamin A delivery in Senegal is organised by the La Division de l'Alimentation, de la Nutrition et de la Survie de l'Enfant (DANSE), each district is provided with Vitamin A capsules and a budget of 1,200,000 CFA for each round of delivery. To compare these costs with our costs, the economic costs of district logistics, transport etc used in Vitamin A campaigns will need to be taken into account.

Table 4. Resources involved in IPTc delivery

		Number / mean	Health post range	
			Low	High
Health structures	**Regions**	3		
	Districts	4		
	Health posts[1]	46		
Health workers	**Head nurses**	46		
	Assistant nurses[2]	46		
	CHWs administering IPTc each month (mean)	831		
	CHWs administering IPTc each month per health post (mean)	18.1	4.0	68.0
	Number of days worked on IPTc per month per CHW (mean)	4.2	2.3	5.0
Outputs per structure/ worker	**IPTc courses administered each month per health post (mean)**	3,456	502	16,720
	IPTc courses administered each month per CHW (mean)	189.2	104.5	268.9
	IPTc courses administered each month per CHW per day (mean)	45.3	31.5	89.0

[1] *45 government health posts were randomized to receive IPTc; an additional Catholic mission health post within the catchment area of one of the government posts also participated and is included here.*
[2] *All head nurses have an assistant, but some assistants are community health agents while others are members of the health service.*

High coverage was obtained in our study area, the coverage estimates may somewhat overestimate the true coverage as they are based on estimates of the eligible population from the demographic surveillance system. Children present in the household on the day of IPT delivery who were aged between 3 and 120 months, who were not in the DSS list, were also offered IPT if they were normally resident in the village. However the estimates are consistent with survey estimates of coverage in 2009, based on recorded doses on the DSS card and parental recall. The survey also showed that a high proportion of children received three monthly doses (2009 data: 89.6% had three courses, 3.2% two courses, 1.6% one course, and 5.6% received no IPT).

Costs of publicity campaigns run each month just before each round of IPT were included in these costings, these campaigns were important in ensuring good uptake.

The fact that listings of children were provided from the DSS may have helped to identify eligible children. The costs of the DSS have not been included, although the costs of printing the materials for them to keep track have been printed. On the other hand, completing the registers took additional time. In Vitamin A campaigns there is a tally of total doses delivered but no individual recording of children treated. In our

study IPTc doses were recorded in a register and on the mother's card, however accurate recording of doses received is essential if impact is to be monitored for example using case control studies to measure efficacy of the intervention or rebound effects, and for adverse event monitoring.

Table 5. Financial costs of IPTc by cost category

	Total Costs		Cost per course		Cost profile	
	(XOF)	(USUS)	(XOF)	(USUS)	*including research incentives* (%)	*excluding research incentives* (%)
TOTAL	**115 719 136**	**$233 714**	**245,54**	**$0.50**	**100%**	**100%**
Cost IPTc Drugs (SP+AQ)	21,991,407	$44,415	46.66	$0.09	19%	24%
Drug Transport/Supply Chain	454,814	$919	0.97	$0.00	0%	1%
Drug Administration (CHWs)	39 808 879	$80,401	84.47	$0.17	34%	44%
Supervision	13 972 312	$28,219	29.65	$0.06	12%	15%
Training of CHWs	3,554,337	$7,179	7.54	$0.02	3%	4%
Training of ICPs	951,241	$1,921	2.02	$0.00	1%	1%
Meetings - evaluation & planning	1,170,500	$2,364	2.48	$0.01	1%	1%
Sensitisation	770,100	$1,555	1.63	$0.00	1%	1%
Drugs for side effects	604,025	$1,220	1.28	$0.00	1%	1%
Supplies	7 346 521	$14,837	15.59	$0.03	6%	8%
Research participation incentives	25,095,000	$50,683	53.25	$0.11	22%	x

In most of the clinical trials of IPTc the intervention has been administered to children up to 5 years of age. In this study the inclusion of children up to ten years of age may allow for significant economies of scope to be gained in administering IPTc to a greater proportion of the children within each household visited. Coverage amongst children over 5years old was similar to that achieved in under 5's (data not shown). During the year community health workers may visit households a number of times for Vitamin A and mebendazole delivery, bednet distribution, mass vaccination campaigns and other programmes, opportunities therefore exist for further economies of scope by combining IPTc with delivery of other interventions.

