How to scale up delivery of malaria control interventions:
A systematic review using insecticide-treated nets, intermittent preventive treatment in pregnancy, and artemisinin combination treatment as tracer interventions.

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Background paper for the global symposium on health systems research
16-19 November 2010 • Montreux, Switzerland
This paper is one of several in a series commissioned by the World Health Organization for the First Global Symposium on Health Systems Research, held 16-19 November, 2010, in Montreux, Switzerland. The goal of these papers is to initiate a dialogue on the critical issues in health systems research. The opinions expressed in these papers are those of the authors and do not necessarily reflect those of the symposium organizers. This paper has financial support from the Global Fund to Fight AIDS, Tuberculosis and Malaria.

All papers are available at the symposium website at www.hsr-symposium.org
Table of contents

LIST OF FIGURES AND TABLES ..........................................................................................................................2
KEY MESSAGES ................................................................................................................................................3
EXECUTIVE SUMMARY .....................................................................................................................................4
INTRODUCTION ...............................................................................................................................................7
  GLOBAL MALARIA EPIDEMIOLOGY .................................................................................................................7
  MALARIA CONTROL INTERVENTIONS ...............................................................................................................8
  LEVELS AND TRENDS IN COVERAGE OF MALARIA CONTROL INTERVENTIONS .............................................10
AIM AND OBJECTIVES ....................................................................................................................................11
METHODS ......................................................................................................................................................12
  SEARCH METHODS FOR THE IDENTIFICATION OF PAPERS .................................................................12
  CRITERIA FOR SELECTING PAPERS ............................................................................................................12
  SCREENING OF ABSTRACTS AND FULL PAPERS FOR INCLUSION ....................................................15
  DATA EXTRACTION .......................................................................................................................................15
ANALYSIS OF INCLUDED PAPERS ....................................................................................................................16
RESULTS .........................................................................................................................................................16
  SEARCH RESULTS .......................................................................................................................................16
  STRATEGIES FOR DELIVERING MALARIA INTERVENTIONS AT SCALE .....................................................18
  COVERAGE AND EQUITY ............................................................................................................................18
  COSTS ............................................................................................................................................................30
  FACILITATORS AND BARRIERS TO ACHIEVING DELIVERY AT SCALE ....................................................35
DISCUSSION ...................................................................................................................................................41
REFERENCES ...................................................................................................................................................46
ABBREVIATIONS AND GLOSSARY ..................................................................................................................51
APPENDIX ......................................................................................................................................................52
List of figures and tables

Figure 1: Spatial distribution of *P.falciparum* (2007) and *P.vivax* (2009) malaria endemicity

Figure 2: Components of methods for scaling up delivery of IPTp and ITN or LLIN for malaria control

Figure 3: Selection criteria applied to full paper screening

Figure 4: Flow diagram or review search results

Figure 5: Distribution of IPTp, ACT and ITN/LLIN interventions by scale, target, sector, and cost of scale up strategy

Figure 6: IPTp logic model

Figure 7: ACT logic model

Figure 8: ITN/LLIN logic model

Figure 9 (Appendix): Ovid Medline search

Figure 10 (Appendix): Embase search strategy

Figure 11 (Appendix): Search strategy for CAB Abstracts and Global Health databases

Figure 12 (Appendix): Africa Wide search (EBSCOhost interface)

Table 1: Health system elements (from WHO building blocks)

Table 2: Malaria interventions included in systematic review

Table 3: Information extracted from papers

Table 4: Characteristics of delivery strategies for IPTp, ACT and ITN/LLIN programmes included in this review

Table 5: Coverage & equity for IPTp, ACT and ITN/LLIN programmes included in this review

Table 6: Quality of the evidence from papers included using GRADE

Table 7: Costs for IPTp, ACT and ITN/LLIN programmes included in this review

Table 8: Summary of important influences on scale up of delivery of IPTp, ACT and ITN/LLIN interventions categorised by health system building block

Table 9 (Appendix): Search results by source

Table 10 (Appendix): Exclusion reasons applied to title and abstract screening, before and following piloting of 100 titles and abstract
Key messages

Aim: To synthesise recent evidence on how to scale up the delivery of malaria interventions in endemic regions through a systematic review of the available literature by:

- Documenting delivery strategies for the WHO-recommended malaria interventions.
- Summarising information on coverage reached, equity of coverage, and costs.
- Identifying facilitators and barriers from a health systems perspective.

Findings: 39 papers related to delivery at scale of intermittent preventive treatment in pregnancy (IPTp) (n=4), artemisinin combination therapy (ACT) (n=3) or insecticide treated nets (ITN) (n=32).

- Relatively few strategies for scaling up have been reported in published literature.
- Acute knowledge gaps exist for scale up of diagnostics and treatment.
- The geographical range of data is narrow (19 African countries). Countries with large numbers of deaths, such as the DRC and Ethiopia, are not represented.
- The majority of information on delivering interventions at scale is drawn from district level experience, with very little information from scale up to national level.
- Coverage & equity: The evidence to link changes in coverage to any specific strategy is weak: only 3 of 24 studies reporting coverage had a concurrent comparison group, and only one was classified as high-level evidence using the GRADE criteria.
  - IPTp coverage was low (4%-47% pregnant women receiving two doses), despite high ANC attendance (>80%).
  - For ACT, an associated increase in treatment among children (73% to 88%) was reported with delivery through accredited drug dispensing outlets and health facilities in Tanzania; a reduction in parasitaemia in children in one district of Zanzibar (9% to 4.3%) was associated with free delivery in health facilities.
  - For ITNs/ LLINs programmes, household ownership (n=2) or use (n=2) reaching RBM targets of 80% was associated with free delivery through campaigns. Delivery strategies involving a fee for the end user tended to be associated with lower household ownership. Campaigns distributing free nets showed less socio-economic inequity than other ITN/ LLIN strategies. No information on socio-economic status of coverage was available for IPTp or ACT.
- Facilitators & Barriers: There is scant information on facilitators and barriers to scale up and most are setting-specific.
  - Facilitators included good access to interventions; amended record keeping methods; integration between malaria control programmes and other departments both within and outside the MoH; the involvement of stakeholders in planning stages; and sharing experience.
  - Barriers included lack of infrastructure; stock outs; costs of ACTs and lack of uptake of subsidies for ACTs by private retailers; challenges in funding; lack of clear and well-disseminated guidelines.

Comment: In order to prioritise strengthening of health system elements for scale up, systematic review alone is not sufficient and additional research methods are needed.

- New studies, linked to ongoing major scale up efforts could add substantially to the evidence base.
- Qualitative methods, a systems approach, and the prospective and systematic collection of process and monitoring data could help to fill the knowledge gap.
Executive summary

Objectives

The aim of this review was to synthesise recent evidence on how to scale up the delivery of malaria interventions in endemic regions through a systematic review of the available literature. We documented the strategies of delivering the WHO-recommended malaria interventions at scale (district level or higher). We summarised the coverage achieved post intervention, including that stratified by socio-economic status where available, and costs reported by included papers. We synthesised the qualitative evidence for how to deliver interventions at scale, through identifying facilitators and barriers to achieving universal coverage of malaria control interventions. We reported these factors using the perspective of the WHO health systems building block framework of health services; workforce; information; medical products, vaccines and technology; financing; and leadership and governance. We discussed gaps and weaknesses in the existing knowledge base.

Background

In 2008 there were an estimated 863,000 deaths worldwide due to malaria, with an estimated 243 million cases, 93% of which were caused by Plasmodium falciparum. A total of 74 countries or territories at risk of malaria experience relatively low transmission and burden of disease, with 37 in the elimination or pre-elimination phase. Thirty countries in Africa and five in Asia include 98% of worldwide malaria deaths, and 96% of cases. Approximately half of world’s malaria deaths and cases were in only five countries: Nigeria, the Democratic Republic of Congo, Ethiopia, Tanzania and Uganda, illustrating the continuing need to scale up malaria interventions in such countries.

Current malaria control tools include indoor residual spraying (IRS), long lasting insecticide treated nets (ITNs/LLINs), and intermittent preventive treatment in pregnant women (IPTp) and infants (IPTi) for prevention, and timely diagnosis and treatment for all episodes. Targets aim to provide universal coverage with ITNs (over 80%) to all persons at risk of malaria. For IPTp, the current targets are for over 80% of pregnant women attending ANC in high transmission regions to receive at least two doses of IPTp with SP. For diagnosis and treatment interventions, the aim is for universal coverage with prompt and effective treatment of malaria. This constitutes treatment of at least 80% of parasitologically-confirmed malaria within 24 hours of onset of fever with an effective anti-malarial, in most cases an ACT.

Despite widespread adoption of these policies and targets by endemic countries, progress towards them is mixed. This mixed success of scaling up effective malaria prevention and control interventions is of particular concern in sub-Saharan Africa where 90% of the Plasmodium falciparum burden lies, and there is a need to know more about what works in the scaling up process. As a background paper to the First Global Symposium of Health Systems Research, the WHO/UNDP/World Bank Special Programme for Research and Training in Tropical Diseases (TDR) commissioned this systematic review to address the question of how to scale up malaria interventions from a health systems perspective.

Methods

The search strategy was developed in Ovid Medline, using both subject heading (thesaurus) classification terms and free text words. Ten databases were searched using the strategy for combinations of malaria terms; AND prevention, control, treatment and diagnosis terms; AND scaling up terms. The final search was then limited using filters to ‘humans’ and a publication date...
range of January 2000 to May 2010. The search strategy was not restricted by language or study design.

To be included in this review studies had to be carried out under operational circumstances in at least one district. Relevant study designs included those that compared strategies of delivering interventions at scale with control groups or districts, those using surveys before and after the intervention (temporal, but no external control), and cross sectional surveys where the malaria interventions may be linked to a particular scale up method or delivery strategy. Qualitative studies, case studies, process evaluations and cost effectiveness studies were also included, particularly if linked to a publication describing an observational study design, to inform work on facilitators and barriers to achieving universal coverage.