Table 6. Unit costs of key cost drivers

	Article	Unit costs		Total quantity	
		XOF	USUS		
IPTc Drugs	Sulphadoxine-pyremethamine (SP)	11	0.02	515,126	Tablets
	Amodiaquine (AQ)	11	0.02	1,514,054	Tablets
Incentive payments for IPTc administration	CHW daily per diem (mean)	3,755	7.59		CHW-days
	CHW per diems received for one month of IPTc administration (mean)	15,723	31.76		CHWs
	Head nurse IPTc incentive payments (total per year per nurse) [1]	120,000	242.42	46	Nurses
	Head nurse IPTc incentive payments (as % of mean annual net salary)	4.2%		46	Nurses
	Assistant nurse IPTc incentive payments (total per year per nurse)	60,000	121.21	46	Assistant nurses
	Assistant nurse IPTc incentive payments (as % of mean annual net salary)	25.0%		46	Assistant nurses
Funds provided for fuel costs for supervision	District payments (total per year per district)	289,800	585	4	Districts
	Prefecture payments (total per year per prefecture)	193,200	390	4	Prefectures
Research participation incentives	Head nurse (Total per year per nurse)	200,000	404	45	Nurses
	District (Total per year per district)	2,820,000	5697	4	Districts
	Region (Total per year per region)	900,000	1818	3	Regions

[1] Incentives received over the 4 months of IPTc delivery

4. General discussion and conclusions

Across the studies, supervision, training and remuneration of CHWs and ensuring IPTc drug delivery were identified as the main cost components and key determinants to the success of the delivery strategy of IPTc. There is scope for the costs associated with supervision and training to be reduced if IPTc is integrated into existing routine activities. Alternatively, in settings where supervision and training of CHWs is weak, IPTc may offer an opportunity to strengthen both these important aspects of service delivery which will offer benefits beyond reducing malaria morbidity and mortality.

How does IPTc compare to other malaria intervention costs?

i)Costs of IPTi

Two types of unit costs for IPTc have been presented in this report. The first is the 'cost per course' which reflects total costs divided by total courses delivered. In Senegal, the recently calculated financial cost per IPTc course is US$0.50. Across all studies, the financial costs per course range from US$0.24 to US$3.44 and the economic costs per course from US$0.31 to US$3.44. The second option for assessing the unit cost of IPTc is 'the cost of delivering at least the first one dose of each course of IPTc' to take into account the number of children who fully engaged with the intervention as intended.

At between US$8.30 and US$15.03 the annual cost of delivering IPTc under trial conditions was higher in Hohoe, Ghana than that of other interventions designed to protect children against malaria. However, the highest costs in this study relate to a regimen which involved the administration of up to 6 courses of IPTc as opposed to the three courses used in most other studies. When unit costs were scaled up to a district wide level, costs of delivery in this region of Ghana fell to between US$1.74 and US$4.20 per child, comparable to the findings obtained in a larger study conducted in Basse, Gambia where the cost per child who received at least the first dose of each of 3 courses of IPTc was US$1.66 when this was administered via CHWs and $3.53 when it was given through outreach services. These costs are within the range of the costs associated with delivering existing malaria control interventions. For example, the costs per year of protection in US$2010 associated with insecticide treated nets (ITNs) are reported to be US$1.48-4.05[24], US$3.67-6.14 for indoor residual spraying (IRS)[25], US$0.76 for intermittent treatment of malaria (IPT) in infants using three doses of SP [26], US$2.05 for IPT in school children [27] and US$2.73 for delivery of 2 doses of IPT to pregnant woman (using SP) via community care and US$2.42 when delivered via health centres[28].