The review was restricted to populations living in endemic countries and did not include complex emergencies including international refugees and internally displaced populations. We focussed on WHO-recommended policy interventions to control *Plasmodium falciparum* and *Plasmodium vivax*.

Publications were exported to EndNote, duplicate records removed, and titles and abstract independently screened by two authors. Full papers were obtained for all selected abstracts and reviewed independently by both reviewers. Due to time constraints, interventions were limited to intermittent preventive treatment in pregnancy (IPTp), artemisinin combination therapy (ACT), and insecticide treated nets (ITNs) or long-lasting insecticidal nets (LLINs).

Strategies of delivering IPTp, ACT or ITN/LLIN interventions at scale were recorded according to characteristics outlined in the framework by Kilian et al. Data was extracted on coverage achieved post intervention, including that stratified by socio-economic status where available, and costs reported by included papers. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria were used to evaluate the quality of evidence from papers using observational and controlled study designs, in order to determine the extent to which changes in coverage may be due to the intervention described.

Narrative synthesis was used to analyse the qualitative information on how to scale up. Extracted data was presented in the form of descriptions, and tables were used to present summarised data in groups for comparison. Thematic analysis was used to summarise extracted data on health system elements that influence delivery at scale of IPTp, ACT and ITNs or LLINs, based on the WHO health systems building block framework (health services; workforce; information; medical products, vaccines and technology; financing; and leadership and governance).

**Findings**

Our initial search produced a total of 1295 papers, with a further 29 found through searching websites and email alerts. After removing duplicates, 583 papers remained for title and abstract screening, of which 109 were retained for screening of the full paper. Of these, 63 were excluded, mainly because they did not include information on implementation (n=26) or were at a scale smaller than district level (n=21). Of the remaining 46 papers, 39 related to IPTp (n=4), ACT (n=3) or ITN/LLIN interventions (n=32), and were included in the final analysis, the seven that were not were excluded due to time constraints.

IPTp was delivered free through ANC, while strategies to deliver ACTs included free delivery through health facilities, and subsidised delivery through accredited drug outlets. A variety of strategies for ITN/LLIN interventions delivery were recorded, the most frequent of which were campaigns to a targeted population (children or pregnant women) at no cost to the end user.
Measures of coverage were available for most ITN/ LLIN papers, but not all of IPTp or ACT papers. Reported coverage of IPTp was low (4%-47% pregnant women receiving two doses), despite high ANC attendance. Reported coverage of ACT was high in included studies, although these papers represented a small range of delivery strategies (health facility and drug outlet only) and were all based in Tanzania or Zanzibar, the latter with low malaria prevalence. Coverage measures achieved with ITNs/ LLINs varied; programmes with low coverage (22%-43% household ownership) tended to be delivered at subsidised cost, while those programmes with ownership (n=2) or use (n=2) meeting RBM targets of 80% coverage involved free delivery through campaigns.

Socio-economic status (SES) information was available for two thirds of ITN/ LLIN programmes. In general, campaigns distributing free nets showed better SES equity than strategies delivering nets at subsidised cost with some even being pro-poor. Just two programmes distributed free nets through the routine health system alone, one of which achieved equity, and the other did not report coverage by socio-economic status. Stratification of coverage by SES was not reported by any of the IPTp or ACT studies.

Cost information was available for 10 ITNs/ LLINs studies, and one ACT paper. The annual financial cost estimate for delivery of ACT through public health facilities in one district in Tanzania was $1.63 per capita. Overall, the financial cost per ITN delivered ranged from $4.72 in Eritrea to $8.49 in Tanzania; the economic cost per ITN delivered ranged from $2.63 in Malawi to $7.57 in Tanzania. Of those studies that presented some measure of health impact, the economic cost per child death averted ranged from $873 in the national voucher scheme to $1559 in the district level study of delivery through social marketing, both in Tanzania; the economic cost per DALY averted ranged from $44 in Eritrea to $57 in Tanzania. It is important to note that these figures should be compared cautiously due to differences between studies, including scope and perspective of the economic analyses.

Qualitative information on health system facilitators and barriers to delivering IPTp (n=4), ACT (n=1) and ITNs/ LLINs (n=9, although most information from 4 studies) was extracted, although it is important to note that identification of these issues was not the main aim of the large majority of these papers.

Facilitators to delivering these interventions at scale included good access to and awareness of control interventions: access was particularly important for treatment interventions and awareness was important for ITN/ LLIN distribution interventions. Amended record keeping methods also aided implementation of ITN/ LLIN programmes. Integration between malaria control programmes and other departments was important (ANC and reproductive health for IPTp, EPI for ITN/ LLINs); the involvement of stakeholders in planning stages; and sharing experience were also highlighted as facilitators.

Barriers included the negative impact of stock outs of SP, nets and vouchers; the costs of ACTs and lack up uptake of subsidies for ACTs by private retailers; and challenges in funding intervention distribution activities. The lack of well-developed guidelines that are clearly communicated to all parties, and effective staff training and supervision to implement these guidelines were highlighted by many IPTp and ITN/ LLIN programmes as important barriers to delivery of these interventions at scale.
Introduction

Global malaria epidemiology

Malaria is a vector-borne disease caused by the *Plasmodium* parasite and transmitted to humans by the female *Anopheles* mosquito. Five species of *Plasmodium* can cause disease in humans: *falciparum*, *vivax*, *ovale*, *malariae* and *knowlesi*. In 2008 there were an estimated 863,000 deaths worldwide, with an estimated 243 million cases, 93% of which were caused by *Plasmodium falciparum* (1).

Data from 2008, reported in the World Health Organization’s World Malaria Report 2009, show that malaria is endemic in 109 countries or territories spread throughout Africa (n=50), Asia-Pacific (n=20), Central and South America (n=22), and the Middle East and Eurasia (n=17), representing 3.3 billion people at risk (1). Figure 1 shows the spatial distribution of *P. falciparum* for 2007 and *P. vivax* for 2009, as produced by the Malaria Atlas Project (MAP) (2-3).

Figure 1: Spatial distribution of *P.falciparum* (2007) (top) and *P.vivax* (2009) (bottom) malaria endemicity

![Map showing malaria endemicity](map.png)
Transmission was defined as stable (red areas, where \(Pv\text{API} \geq 0.1\) per 1,000 people p.a.), unstable (pink areas, where \(Pv\text{API} < 0.1\) per 1,000 p.a.) or no risk (grey areas). The boundaries of the 95 countries defined as \(P.\) vivax endemic are shown. The medical intelligence and predicted Duffy negativity layers are overlaid on the \(P.\) vivax limits of transmission as defined by the \(Pv\text{API}\) data and biological mask layers. Areas where Duffy negativity prevalence was estimated as \(\geq 90\%\) are hatched, indicating where PAR estimates were modulated most significantly by the presence of this genetic trait.

Regions vary in the species of \textit{Plasmodium} parasite transmitted, \textit{Anopheles} vector, intensity of transmission, and the mortality and morbidity burden. A total of 74 countries experience relatively low transmission and burden of disease, with 37 in the elimination or pre-elimination phase. However, the remaining 35 countries (30 in Africa and 5 in Asia) represent 98\% of worldwide malaria deaths, and 96\% of cases (1). Indeed it is estimated that approximately half of malaria deaths and cases in 2008 were in only five countries: Nigeria, the Democratic Republic of Congo, Ethiopia, Tanzania and Uganda, illustrating the continuing need to scale up malaria interventions in such countries to successfully control this epidemic (1).

**Malaria Control Interventions**

*Preventive Interventions*

The World Health Organization (WHO) recommends the use of insecticide treated nets (ITNs), particularly long-lasting insecticidal nets (LLINs), and indoor residual spraying (IRS) in endemic regions (4-5). Additionally, in areas where mosquito breeding sites are few, fixed, and easily identified, ITNs and indoor residual spraying may be complemented by the use of larviciding and environmental management (6). In areas of moderate to high transmission of \(P.\) falciparum malaria, intermittent preventive treatment (IPT) for pregnant women is recommended (7). Finally in certain epidemiological situations interventions targeting high risk groups (e.g. infants with IPT [IPTi]) may also be appropriate.

*Insecticide treated nets (ITNs) and long-lasting insecticidal nets (LLINs)*

ITNs have been shown to be a cost-effective vector control measure in endemic regions (8-10). A Cochrane review of the effect of ITNs that included 14 trials reported a 50\% reduction in malaria episodes in stable malaria transmission areas compared to no net use, and a 62\% reduction in episodes in \(P.\) falciparum and a 52\% reduction in \(P.\) vivax in unstable transmission areas (11). Five of the included trials assessed mortality, and together suggested that ITNs reduce all-cause under five mortality by 17\% compared to no nets (11).
Insecticide treated nets provide a physical barrier, preventing biting by the malaria vector and as such offer personal protection to the individual sleeping under the net. As ITNs are treated with insecticides that provide toxic effects to the mosquito (12), ITNs also have a community effect, providing protection even for those who do not sleep under nets themselves, by reducing the vector population (13). LLINs are nets that are treated at factory level by a process that binds or incorporates insecticide into the net’s fibres. The WHO currently recommends three types of LLIN (Permethrin-incorporated, Deltamethrin-coated, and Alphacypermethrin-coated nets) which are designed to maintain their effects against mosquitoes for at least three years without the need for re-treatment (4).

Intermittent preventive treatment for pregnant women (IPTp)

The WHO recommends IPT for pregnant women (IPTp) in areas of moderate to high *P.falciparum* malaria transmission, as part of a package of interventions that also includes ITNs and prompt and effective case management of anaemia and malaria, delivered through routine antenatal care (ANC) services (14). Women in these regions may have high levels of acquired immunity and are susceptible to asymptomatic malaria infection with high levels of placental parasitaemia, which can cause severe maternal anaemia and, increased risk of low birth weight infants (15). IPTp with Sulphadoxine Pyrimethamine (SP) has been shown to be effective in reducing placental parasitaemia, maternal anaemia and low birth weight (16-20).

Here we refer to IPTp as the administration of a treatment dose of Sulphadoxine Pyrimethamine (SP), after the first trimester of pregnancy, regardless of whether or not the woman has symptoms of malaria. It is recommended that women should receive at least two doses at intervals of at least one month during the second and third trimesters, and three doses in areas with high HIV prevalence (7).

Diagnosis and Treatment

Treatment guidelines for non-severe malaria in regions with *P.falciparum* recommend the use of an artemisinin-based anti-malarial in combination with a differently-acting anti-malarial, termed artemisinin combination therapy (ACT). These therapies have been proved to be highly effective (21-23). ACT should be co-formulated and the production, sale and use of artemisinin monotherapy, or co-blistered formulations, are not recommended. Recommended treatment for *P.vivax* is chloroquine followed by radical cure using primaquine to target the liver stage of *plasmodium* development if the patient is not G6PD-deficient, because primaquine can cause haemolytic anaemia in this group(1). Where *P.vivax* demonstrates resistance to chloroquine, ACT are recommended (1). Guidelines for the treatment of severe malaria recommend quinine or ACT at a health facility, or in situations where timely access to a health facility is not possible, administration of a dose of rectal artesunate followed by referral to the nearest health facility able to treat severe malaria (1).

In 2010 the WHO issued new guidelines on the diagnosis and treatment of malaria, recommending parasitological confirmation by microscopy or rapid diagnostic test (RDT) of all suspected cases of non-severe malaria prior to anti-malarial treatment, where testing is possible (24). Guidelines for prompt and effective treatment for all cases of malaria within 24 hours of onset of symptoms remain (1). RDTs use immuno-chromatographic methods to detect malaria parasite-specific antigens and are relatively simple to use. There are now a number of RDTs available that are relatively inexpensive, sensitive (90-95%), specific (>95%), and temperature stable (25-27), although performance under operational conditions has varied (28).
Levels and trends in coverage of malaria control interventions

The current Roll Back Malaria (RBM) goal is to reduce global malaria cases from year 2000 levels by 50% by 2010, and by 75% by 2015, and to reduce malaria deaths from year 2000 levels by 50% by 2010, and to near-zero prevalence by 2015 (29). This is to be achieved through universal coverage with previously discussed effective prevention and treatment interventions that are currently available, including ITNs and prompt and effective treatment (1). Universal coverage is defined as greater than 80% coverage of all populations at risk of malaria; this represents a shift from the previous focus on pregnant women and children aged less than five years, although emphasis on these biologically vulnerable groups remains.

Targets for preventive, and diagnosis and treatment interventions

Current targets aim to provide universal coverage with ITNs (over 80%) to all persons at risk of malaria. The WHO recommends that ITNs should be provided free of charge to the end user, or highly subsidised (29). With regard to delivery strategies, a combination of “catch-up” and “keep-up” is recommended, utilising both periodic mass campaigns (“catch-up”) and continuous routine delivery channels (“keep-up”) (29). Periodic mass ITN delivery campaigns may be integrated with existing activities such as measles or polio campaigns, or other outreach activities such as child health days or weeks. Stand-alone ITN distribution campaigns have also been conducted in a number of countries. Continued ITN delivery during routine contact with the health system includes distribution in pregnancy at antenatal clinics and distribution for young children in vaccine clinics. Such strategies may be implemented by the national health service and by private sector providers or non-governmental organisations. Other strategies include efforts to support the existing commercial sector and the use of vouchers exchangeable for subsidised ITNs through the private sector (5). Social marketing, by which we mean the application of marketing technologies developed in the commercial sector to the solution of social problems where the bottom line is behaviour change (30) has been used to support many different types of strategy. RBM targets for IPTp are for over 80% pregnant women attending ANC in high transmission regions receive at least two doses of IPTp with SP. Universal coverage with prompt and effective treatment of malaria is defined as treatment of at least 80% of parasitologically-confirmed malaria with an effective anti-malarial within 24 hours of onset of fever, in most cases an ACT; however, clinical diagnosis is recognised where RDTs and quality microscopy are not available.

Trends towards achieving universal coverage

By 2008 all endemic countries in the African region had policies to improve the use of LLINs by pregnant women and children aged less than five years; 33 countries had adopted strategies for free distribution and 14 had expanded the reach of their LLIN strategy to cover all age groups at risk of malaria. Forty-two countries in Africa, and 35 in other regions had a policy of ACT as first line treatment for *P. falciparum* by 2008, with 60 actually deploying ACT; furthermore, 20 countries within the African region, and 51 in other regions, had adopted a policy of parasitological testing of all patients with symptoms of malaria. IPTp had been adopted as a policy in 33 high burden *P. falciparum* endemic countries (7).

However despite widespread policy adoption, average household net ownership in the 35 highest-burden countries was estimated in 2008 at 31%, and use by children aged less than five years at 24%. Household surveys from 11 African countries (2006-2008) showed that less than 15% of young children received ACT treatment for malaria within 24 hours of onset of fever, and survey data from nine African countries (2007-2008) suggest that an average of 20% of women received two doses of IPTp during pregnancy (7).
More encouragingly, seven countries in the African region (Equatorial Guinea, Ethiopia, Gabon, Mali, San Tome, Senegal and Zambia) reported net use of over 60% by children aged less than five years, and some countries have reported declines of over 50% in malaria cases and deaths (Eritrea, Rwanda, Sao Tome, Zambia, Zanzibar; Botswana, Cape Verde, Namibia, South Africa, and Swaziland).

This mixed success of scaling up effective malaria prevention and control interventions is of particular concern in sub-Saharan Africa where over 90% of the *Plasmodium falciparum* burden lies. There is a need to know more about what works in the scaling up process, in order to inform implementation in other malaria endemic countries. As a background paper to the First Global Symposium of Health Systems Research, the WHO/UNDP/World Bank Special Programme for Research and Training in Tropical Diseases (TDR) commissioned this systematic review to synthesise published evidence on how to deliver malaria interventions at scale, from a health systems perspective.

**Aim and Objectives**

The aim of this review was to synthesise recent evidence on how to deliver malaria interventions at scale in endemic regions through a systematic review of the available literature.

The objectives were:

i. To document the strategies of taking the WHO-recommended malaria interventions to scale, meaning at a district level or higher.

ii. To summarise the coverage achieved post intervention, including that stratified by socio-economic status where available, and costs reported by included papers.

iii. To synthesise the evidence for how to scale up through identifying barriers, facilitators, and influences on achieving universal coverage of malaria control interventions at scale, and report these using the perspective of the WHO health systems building block framework of health services (31).

The gaps and weaknesses in the existing knowledge base were discussed, including methodological gaps, weaknesses and constraints that prevent a better understanding of how to reach universal coverage with selected malaria interventions.

**Health system elements**

Health system elements are guided by the WHO ‘building blocks’ framework of health services, which include health services; workforce; information; medical products, vaccines and technology; financing; and leadership and governance, as detailed in table 1(31).

<table>
<thead>
<tr>
<th>Building blocks</th>
<th>Characteristics and priority areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health services</td>
<td>Demand for services; Package of integrated services; Organization of the provider network; Management; Infrastructure and logistics</td>
</tr>
<tr>
<td>Health workforce</td>
<td>Planning and/ or scaling up workforce; training; financing of workforce scale up; retention of workforce</td>
</tr>
<tr>
<td>Health information</td>
<td>Production, analysis and dissemination of reliable and timely information; Health systems performance; Health determinants; Health status; Reporting systems</td>
</tr>
<tr>
<td>Medical products, vaccines and technologies</td>
<td>Policies, guidelines; Prices; Quality assessment; Procurement, storage, supply, distribution</td>
</tr>
<tr>
<td>Health financing</td>
<td>Pre-payment and risk pooling; Information; Domestic and international sources of funding</td>
</tr>
<tr>
<td>Leadership and governance</td>
<td>Strategy; Oversight; Collaboration and coalition building; Regulation; System design; Accountability</td>
</tr>
</tbody>
</table>

Health system elements (from WHO building blocks (31))
Methods

The development of this review was guided by a number of sources (32-35), including guidelines from the Campbell and Cochrane Equity Methods group (36), and the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) Statement was used to guide presentation (37).

Search methods for the identification of papers

The search strategy was developed in Ovid Medline, using both subject heading (thesaurus) classification terms and free text words. The detailed search strategy is shown in Table 9, and figures 9-12 in the Appendix. Briefly, ten databases were searched and the strategy included searching for combinations of malaria terms; AND prevention, control, treatment and diagnosis terms; AND scaling up terms. The final search was then limited using filters to ‘humans’ and a publication date range of January 2000 to May 2010. The search strategy was not restricted by language or study design.

Following the development of the search strategy in Ovid Medline, this was translated into EMBASE, CAB Abstracts, Global Health, and Africa Wide. In order to identify potential grey literature, the ELDIS and WHO Global Health databases were searched by browsing all titles under the ‘Malaria’ and ‘Health systems/priority diseases/malaria’ index headings. Also, the following websites were purposively selected and searched: WHO (topic- malaria), WHO Roll Back Malaria, Malaria Consortium, Africa Malaria Network Trust, Global Fund, and the following email alerts were browsed: RBM news alert, Malaria World alert, and Tropika.net alert.

The last search was conducted May 2010. Following screening and application of inclusion criteria, reference lists from all included papers were hand searched for any additional relevant citations, and those relevant were added to the review.

Criteria for selecting papers

Types of studies

Study designs were selected on a basis of ‘fitness for purpose’ to address the review’s aims and objectives, rather than a strict evidence hierarchy, as recommended by the Campbell and Cochrane Equity Methods group (36). To be included in this review studies had to be carried out under operational circumstances, at scale- meaning in at least one district. Relevant study designs, used to show the extent to which coverage increased, included those comparing strategies of delivering interventions at scale with control groups or districts, those using surveys before and after the intervention (temporal, but no external control), and cross sectional surveys where the malaria interventions may be linked to a particular scale up method or delivery strategy. Qualitative studies, case studies, process evaluations, and cost effectiveness studies were used, particularly if linked to a publication describing an observational study design, to inform work on barriers, facilitators and influences to achieving universal coverage. Although qualitative methodologies and expert opinions were important to identify barriers and facilitators to scaling up, general opinion pieces not linked to specific scale up studies were excluded.