ii) *Cost-effectiveness of IPTi*

Comparisons of ICERs across studies should be interpreted with caution due to methodological differences (e.g. some take account of resource savings and some do not, some take a societal perspective while others take a provider perspective) and cultural and epidemiological profiles may differ. With this in mind, based on intervention costs alone, the cost of averting an episode of malaria in Hohoe with IPTc is high (US$67.77) compared to other malaria interventions which report the cost per malaria episode averted among under fives of between US$3.71 for ITNs [18] and US$24.00 to US$26.58 for IRS [19]. Figure 3, taken from a summary report recently compiled for the Roll Back Malaria Partnership reviews the available data on the costs and cost effectiveness of various malaria strategies [20]. While caution should be taken when interpreting the data as there was considerable variation in the definition of a case of malaria across the 57 cost and 24 cost effectiveness studies included in the review, the costs of averting a case of malaria via IPTc are comparable to other malaria interventions. In addition, IPTc was predicted to fall within the bounds of being cost-effective (<$223 per DALY) for nearly all of the simulated scenarios[7]. The differences between the predictions and the trial estimates are likely to be due to the inclusion of deaths and severe episodes, the inclusion of all episodes as opposed to those detected by passive case detection alone, and careful exclusion of costs related specifically to research.

The calculations considered above are based on the findings of administration of IPTc under trial conditions for one year although it is proposed that IPTc would be given for the first few years of life. Provided that the same level of protection is achieved each year that IPTc is given, the cost effectiveness ratios achieved in the first year should be repeated in subsequent years, in fact CERs could improve if protection remained constant and costs reduced as the intervention was delivered more efficiently over time. Studies undertaken so far have shown little evidence of a rebound in the incidence of malaria in the year after IPTc was given [2]. However, previous studies in which children were protected against malaria by seasonal chemoprophylaxis indicated that there was a significant increase in clinical attacks of malaria in the year after the intervention stopped in children who had received chemoprophylaxis from the age of 3 months to 5 years [21]. If several years of IPT have a similar effect, this would need to be taken into account in assessing the overall cost effectiveness of the intervention.

Supply side –the impact of IPTc on the health system

IPTc studies have used various delivery systems to achieve high levels of IPTc coverage. There is scope to deliver IPTc using one delivery strategy or a combination of two or more different strategies depending on the setting. However, evidence gained to date suggests that, in most settings, community health workers are likely to be the most effective way of delivering IPTc as they have achieved higher levels of coverage

and lower costs than IPTc delivered by staff of outpatient departments and trekking/outreach clinics [4,5,22].