Populations

Endemic countries and territories exposed to Plasmodium falciparum and Plasmodium vivax were included. This review excluded travellers from non-endemic countries or territories, foreign military
personnel, and populations in areas experiencing complex emergencies including international refugees and internally displaced populations.

Interventions

We focussed on WHO-recommended policy interventions, which are listed in table 2. A number of interventions were not included in the review; namely, insecticide coils and electrically heated dispensers; insecticide-treated matting (for use on the inside of walls); insecticide-treated tents or sheeting; vaccines; and large-scale environmental management such as civil engineering projects to fill in mosquito breeding sites.

Table 2: Malaria interventions included in systematic review

<table>
<thead>
<tr>
<th>Prevention</th>
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<tbody>
<tr>
<td>Vector Control</td>
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<tr>
<td>Insecticide treated nets (ITN)</td>
</tr>
<tr>
<td>Long-lasting insecticide nets (LLIN)</td>
</tr>
<tr>
<td>Indoor residual spraying (IRS)</td>
</tr>
<tr>
<td>Larviciding and environmental management</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intermittent preventive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant women (IPTp)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment &amp; Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis with microscopy or rapid diagnostic test</td>
</tr>
<tr>
<td>Treatment with artemisinin combination therapy, chloroquine, primaquine as appropriate for species of Plasmodium and severity of infection</td>
</tr>
<tr>
<td>Home or community management of malaria</td>
</tr>
</tbody>
</table>

Outcome measures

Strategies to deliver interventions at scale

Identifying strategies to deliver malaria control interventions at scale was the first objective of this review and a framework, adapted from Kilian et al., guided our classification of strategies of scaling up IPTp, ACT, and ITN/LLIN interventions (figure 2)(38). The framework was classified according to six complementary criteria: the intervention delivered, target group, sector of delivery, agent of delivery, duration of implementation, and cost to user.
Coverage, equity and costs

Outcome measures relating to coverage, equity and costs (second objective) are listed below.

- Proportion of targeted population reached
- Proportion of population reached, stratified by SES status
- Proportion of pregnant women attending ANC who receive at least one dose of IPTp, and that receiving two or more doses
- Household ownership of an ITN/LLIN
- Proportion of children aged less than five years who used an ITN/LLIN during the night preceding survey
- Proportion of non-severe malaria cases in children aged less than five years that received appropriate anti-malarial treatment within 24 hours of onset of fever
- Costs included
- Economic costing (annuitization, discount rates, opportunity costs)

Facilitators and barriers to delivery at scale

Facilitators and barriers to implementing a malaria control intervention at scale were identified from a health system’s perspective, guided by the WHO building blocks (table 1). Qualitative data was extracted from included papers, and analysed using narrative synthesis as detailed below.
**Time frame and language**

This review addresses how to scale up malaria control interventions during the last 10 to 15 years and the search strategy covered papers published between 2000 to May 2010, describing interventions from 1995 onwards. Historical accounts of malaria control published during this period, but which address historic activities were excluded, as this was outside the scope of the review, and this literature was not searched systematically.

The search strategy did not include any filters on language; however publications in languages other than English were excluded at the screening stage.

**Screening of abstracts and full papers for inclusion**

Following the database searches, resulting publications were exported to EndNote where duplicate records were removed. All titles and abstracts were independently screened by two authors (BW and LS) in accordance with the study inclusion and exclusion criteria (figure 3). Discrepant results were discussed and resolved between the two reviewers. Full papers were obtained for all selected abstracts and assessed for inclusion by both reviewers. Where there was disagreement at the full paper screening stage, a third reviewer (JS) reviewed the full paper and a final decision was made.

Figure 3: Selection criteria applied to full paper screening

- Is the malaria intervention relevant to this review?
- Is the population relevant to this review?
- Is the report describing scale up in at least one district?
- Is the report a description of how to scale up a malaria intervention, or a comparative study of how to scale up a malaria intervention, or a before and after study of a scaled up malaria intervention, or did the report allow attribution of a change in outcome to a scaled up malaria intervention?
- Does the report describe a scaled up intervention, or does it identify barriers to/ facilitators of/ influences on scaling up, or comment on health system elements required to allow scale up, or describe how to strengthen health systems to allow scale up?
- Is the report in English?

**Data extraction**

Data were extracted from the final included papers into an Access database as detailed in table 3. Half of the papers were extracted independently by both reviewers (BW & LS), and the remaining by BW only.

Table 3: Information extracted from papers

<table>
<thead>
<tr>
<th>Category</th>
<th>Detail of information extracted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Publication details</td>
<td>Author, year, citation details, type of publication, reviewer ID, unique identifier for each paper, database source</td>
</tr>
<tr>
<td>Study design</td>
<td>Study design, use of controls/ comparison group</td>
</tr>
<tr>
<td>Setting</td>
<td>Country, geographical location</td>
</tr>
<tr>
<td>Context</td>
<td>Malaria transmission, seasonality of malaria, malaria control policy</td>
</tr>
<tr>
<td>Malaria intervention</td>
<td>IPTp, ACT, ITN/ LLIN (narrowed focus of review)</td>
</tr>
<tr>
<td>Level of scale up</td>
<td>District, Regional, National</td>
</tr>
<tr>
<td>Details of scale up</td>
<td>Strategy to deliver intervention at scale, timing of scale up, selection of districts or regions</td>
</tr>
<tr>
<td>Evaluation</td>
<td>Timing of evaluation, sample size, coverage achieved</td>
</tr>
<tr>
<td>Equity</td>
<td>Equity measure, coverage by subgroup</td>
</tr>
<tr>
<td>Costs</td>
<td>Study perspective (societal, provider, user), costs included, economic costing (annuitization, discount rates, opportunity costs), sensitivity analyses and outcomes (in terms of costs and effectiveness, where measured)</td>
</tr>
<tr>
<td>Health system elements</td>
<td>Classified as facilitators or barriers, suggestions for improvement</td>
</tr>
<tr>
<td>Study quality</td>
<td>Methodological issues, bias, external validity (generalisability)</td>
</tr>
</tbody>
</table>
Analysis of included papers

Strategy of delivering IPTp, ACT or ITN/LLIN interventions at scale were recorded according to characteristics outlined in the framework by Kilian et al. described above (figure 2). With regard to the second objective of this review, reporting coverage and the extent to which changes in coverage may be due to the intervention described, we used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria to evaluate the quality of evidence from papers using observational and controlled study designs (39).

Analysis of information relevant to the third objective of this review was carried out using narrative synthesis (40): quantitative methods such as meta-analysis are not appropriate for the study question or the qualitative data available, which did not provide a measure of efficacy or effectiveness. Extracted qualitative data was presented in the form of descriptions, and tables were used to present summarised data in groups for comparison. Thematic analysis was used to summarise extracted data on health system elements that influence scale up of IPTp, ACT and ITNs or LLINs as highlighted in the included papers.

Guidelines to assess the quality of qualitative study designs are less established than those to assess controlled studies (Cochrane) or observational studies (Campbell Collaboration). A systematic assessment of the quality of qualitative evidence was not attempted in this review.

Results

Search results

Our initial database search produced a total of 1295 papers. An additional 29 reports were found through searching pre-specified websites and email alerts. After checking for duplicates, 583 papers remained for title and abstract screening, of which 105 were retained for screening of the full paper. At this stage 63 papers were excluded with 42 papers retained, the main reasons being that they did not include information on implementation (n=26) or were not at scale (defined in this review as implemented in at least one district) (n=21). Other papers were excluded because they did not contain primary data (n=9), involved a malaria intervention not included in this review (n=3), or discussed the process of anti-malarial drug policy change rather than the implementation of that policy (n=2), or for other reasons (n=2). A further four papers were identified and included by hand searching reference lists of included papers, giving 46 papers in total (figure 4).

Restriction of scope of review

Given the time frame available for this review, it was necessary to narrow the focus of the work to particular malaria control interventions. Of the 46 papers meeting the full inclusion criteria, three related to ACT, three to integrated vector control, four to multiple interventions, four to IPTp and 32 to ITNs. It was decided to restrict the review ITNs/LLINs, ACT and IPTp. Reviewers excluded papers describing multiple interventions on the basis that these did not contain the same level of detail those discussing a single intervention only. Papers covering integrated vector control were excluded on the assumption that many of the ‘lessons learned’ from these would be covered by papers discussing ITNs, as ITNs form a cornerstone of integrated vector management. As such 39 papers addressing the delivery of IPTp, ACT, and ITNs/LLINs at scale were included (figure 4).
Figure 4: Flow diagram or review search results

Identification

1295 records identified through database searching

29 additional records identified through other sources

583 records after duplicates removed

Screening

583 records screened

478 records excluded

Doesn’t address scale up (n=26)
Less than district level (n=21)
Not primary data (n=9)
Not relevant malaria intervention (n=3)
Discusses policy change not scale up (n=2)
Other (n=2)

105 full-text articles assessed for eligibility

46 articles meeting inclusion criteria

63 full-text articles excluded

Integrated vector control (n=3)
Multiple interventions (n=4)

Eligibility

4 articles from hand searching reference lists

7 not included due to narrowed focus of review: ITN or IPTp

Included

39 articles meeting narrowed focus criteria

39 articles included for narrative synthesis
Strategies for delivering malaria interventions at scale

Our review included 39 publications covering 28 programmes (table 4), where a programme is defined as scaled up delivery of IPTp, ACT, ITNs or LLINs, delivered through the same sector in a particular country.