Figure 3: Cost per malaria case averted broken down by prevention strategy

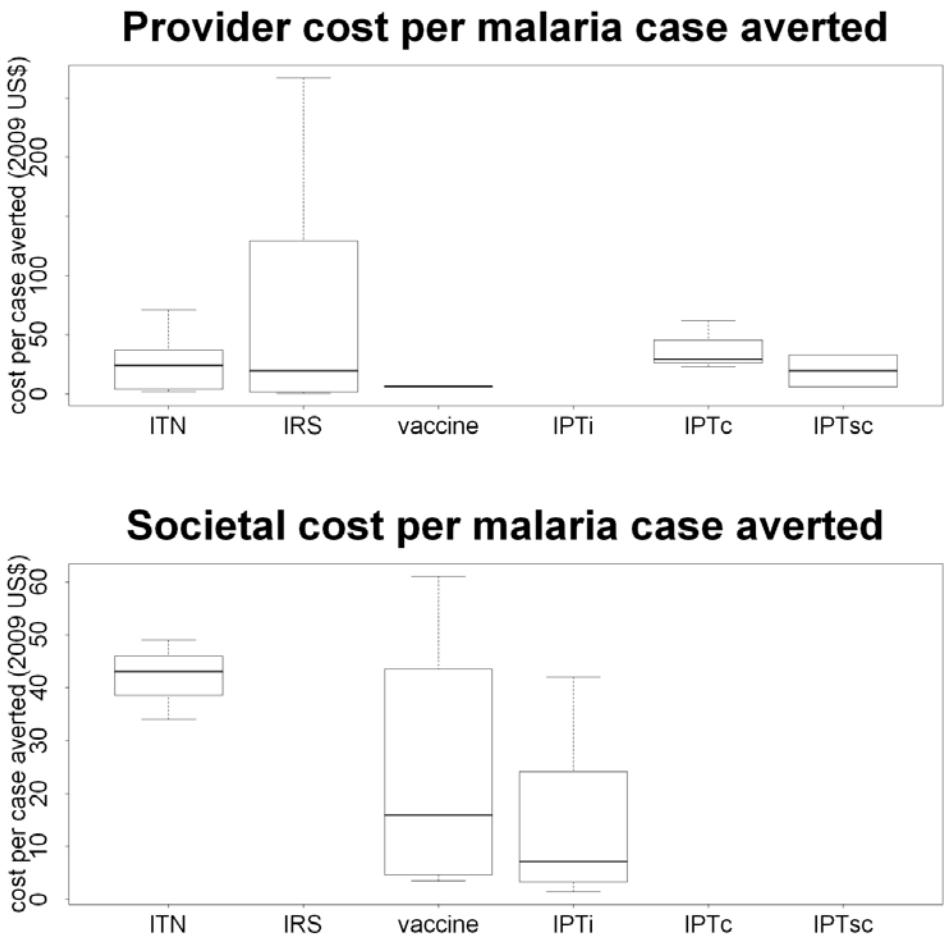


Figure based on [20]; ITN: Insecticide treated nets; IRS: Indoor residual household spraying; IPTsc: IPT in school children

Central to the success of IPTc is the sustainability of the community health worker network. Increasing attention is being given to the role of CHWs in public health programmes [23,24]. Although we refer to CHWs throughout this report, we recognise that there is a wide spectrum of lay health workers and volunteers with varying roles and responsibilities contributing to health and other community programmes. We use the term CHW as an umbrella for all community based health agents and recognise that the potential role of different categories of CHWs in IPTc delivery is an area for future research. The challenges of scaling up and sustaining community–based interventions are varied and, if IPTc is to be launched on a large scale, those responsible for its implementation could learn from some of the

constraints to scaling up identified by other community based studies that have successfully scaled up from small scale experiments to districts [25,26]. Challenges are likely to include managing the time lag between the onset of planning and the launch of services, discrepancies between the knowledge about the intervention held by the different stakeholders and their perceived roles and responsibilities and the need for additional resources at the primary health care level, if staff, materials and supplies are already severely constrained. While these challenges are to be expected, findings from both studies in Senegal suggest that they can be overcome if there is absorption capacity and genuine commitment at all tiers of the health system [6].

The role of incentives

As well as political will and commitment among health care providers, the issue of remunerations, be they financial or non-financial, is crucial to the sustainability of IPTc. The recognition that CHWs need to be compensated was central to the success of the studies considered in this report and an important factor in other successful community health interventions[27]. In the studies costed, CHW were paid as an incentive between US$ 11 and 32 per month (US$ 2010) to deliver IPTc, see Table 7. Health staff were also paid incentives to help motivate them and support the delivery of IPTc. The role of incentives was most pronounced in both studies based in Senegal. For example in Tivaouane, the district-led implementation site, where incentives comprised approximately 10% of total intervention costs. At $31.76 per month the incentives given to CHW in the 4 district study is high, but the daily rate is consistent with what CHWs receive for many other health activities in Senegal, although somewhat higher than is paid in Vitamin A campaigns. Across the studies, the level of incentives was decided by the research teams, health professionals and by assessing the payments CHW received from existing campaigns. If and how these incentives could/should be sustained needs to be explored further. It is important to consider carefully what level the incentive should be set at to avoid wage inflation and market distortions, as setting the incentive too high or low will impact other CHW programmes and have implications on the equilibrium market price of CHW services.