Interventions delivered included IPTp, ACT, LLINs, ITNs either pre-treated or bundled with a treatment kit, or a voucher (to be exchanged for an ITN or LLIN). Targeted populations included pregnant women, young children (less than five years, although other age cut offs were also used), and the general population. The sector of delivery was categorised into routine health services (e.g. ANC, maternal and child health (MCH) clinics or other health facility (HF) contact), campaign (meaning integrated or targeted campaigns), and the formal private retail sector. Interventions scaled up through these sectors were implemented by routine health staff, community workers, volunteers, private retailers, or civic/ NGO/ academic organisations. Interventions were delivered on a continuous or a time limited basis, and were free (100% subsidy) or provided at a partially subsidised cost to the end user (figures 2 & 5).

IPTp

Four papers related to the delivery of IPTp, one from Mozambique (41), one from Tanzania(42), and two reviews of delivery in a number of East African (Kenya, Malawi, Tanzania, Uganda, Zambia) (43) and West African (Benin, Burkina Faso, Cameroon, Cote d’Ivoire, Mali, Senegal, Togo) countries (44). All were delivered to pregnant women through the routine ANC sector by ANC staff in a continuous manner, and were free to the end user. All papers described IPTp delivery at a national scale, except in Mozambique where IPTp was initially delivered in 2 pilot districts before roll-out nationwide (table 4 & figure 5).

ACT

Three papers related to the delivery of ACT at district level in mainland Tanzania (n=2) and Zanzibar, and all targeted the general population. Those from the North A district of Zanzibar (45), and Rufiji district in Tanzania (46) delivered free (100% subsidy) ACT through government and mission (Rufiji only) health facilities. The study from Kilombero and Ulanga districts in Tanzania delivered ACT through private retailers (accredited drug dispensary outlets (ADDOs)) who were eligible to sell partially subsidised ACTs (available from a central wholesaler) (47) (table 4 & figure 4).

ITN/ LLIN

Thirty-two papers described 21 programmes delivering ITNs/ LLINs in 12 countries (Burkina Faso, Eritrea, Ghana, Kenya, Madagascar, Malawi, Niger, Nigeria, Tanzania & Zanzibar, Togo, Uganda and Zambia). Of these, seven were implemented at a national level (Eritrea, Kenya, Malawi, Niger, Tanzania & Zanzibar, Togo) (48-60), three at regional (61-63), and 11 at district level (one or more districts, with four programmes taking place in one district only) (64-78) (table 4 & figure 4).

Nine programmes delivered nets bundled with an insecticide treatment kit, two of these were delivered by means of a voucher (9, 50-53, 58, 60, 63-64, 67, 71-72, 74, 78-80). Four programmes delivered a pre-treated ITN (59, 67, 70-71), seven delivered LLINs (48, 55-57, 61, 68, 73, 77), and one involved a split delivery strategy, namely direct LLIN delivery in rural areas and a voucher for redemption at a private retail outlet in urban areas (69). In total, six ITN or LLIN programmes involved the general population (9, 53, 58-59, 64-66, 72, 74, 78-79), eight targeted children aged less than five years (48, 55-57, 61, 63, 68-69, 73, 77), three targeted pregnant women (62, 70-71), while
four targeted both children aged less than five years and pregnant women (50-52, 60, 67, 80) (table 4).

The most common sector for delivering ITNs or LLINs, or vouchers for these, was through campaigns, comprising nine programmes; seven of these involved delivery of nets through integration with an existing mass campaign delivering a public health intervention such as measles or polio vaccination (57, 61, 63, 67-69, 73, 77); the remaining two involved mass campaigns that delivered ITN or LLINs only (48, 55-56). Three programmes used the routine health sector only (59, 70-71), and the remaining programmes used the routine health sector in combination with: (i) formal private retail (n=5) (50-52, 58, 60, 62, 65-66, 72, 74, 76, 78); (ii) campaign (n=1) (75); (iii) community delivery (n=2) (9, 53, 64, 79); and (iv) both the formal private retail and campaign sectors (n=1) (80).

In total, 10 of the 21 ITN/LLIN programmes delivered interventions on a continuous (routine) basis, nine were time limited (48, 55-56, 61, 63, 67-69, 72-74, 77-78), involving mass distribution campaigns conducted over short periods of time, and two were a combination of both continuous (routine) and time limited (campaign) time frames (75, 80). Finally, a large proportion of the programmes reviewed involved delivery of free nets (100% subsidy) (n=11) (48, 55-57, 59, 61, 63, 67-69, 71, 73, 75, 77); one was initially delivered at cost to end users but this was altered to a free programme as implementation proceeded (59); seven were delivered at a partially subsidised cost to the end user (9, 50-53, 58, 60, 62, 68, 72, 74, 78-79); and in two programmes nets were either free or partially subsidised to the end user according to their socio-economic eligibility status (65-66, 76, 80) (table 4).

Figure 5: Distribution of IPTp, ACT and ITN/LLIN programmes by scale, target, sector, and cost of scale up strategy
Table 4: Characteristics of delivery strategies for IPTp, ACT and ITN or LLIN programmes included in this review