Table 7: Monthly Incentives paid by studies to individual health providers for IPTc Delivery* (US$ 2010)

		CHW	Nurses	DHMT	Driver
Basse, Gambia	CHW	11.10	no incentives	no incentives	13.88
	Outreach	no incentives	25.98	no incentives	13.88
Jasikan, Ghana	CHW	10.60	53.65 (Senior)	no incentives	16.10
	Outreach	no incentives	53.65 (Senior) 10.60 (Dispensers)	no incentives	16.10
	OPD	no incentives	53.65 (Senior) 10.60 (Dispensers)	no incentives	16.10
Hohoe, Ghana		12.00	no incentives	no incentives	no incentives
Tivaouane, Senegal	CHW	20.98	96.21	149.86 (DMO) 99.91 (Deputy DMO)	14.34
4 Districts, Senegal	CHW	31.76	60.61 (Head) 30.30 (Assistant)	157.50 (DMO) 105.00 (Deputy DMO) 73.50 (Supervisor)	no incentives
Average		17.29	42.09	117.15	14.77
Min		10.60	25.98	73.50	13.88
Max		31.76	96.21	157.50	16.1

* Incentives for the research component of the studies are not included
DHMT: District Health Medical Team
DMO: District Medical Officer

Demand Side –household engagement

This report has focused on the costs and potential benefits of IPTc to the health system and the providers who are responsible for supplying health care, with limited discussion on the costs and benefits of IPTc to households. In the Gambia, the costs of accessing IPTc (directly and indirectly in terms of time lost) were calculated and only one caregiver reported a loss of income. In all studies there has been a willingness to give time to receive IPTc and, if IPTc is delivered in the community the cost of accessing IPTc appear to be negligible. Even in the trials in Mali and Burkina Faso where caretakers were asked to visit a health facility on 3 consecutive days with the study children, those who had initially dropped out or felt it was too much of an onerous task, subsequently wished to join the programme after they had witnessed firsthand the benefits the IPTc trial was having on the children in their communities[28]. This enthusiasm of caretakers to enrol in a study that averts malaria is totally rational given the heavy direct and indirect costs a visit to a hospital can have on a household when a child suffers an episode of malaria.

To conclude, in this report we present the costs and cost-effective of IPTc using three different drug regimens and various delivery strategies. While the cost of the intervention is marginally higher than that of delivering other prevention strategies, possibilities exist for reducing the costs of IPTc by scaling up delivery to the district level and by incorporat delivery of IPTc with the delivery of other interventions such as the distribution of Vitamin A or HMM. Supervision, training and remuneration of CHWs and IPTc drug delivery have been identified as the main cost components and key determinants to the success of the delivery strategy.

Annex 1: Studies with a Socio-Economic Component

Adapted from [2]