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of scale up</th>
<th>Intervention</th>
<th>Target group</th>
<th>Sector</th>
<th>Delivered by</th>
<th>Duration</th>
<th>Cost to user</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IPTp</strong></td>
<td></td>
<td></td>
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<tr>
<td>East Africa: Kenya, Malawi, Tanzania, Uganda, Zambia(43)</td>
<td>National</td>
<td>IPTp with SP</td>
<td>Pregnant women (PW)</td>
<td>Routine: ANC</td>
<td>ANC staff</td>
<td>Continuous</td>
<td>Free</td>
</tr>
<tr>
<td>Mozambique(41)</td>
<td>District (n=2)</td>
<td>IPTp with SP</td>
<td>PW</td>
<td>Routine: ANC</td>
<td>ANC staff</td>
<td>Continuous</td>
<td>Free</td>
</tr>
<tr>
<td>Tanzania(42)</td>
<td>National</td>
<td>IPTp with SP</td>
<td>PW</td>
<td>Routine: ANC</td>
<td>ANC staff</td>
<td>Continuous</td>
<td>Free</td>
</tr>
<tr>
<td>West Africa: Benin, Burkina Faso, Cameroon, Cote d'Ivoire, Mali, Senegal, Togo(44)</td>
<td>National</td>
<td>IPTp with SP</td>
<td>PW</td>
<td>Routine: ANC</td>
<td>ANC staff</td>
<td>Continuous</td>
<td>Free</td>
</tr>
<tr>
<td><strong>ACT</strong></td>
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<tr>
<td>Tanzania</td>
<td>District (n=2)</td>
<td>ACT (ALu)</td>
<td>General population (GP)</td>
<td>Private retail</td>
<td>Private retail</td>
<td>Continuous</td>
<td>Subsidised</td>
</tr>
<tr>
<td>Tanzania</td>
<td>District (n=1)</td>
<td>ACT (AS-SP)</td>
<td>GP</td>
<td>Routine: HF</td>
<td>HF staff</td>
<td>Continuous</td>
<td>Free</td>
</tr>
<tr>
<td>Zanzibar</td>
<td>District (n=1)</td>
<td>ACT (AS-AQ)</td>
<td>GP</td>
<td>Routine: HF</td>
<td>HF staff</td>
<td>Continuous</td>
<td>Free</td>
</tr>
<tr>
<td><strong>ITN/ LLIN</strong></td>
<td></td>
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<tr>
<td>Burkina Faso(65-66, 76)</td>
<td>District (n=1)</td>
<td>LLIN</td>
<td>GP via private retail sector; PW via ANC</td>
<td>Routine: ANC &amp; Private retail</td>
<td>ANCA staff &amp; private retailers with PSI for social marketing (SM)</td>
<td>Continuous</td>
<td>Free to PW attending ANC; subsidised to clients at private retail outlets</td>
</tr>
<tr>
<td>Eritrea(59)</td>
<td>National</td>
<td>ITN (pre-treated)</td>
<td>GP via CHAs; PW via ANC</td>
<td>Routine: ANC, MCH &amp; HF; Community</td>
<td>ANCA, MCH, HF, and CHAs</td>
<td>Continuous</td>
<td>Initially at cost to GP via CHAs and HFs; free to GP after 2003; free to PW at ANC</td>
</tr>
<tr>
<td>Ghana(70)</td>
<td>District (n=1)</td>
<td>ITN (pre-treated) or voucher exchangeable for ITN at private retailer</td>
<td>PW</td>
<td>Routine: ANC</td>
<td>ANCA staff</td>
<td>Continuous</td>
<td>Subsidised</td>
</tr>
<tr>
<td>Ghana (62)</td>
<td>Region</td>
<td>Voucher exchangeable for an ITN (pre-treated)</td>
<td>PW</td>
<td>Routine: ANC and private retail</td>
<td>ANCA staff, and private retail outlets</td>
<td>Continuous</td>
<td>Subsidised</td>
</tr>
<tr>
<td>Ghana (68)</td>
<td>District (n=1)</td>
<td>ITN (pre-treated); LLIN (45%)</td>
<td>Children &lt; 5 yrs</td>
<td>Measles campaign</td>
<td>Campaign and volunteers</td>
<td>Time limited</td>
<td>Free</td>
</tr>
<tr>
<td>Country</td>
<td>Level</td>
<td>Distribution Method</td>
<td>Routine</td>
<td>ANC Staff</td>
<td>Continuity</td>
<td>Cost</td>
<td></td>
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</tr>
<tr>
<td>Kenya (71)</td>
<td>District (n=35)</td>
<td>ITN (pre-treated or bundled with treatment kit)</td>
<td>PW</td>
<td>Routine: ANC</td>
<td>Continuous</td>
<td>Free</td>
<td></td>
</tr>
<tr>
<td>Kenya (58)</td>
<td>National</td>
<td>ITN bundled with treatment kit</td>
<td>GP through formal private retail, PW and &lt;5yr via MCH</td>
<td>Routine: MCH, Private retail</td>
<td>MCH staff and SM by PSI</td>
<td>Continuous Free</td>
<td></td>
</tr>
<tr>
<td>Kenya (73, 77)</td>
<td>District (n=4)</td>
<td>LLIN</td>
<td>Children &lt; 5 yrs</td>
<td>Measles campaign</td>
<td>Campaign</td>
<td>Time limited Free</td>
<td></td>
</tr>
<tr>
<td>Madagascar (61)</td>
<td>Region</td>
<td>LLIN</td>
<td>Children &lt; 5 yrs</td>
<td>Measles campaign</td>
<td>Campaign and NGO partners</td>
<td>Time limited Free</td>
<td></td>
</tr>
<tr>
<td>Malawi (49, 53-54)</td>
<td>National</td>
<td>ITN bundled with treatment kit</td>
<td>GP via private retail and after 2003 via community-based groups, PW and &lt;5yr children via MCH</td>
<td>Private retail, Routine: MCH, community-based groups</td>
<td>Private retail with SM by PSI, MCH clinic staff</td>
<td>Continuous Subsidised</td>
<td></td>
</tr>
<tr>
<td>Niger (57)</td>
<td>National</td>
<td>LLIN</td>
<td>Children &lt; 5 yrs</td>
<td>Polio campaign</td>
<td>Campaign, NGO partners, community volunteers</td>
<td>Time limited Free</td>
<td></td>
</tr>
<tr>
<td>Nigeria (67)</td>
<td>District (n=2)</td>
<td>ITN (pre-treated or bundled with treatment kit)</td>
<td>Children &lt; 5 yrs and PW</td>
<td>MDA for LF campaign</td>
<td>Campaign and community volunteers</td>
<td>Time limited Free</td>
<td></td>
</tr>
<tr>
<td>Tanzania (50-52, 60)</td>
<td>National</td>
<td>ITN bundled with treatment kit</td>
<td>Children &lt; 5 yrs and PW</td>
<td>Routine: ANC, Formal private retail</td>
<td>ANC staff to provide voucher exchanged at private retailers</td>
<td>Continuous Subsidised</td>
<td></td>
</tr>
<tr>
<td>Tanzania (72, 74, 78)</td>
<td>District (n=2)</td>
<td>ITN bundled with treatment kit</td>
<td>GP</td>
<td>Private retail and HF or community</td>
<td>Private retail with HF and community sellers</td>
<td>Continuous Subsidised</td>
<td></td>
</tr>
<tr>
<td>Tanzania (63)</td>
<td>Regional</td>
<td>ITN bundled with treatment kit</td>
<td>Children &lt; 5 yrs</td>
<td>Measles campaign</td>
<td>Campaign</td>
<td>Time limited Free</td>
<td></td>
</tr>
<tr>
<td>Tanzania (80)</td>
<td>District (n=1)</td>
<td>ITN bundled with treatment kit, or voucher for this via ANC exchangeable at private retailer</td>
<td>Children &lt; 5 yrs via campaign and PW via TNVS</td>
<td>Routine: ANC, measles campaign, private retailer</td>
<td>ANC staff, Campaign, private retailers</td>
<td>Continuous for TNVS, Time limited for campaign Free to children &lt; 5 yrs, voucher to PW subsidised- requires top up fee</td>
<td></td>
</tr>
<tr>
<td>Zanzibar (48)</td>
<td>National</td>
<td>LLIN</td>
<td>Children &lt; 5 yrs</td>
<td>Campaign</td>
<td>Campaign HF and community volunteers</td>
<td>Time limited Free</td>
<td></td>
</tr>
<tr>
<td>Togo (55-56)</td>
<td>National</td>
<td>LLIN</td>
<td>Children &lt; 5 yrs</td>
<td>Campaign</td>
<td>Campaign, community</td>
<td>Time limited Free</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>District (n=)</td>
<td>Distribution</td>
<td>Target Population</td>
<td>Routine</td>
<td>Volunteers and NGO partners</td>
<td></td>
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</tr>
<tr>
<td>Uganda (75)</td>
<td>District (n=2)</td>
<td>LLIN</td>
<td>Children &lt; 5yrs and PW</td>
<td>ANC, Campaign</td>
<td>ANC staff, Campaign and community volunteers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zambia (64)</td>
<td>District (n=3)</td>
<td>ITN bundled with treatment kit</td>
<td>GP</td>
<td>HF, Community</td>
<td>HF staff, and community volunteers, with SM by MoH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zambia (69)</td>
<td>District (n=4)</td>
<td>LLIN in rural areas and voucher exchangeable for a pre-treated ITN at private retailers in urban areas</td>
<td>Children &lt; 5yrs</td>
<td>Measles campaign</td>
<td>Campaign with NGO partners, private retailers</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACT = Artemisinin combination therapy; ANC = Antenatal care; CHA = Community health assistant; GP = General population; HF = Health facility; IPTp = Intermittent preventive treatment in pregnancy; ITN = Insecticide treated net; LF = Lymphatic filariasis; LLIN = Long-lasting insecticidal nets; MCH = Maternal and child health; MDA = Mass drug administration; MoH = Ministry of health; NGO = Non-governmental organisation; PSI = Population services international; PW = Pregnant women; SM = Social marketing; SP = Sulphadoxine Pyrimethamine; TNVS = Tanzania national voucher scheme.
Coverage and Equity

Three of four IPTp papers reviewed included the proportion of pregnant women attending ANC who received two doses of IPTp (IPTp2) as a measure of coverage (41-43). This ranged from 4% in Kenya to 47% in Malawi. Equity of coverage across subgroups was not reported for any of the four IPTp programmes, although Hill et al. in their review report that ANC use was higher in urban than in rural areas of Kenya, Malawi, Tanzania, Uganda, and Zambia (DHS data) (table 5).

Of the three ACT papers reviewed, one reported treatment of febrile children (≤5 years) with a recommended anti-malarial within 24 hours, as recorded from self-report for illness within the last 14 days in cross sectional surveys (47), another reported parasitaemia in children aged less than five years from cross sectional surveys in Zanzibar (45), while the third was a cost effectiveness study of delivery through health facilities with no coverage reported (46). Prompt and effective treatment among children improved by 15% (73-88%) during the two year period in Kilombero and Ulanga districts where ACT were available through ADDOs as well as from health facilities, while parasitaemia in children in North A district, Zanzibar was reduced by almost 5% (9-4.3%); note these differences are temporal comparisons only as neither study included a control group. Coverage across SES subgroups was not reported for any of the three ACT papers, although SES was collected in the Kilombero/ Ulanga study (table 5).

Nineteen of the 21 ITN/ LLIN programmes reported household LLIN or ITN ownership or use by children aged less than five years, ranging from 22% to 94% for ownership and 13% to 94% for use. Nine programmes achieved ownership of ITN or LLINs greater than 60% (56-57, 59, 61, 67, 69-70, 73, 77), meeting the original Abuja target set in 2000, of which two achieved ownership over 80% (68-69), meeting the more recent WHO RBM target for universal coverage. Two further programmes which reported use in children aged less than five years rather than ownership, reported use of 86% and 93% (48, 75). Ten of these 11 programmes (13 papers) which achieved high ITN ownership or use, delivered nets free of charge to the end user, nine through mass campaigns. Four were at national scale (three were vaccination-integrated national campaigns in Niger, Togo and Zanzibar (48, 55-57); the fourth used the routine health system in Eritrea (59)); one programme was implemented at regional level (a measles vaccination-integrated campaign in Madagascar) (61); and the remaining six were implemented at district level (three through integrated campaigns with measles vaccination in Ghana, Kenya and Zambia (68-69, 73, 77); one through an integrated campaign with mass drug administration for lymphatic filariasis (LF) in Nigeria (67); one was implemented through routine ANC in Uganda (75); and one using a voucher scheme (subsidised cost to user) in Ghana(70) (table 5).

Fourteen programmes reported coverage stratified according to SES as a measure of equity. Of these, three were pro-poor: the national campaign targeting children in Zanzibar (pro-poor in North A district, but pro-rich in Micheweni district where the most poor quintile were less likely to register (largest disparity), attend the distribution point, and receive an LLIN) (48); the regional campaign integrated with measles vaccination in Madagascar (61); and the national level campaign to the general population using routine distribution through ANC, MCH, and community health workers in Eritrea (59). The national campaign in Togo (55-56), and district-level measles-integrated campaigns in Kenya (73, 77) and Ghana (68) achieved similar coverage across socio-economic groups; the campaign elements of the national programme in Niger (57) and district-level programme delivering to children through a campaign and to pregnant women through ANC in Uganda also neared equity (75). In three measles or LF-integrated campaigns that delivered free nets in Nigeria (67), Tanzania (63) and Zambia (69), and three programmes that delivered partially subsidised nets, through a voucher scheme to pregnant women in Tanzania (50-52, 60), and through sales to pregnant women and young children at MCH clinics at a national scale in Kenya (58) and Malawi (9, 53, 79), increased
ownership of nets remained higher in less poor socioeconomic groups and in urban populations (table 5).
Table 5: Coverage & equity for IPTp, ACT and ITN or LLIN programmes included in this review

<table>
<thead>
<tr>
<th>Country</th>
<th>Intervention</th>
<th>Level of scale up</th>
<th>Study design</th>
<th>Method of evaluation</th>
<th>Timing of evaluation</th>
<th>Baseline coverage</th>
<th>Coverage</th>
<th>Equity indicator</th>
<th>Coverage by SES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IPTp</strong></td>
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</tr>
<tr>
<td>East Africa: Kenya, Malawi, Tanzania, Uganda, Zambia(43)</td>
<td>IPTp with SP</td>
<td>National</td>
<td>Review</td>
<td>DHS (national) household surveys &amp; HMIS</td>
<td>Malawi 2004; Uganda 2003; Kenya 2003; Zambia 2002; Tanzania (data NA)</td>
<td>NR</td>
<td>IPTp2: Malawi 47%; Uganda 30%; Kenya 4%</td>
<td>Urban/rural residence; Kenya MOH v non-govt HF</td>
<td>ANC use and SP uptake higher in urban areas</td>
</tr>
<tr>
<td>Mozambique(41)</td>
<td>IPTp with SP</td>
<td>District (n=2)</td>
<td>Qualitative</td>
<td>Routine monitoring by ANC nurses (cross sectional survey)</td>
<td>2004</td>
<td>NR</td>
<td>30% received IPTp2</td>
<td>NR but carried out in poor districts</td>
<td>NR</td>
</tr>
<tr>
<td>Tanzania(42)</td>
<td>IPTp with SP</td>
<td>National</td>
<td>Qualitative</td>
<td>Cross sectional survey 21 districts (1/region)</td>
<td>2007</td>
<td>26% IPTp2 (NMCP Progress report 2006)</td>
<td>45% IPTp2</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>ACT</strong></td>
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<tr>
<td>Tanzania</td>
<td>ACT (ALu)</td>
<td>District (n=2)</td>
<td>Before &amp; After study</td>
<td>Cross sectional survey</td>
<td>2008</td>
<td>AM within 24 hrs (&lt;5 yrs) 73% 2004</td>
<td>AM within 24 hrs (&lt;5 yrs) 88% 2008</td>
<td>Asset index</td>
<td>NR</td>
</tr>
<tr>
<td>Tanzania</td>
<td>ACT (AS-SP)</td>
<td>District (n=1)</td>
<td>Cost effectiveness</td>
<td>Cost effectiveness</td>
<td>2005</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Zanzibar</td>
<td>ACT (AS-AQ)</td>
<td>District (n=1)</td>
<td>Before &amp; After study</td>
<td>Cross sectional survey</td>
<td>2005</td>
<td>Parasitaemia (&lt;5 yrs) 9% 2003</td>
<td>Parasitaemia (&lt;5 yrs) 5.3% 2005</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>ITN/ LLIN</strong></td>
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<tr>
<td>Burkina Faso (65-66, 76)</td>
<td>LLIN</td>
<td>District (n=1)</td>
<td>Cluster RCT, cost effectiveness, qualitative studies</td>
<td>Baseline &amp; follow up surveys SM only vs. SM &amp; ANC distribution</td>
<td>2007</td>
<td>16% LLIN ownership 2002</td>
<td>28% LLIN ownership 2007</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Eritrea(59)</td>
<td>ITN (pre-treated)</td>
<td>National</td>
<td>Cost effectiveness</td>
<td>NMCP survey in 4 regions</td>
<td>2004</td>
<td>NR</td>
<td>62% HH ownership; 59% &lt;5 yr use 2004</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Ghana(70)</td>
<td>ITN (pre-treated) or voucher exchangeable for ITN at local private retailer</td>
<td>District (n=1)</td>
<td>Before &amp; After study</td>
<td>Cross sectional survey</td>
<td>16 February 2006</td>
<td>Ownership ITN 4.4%, use &lt;5yr 4.1% reported by caregiver 2002</td>
<td>74% ITN ownership, 60% use &lt;5 yr 2006</td>
<td>HH asset index; equity index</td>
<td>Equity index 0.95 ITN ownership, 1.08 ITN use &lt;5 yr</td>
</tr>
<tr>
<td>Country</td>
<td>Voucher</td>
<td>Region</td>
<td>Qualitative</td>
<td>Programme Monitoring</td>
<td>March</td>
<td>Volta Region ITN Ownership 2.5% (DHS 2002)</td>
<td>67% vouchers redeemed for ITN at private retailer 2005</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Ghana(62)</td>
<td>Voucher exchangeable for an ITN (pre-treated)</td>
<td>Region</td>
<td>Qualitative</td>
<td>Programme monitoring of vouchers issued and redeemed</td>
<td>March 2005</td>
<td>Volta Region ITN ownership 2.5% (DHS 2002)</td>
<td>67% vouchers redeemed for ITN at private retailer 2005</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Ghana(69)</td>
<td>ITN (pre-treated); LLIN (45%)</td>
<td>District (n=1)</td>
<td>Before &amp; After study</td>
<td>Cross sectional survey</td>
<td>May 2003</td>
<td>Ownership ITN 4%, use &lt; 5 yr 4% reported by caregiver 2002</td>
<td>ITN ownership 94%, use &lt; 5 yr 65% 2003</td>
<td>HH asset index</td>
<td>ITN ownership and &lt; 5 yr use similar across quintiles</td>
</tr>
<tr>
<td>Kenya(71)</td>
<td>ITN (pre-treated or bundled with treatment kit)</td>
<td>District (n=35)</td>
<td>Qualitative</td>
<td>Program monitoring using routine information</td>
<td>July 2001</td>
<td>Ownership ITN 4%, use &lt; 5 yr 4% reported by caregiver 2002</td>
<td>ITN ownership 94%, use &lt; 5 yr 65% 2003</td>
<td>HH asset index</td>
<td>ITN ownership and &lt; 5 yr use similar across quintiles</td>
</tr>
<tr>
<td>Kenya(58)</td>
<td>ITN bundled with treatment kit</td>
<td>National</td>
<td>Case study</td>
<td>National survey 2003; Monitoring of net sales for MCH sales</td>
<td>2003 survey private retail; August 2005 MCH sales</td>
<td>Use &lt; 5 yr 17% 2003</td>
<td>22% ITN ownership, 24% use &lt; 5 yrs; 90% ITN sold via MCH 2005</td>
<td>Urban / rural residence</td>
<td>In 2003 survey showed increased use in urban &lt; 5yr</td>
</tr>
<tr>
<td>Kenya(73, 77)</td>
<td>LLIN</td>
<td>District (n=4)</td>
<td>Time interrupted series, Before &amp; After study</td>
<td>3 cross sectional surveys</td>
<td>Dec 2004, 2005, 2006.</td>
<td>2004 24.5% HH own net, 13% &lt; 5yr slept under net. 2005 46% HH ownership, 32% use &lt;5 yr.</td>
<td>2006 79% HH ownership, 80% use &lt; 5 yrs.</td>
<td>Asset index</td>
<td>In 2006 equity equal across quintiles. Free mass distribution favoured poor.</td>
</tr>
<tr>
<td>Madagascar(61)</td>
<td>LLIN</td>
<td>Region</td>
<td>Cross sectional (no control)</td>
<td>Cross sectional survey</td>
<td>April 2008</td>
<td>Ownership of any net 11-34% Central &amp; S., 62-82% E. and W. provinces (2004 DHS)</td>
<td>77% HH ownership LLIN, &lt;5yr use 81% 2008</td>
<td>Asset index</td>
<td>Campaign pro poor, equity ratio 1.05</td>
</tr>
<tr>
<td>Malawi (9, 53, 79)</td>
<td>ITN bundled with treatment kit</td>
<td>National</td>
<td>Case study (2), cost effectiveness</td>
<td>DHS</td>
<td>2004</td>
<td>13% HH ownership ITN, 8% use &lt; 5 yr (DHS 2000)</td>
<td>43% HH ownership ITN, 38% use &lt; 5 yr 2004</td>
<td>Asset index</td>
<td>Ownership increased in all quintiles, but rural and most poor quintiles still lower ownership</td>
</tr>
<tr>
<td>Country</td>
<td>ITN Type</td>
<td>Study Area</td>
<td>Study Design</td>
<td>Start Date</td>
<td>ITN Ownership</td>
<td>Use (&lt;5yr)</td>
<td>Asset Index</td>
<td>Equity Ratio</td>
<td></td>
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<tr>
<td>Niger (57)</td>
<td>LLIN</td>
<td>National</td>
<td>Cross sectional (no control)</td>
<td>September 2006</td>
<td>6% HH ownership (recall 2006)</td>
<td>63% HH ownership, use 56% (rainy) 2006</td>
<td>Asset index</td>
<td>Equity ratio of ITN ownership increased from 0.17 to 0.79 (pre-/post-campaign)</td>
<td></td>
</tr>
<tr>
<td>Nigeria (67)</td>
<td>ITN (pre-treated or bundled with treatment kit)</td>
<td>District (n=2)</td>
<td>Cross sectional (no control)</td>
<td>April-May 2005</td>
<td>9% HH ownership (recall)</td>
<td>74% HH ownership, use &lt; 5yr 2005</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Tanzania (50-52, 60)</td>
<td>ITN bundled with treatment kit</td>
<td>National</td>
<td>Cost effectiveness, cross sectional (no control), system analysis, case study</td>
<td>July-Aug 2005, 2006 and 2007 (just after rainy season)</td>
<td>NR</td>
<td>HH ownership 18% 2005, 29% 2006, 36% 2007; use &lt;5 yr 12% 2005, 21% 2006, 26% 2007</td>
<td>Asset index</td>
<td>Ownership increased across all quintiles, but inequity favouring least poor remained.</td>
<td></td>
</tr>
<tr>
<td>Tanzania (72, 74, 78)</td>
<td>ITN bundled with treatment kit</td>
<td>District (n=2)</td>
<td>Cost effectiveness, economic study, cross sectional (with nested case control study)</td>
<td>1997, 1998, 1999</td>
<td>NR</td>
<td>1997 37% HH ownership, &lt;2 yr use 10%; 1998 ownership in &lt;1 yr 45%; 1999 ownership &lt;1 yr 54%</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Tanzania (63)</td>
<td>ITN bundled with treatment kit</td>
<td>Regional</td>
<td>Cross sectional (no control)</td>
<td>November 2005</td>
<td>26% HH ownership, use &lt;5yr 8% (DHS 2004), Pre-campaign ITN ownership 16.5% (recall)</td>
<td>ITN ownership 37%, use &lt; 5yr 21.5% 2005</td>
<td>Asset index</td>
<td>Ownership increased in all quintiles but equity ratio improved only from 0.31 to 0.44</td>
<td></td>
</tr>
<tr>
<td>Tanzania (80)</td>
<td>ITN bundled with treatment kit, or voucher for this via ANC exchangeable at private retailer</td>
<td>District (n=1)</td>
<td>Cross sectional (no control)</td>
<td>June - August 2006</td>
<td>NR</td>
<td>Use &lt;5 yr 40% 2006</td>
<td>Asset index</td>
<td>Overall ownership inequitable (index 0.127), free nets campaign equitable (index 0.015)</td>
<td></td>
</tr>
<tr>
<td>Zanzibar (48)</td>
<td>LLIN</td>
<td>National</td>
<td>Cross sectional (no control)</td>
<td>May 2006</td>
<td>Use &lt; 5yr 40% in Zanzibar and 10% in Micheweni (Zanzibar MCP 2005)</td>
<td>Use &lt;5 yr 57% in Micheweni district, 87% in North A district 2006</td>
<td>Asset index</td>
<td>Equity in North A district, but equity ratio in Micheweni was 1.5 (pro rich)</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>LLIN/ITN Type</td>
<td>Location</td>
<td>Study Type</td>
<td>Study Period</td>
<td>HH Ownership</td>
<td>Asset Index</td>
<td>Use by Children</td>
<td>Notes</td>
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<tr>
<td>Togo(55-56)</td>
<td>LLIN</td>
<td>National</td>
<td>Before &amp; After Study</td>
<td>Cross sectional survey</td>
<td>September 2005</td>
<td>&gt;65% in all 3 districts</td>
<td>Use &lt; 5yr similar in poorest (53%) and least poor quintile (46%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uganda(75)</td>
<td>LLIN</td>
<td>District (n=2)</td>
<td>Cross sectional survey (no control)</td>
<td>Cross sectional survey</td>
<td>5-7 months after distribution (Jan-Sept 2007)</td>
<td>NR</td>
<td>Use &lt; 5 yrs 93% in Adjumani, 56% in Jinja districts</td>
<td>Concentration index closer to 0 (equity) post campaign from 0.24 to 0.08</td>
<td></td>
</tr>
<tr>
<td>Zambia(64)</td>
<td>ITN bundled with treatment kit</td>
<td>District (n=3)</td>
<td>Quasi experimental study</td>
<td>Cross sectional survey with control districts</td>
<td>August-September 2000</td>
<td>NR</td>
<td>Use 13% intervention vs. 5% in comparison districts 2000</td>
<td>Concentration index closer to 0 (equity) for intervention (0.374) versus comparison (0.608) districts</td>
<td></td>
</tr>
<tr>
<td>Zambia(68)</td>
<td>LLIN in rural areas and voucher exchangeable for a pre-treated ITN at urban private retailers</td>
<td>District (n=4)</td>
<td>Cross sectional survey (no control)</td>
<td>Cross sectional survey</td>
<td>December 2003</td>
<td>HH ownership in rural 81% and 76% in urban, use &lt; 5yr 56% in rural, 77% in urban 2003</td>
<td>Equity improved in both rural (equity ratio 0.88) and urban areas (equity ratio 1.19)</td>
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</tbody>
</table>