		Kweku *et al* (2008) [29]	**Bojang et al, (2011) [4]**	**Kweku *et al* (2009) [30]**	**Cisse *et al* [6]**	**Dicko *et al*, (2011) [11]**	**Konaté *et al*, (2011) [12]**	**Senegal 4 Districts**
Characteristics of study area	Location	Hohoe, Ghana	Basse, The Gambia	Jasikan, Ghana	Tivaouane, Senegal	Siby, Djoliba and Ouelessebougou, Kati administrative region, Mali	Toeghin, Niou, Laye and Sao, Boussé District Burkina Faso	Mbour, Bambey, Fatick districts, Senegal
	Rainy season	Major Apr-Jul, minor Sept-Nov	July – Nov	Apr-Nov (peaks in May-Jul. and Sept.-Oct.)	Jul. to beginning of Oct	Jun-Oct	Jun-Oct	May/Jun - Sept
	EIR / year	65[B]	1 - 50 per year	65	10	7 – 37	7 – 37	173
	Bednet usage	20% slept under (any) bednet / II% slept under ITN	50% / 62% slept under intact or impregnated bednet	Bednet usage 19% / ITN usage 14%	Bednet usage 28% / ITN usage 13%	>99% ITN usage	>99% ITN usage	93% ITN usage
Study Characteristics	Recruitment Year	2005	2006	2006	2006	2008	2008	2008-2-10
	Design	Individual randomisation	Cluster randomisation	Cluster randomisation	Cluster randomisation	Multi-centre, individual randomisation, double blind		Large-scale implementation
	Control arm	Placebo	Non – Controlled	Non – Controlled	Non – Controlled	Placebo + ITN		Non – Controlled
	For Controlled No. of children randomised, control / active arm or for non-controlled No. of children randomised / enrolled	650 / 1801	12,326	962	5630	1508 / 1509	1505 / 1509	184,795
	Age range enrolled	3-59 months	6-59 months	3-59 months	3-59 months	3–59 months		3-59 months (<120 mths in 2009&2010)
	Drug	SP bimonthly AS+AQ bimonthly AS+AQ monthly	SP+AQ monthly	SP+AQ (May/Jun./Sept./Oct)	SP+AQ monthly	SP+AQ monthly		SP+AQ monthly

		Kweku *et al* (2008) [29]	Bojang et al, (2011) [4]	Kweku *et al* (2009) [30]	Cisse *et al* [6]	Dicko *et al*, (2011) [11]	Konaté *et al*, (2011) [12]	Senegal 4 Districts
Study Characteristics	Dosing	By age: AQ/AS (150mg/50mg) SP (500/25mg) 3-5 months ¼ tab, 6-11 months ½ tab, 12-23 months ¾ tab ≥24 months 1 tab	By weight: SP 25mg S / 1.25 mg P per kg AQ 25mg/kg over 3 days (10mg/kg D1, 10 mg/kg D2, 5mg/kg D3)	By age: SP (500mg/25mg) AQ (150mg) 3-5 months 1/4 tab 6-11 months 1/2 tab 12-23 months 3/4 tab ≥ 24 months 1 tab	By age: SP (500mg/25mg) AQ (150mg) <24 months 1/2 tab ≥24 months 1 tab	By weight: SP (25mg/kg / 1.25 mg/kg) AQ (10mg/kg daily for 3 days)		By age: SP (500mg/25mg) AQ (153mg) 3-23 months 1/2 tab 24-71 months 1 tab 72-120 months 1.5 tab
	Delivery Mechanism	CHW	CHW or Reproductive and Child Health (RCH) trekking team	Health facility (OPD), EPI outreach or CHW	CHW	Health facility		CHW
	Supervision of doses	Directly observed treatment for 3 days	Day 1 directly observed. Day 2 and 3 doses unsupervised	Day 1 directly observed. Day 2 and 3 doses unsupervised	Day 1 directly observed. Day 2 and 3 doses unsupervised	Directly observed for 3 days		Day 1 directly observed. Day 2 and 3 doses unsupervised
Socio-Economic Study Characteristics	Type of Socio-Economic Analysis	Cost effectiveness of trial and modeled for district	Incremental Cost effectiveness	Costing	Costing	Qualitative study on introduction and potential for diffusion of IPTc		Costing
	Costing Perspective	Societal	Provider	Provider	Provider			Provider
	Publication showing results	Conteh et al 2010 [3]	Bojang et al, (2011) [4]	Patouillard E, (in preparation) [5]	Cisse *et al* (in preparation) [6]	Pitt et al [28]		In preparation

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