Note: Newman et al. did not report coverage indicators in their review of scaled up delivery of IPTp in West Africa; therefore this programme is not displayed in the table.

AM= Anti-malarial; ANC= Antenatal care; DHS= Demographic and health survey; GP= General population; HF= Health facility; HMIS= Health Management Information System; HH= Household; IPTp= Intermittent preventive treatment in pregnancy; IPTp2= two doses IPTp; ITN= Insecticide treated net; LLIN= Long-lasting insecticidal nets; MoH= Ministry of health; MCH= Maternal and child health; NA= Not applicable; NMCP= National malaria control programme; NR= Not reported; PW= Pregnant women; RCT= Randomised control trial; SM= Social marketing; SP= Sulphadoxine Pyrimethamine
Study quality using GRADE criteria

A total of 24 papers (3 IPTp, 2 ACT, 19 ITN/ LLIN) included measures of coverage, however only three had concurrent comparison groups. Table 6 shows the study quality, using the GRADE criteria, relating to these three papers, all of which described the implementation of ITNs/ LLINs (64, 76, 78). Muller et al. present results of a cluster RCT in one district of Burkina Faso where social marketing (SM) and partially subsidised sale of LLINs through private retailers alone were compared with SM in addition to free distribution to pregnant women at ANC clinics. Schellenberg et al. describe an intervention to deliver partially subsidised ITNs bundled with treatment kits for sale to the general population through the private retail sector, health facilities and community sellers in two districts of Tanzania. Within the study area a demographic surveillance system was established and a case control study nested within this to investigate child mortality and net use. Agha et al. describe the delivery of partially subsidised ITNs (bundled with treatment kits) to the general population through sales by health facility staff and community volunteers in three districts in Zambia. Net use post intervention in the three intervention districts was compared with two comparison districts.

Despite its randomised design, the RCT was downgraded from high to moderate as no relative measure of effect was provided, and from the information published it was not possible to assess whether the analysis had correctly adjusted for the clustered study design. The Tanzanian study, although a case control, was upgraded to high due to its matched design, good control for confounding and good validation of exposure status. The quasi-experimental study from Zambia was downgraded due to there being no provision of a relative measure of effect, and there being important differences between intervention and comparison districts in important predictors of net use, including socio-economic status (table 6).

The remaining 21 papers are not shown in the table as their study design was not an RCT, quasi-randomised, or in the case of observational studies did not have a concurrent comparison group; as the studies had no measure of effect or control for confounding they did not meet any of the GRADE criteria for upgrading their status, thus making their evaluation using GRADE inappropriate.

Table 6: Quality of the evidence from papers included using GRADE

<table>
<thead>
<tr>
<th>Country</th>
<th>Intervention</th>
<th>Level of scale up</th>
<th>Sector</th>
<th>Study design</th>
<th>Outcomes</th>
<th>Relative effect</th>
<th>Number of participants</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkina Faso(76)</td>
<td>LLIN</td>
<td>District (n=1)</td>
<td>Routine: ANC &amp; Forma</td>
<td>Cluster RCT</td>
<td>Proportion ownership of nets</td>
<td>35% v 23% (p=0.001)</td>
<td>1050 households</td>
<td>+++ Moderate *</td>
</tr>
<tr>
<td>Tanzania(78)</td>
<td>ITN with treatment kit</td>
<td>District (n=2)</td>
<td>Formal private retail and HF or community</td>
<td>Case control (nested)</td>
<td>Net use among children deceased aged &lt; 4yrs (cases) v controls</td>
<td>OR=0.73; 95% CI (0.55-0.97)</td>
<td>2334 children</td>
<td>++++ High †</td>
</tr>
<tr>
<td>Zambia(64)</td>
<td>ITN with treatment kit</td>
<td>District (n=3)</td>
<td>Routine: HF and community</td>
<td>Quasi-experimental design</td>
<td>Proportion usually sleeping under a net</td>
<td>13.3% v 5.4% (p&lt;0.001)</td>
<td>2986 households</td>
<td>+ Very Low ‡</td>
</tr>
</tbody>
</table>

* No measure of effect, analysis does not account for clustering
† matched design, good control for confounding, good validation of exposure status
‡ Differences in intervention and comparison areas in important predictors of net use (e.g. SES), no measure of effect
ANC= Antenatal care; HF= Health facility; ITN= Insecticide treated net; LLIN= Long lasting insecticide treated net; RCT= Randomised control trial
Costs

Eleven of the 39 included papers considered an analysis of the costs or cost effectiveness. One related to the delivery of ACT, and 10 to that of ITNs/LLINs. Of the studies related to ITNs/LLINs, six involved cost elements only, presenting the results as cost per net delivered or cost per treated-net-year (TNY), which combines costs of pre-treated nets and re-treatment as necessary; the remaining four were cost effectiveness studies, presenting costs per death or DALY (disability adjusted life year) averted in addition to cost per net delivered (table 7).

The single study relating to the delivery of ACT (AS SP) through public health facilities under operational conditions was conducted in Rufiji district, Tanzania and reported an estimated annual financial cost of $1.63 per capita (average of annual per capita financial cost over the three years of the study), including drug costs. Modelling was used to extrapolate this to a per capita financial cost of $1.29 following scale up to national level (46).

Overall, the financial cost per ITN delivered ranged from $4.72 in Eritrea (65) to $8.49 in Tanzania (52); the economic cost per ITN delivered from $2.63 in Malawi (9) to $7.57 in Tanzania (52). The alternative measure of economic cost per treated-net-year (TNY) which combines pre-treated nets and any re-treatment activities ranged from $1.18 in Uganda (75) to $6.70 in Tanzania (72). Of those studies that presented some measure of health impact, the economic cost per child death averted ranged from $873 in the national voucher scheme (52) to $1559 in the district level study of delivery through the private retail sector (72), both in Tanzania; the economic cost per DALY averted ranged from $44 in Eritrea(59) to $57 in Tanzania (72).

Of the two studies which evaluated delivery of ITNs through the private retail sector and report their results as cost per ITN delivered, the intervention cost $4.81 per ITN delivered at district level in Burkina Faso (65), compared to $2.63 per ITN delivered at national level in Malawi (9). The third private retail sector study, a district-level intervention in Tanzania (72) found costs of $6.70 per treated-net-year (TNY) which can be compared to $4.41 per TNY in Malawi (9).

Of the five studies that investigated delivery of ITNs through routine ANC, the three conducted at district scale in Uganda, Burkina Faso and Kenya found financial costs of $6.59, $7.21 and $5.26 per ITN delivered, respectively (65, 71, 75); economic costs of $4.39 and $4.81 per ITN delivered, were calculated in Uganda and Burkina Faso respectively (65, 75); the two conducted at national scale in Eritrea and Tanzania reported economic costs of $3.92 and $7.57 per ITN delivered (52, 59).

Although the Tanzanian figure is considerably higher, it is important to note that this presents the provider and user perspective (including user contributions involved in purchasing ITNs through a voucher scheme) whereas all other figures present provider costs only.

Four of the five studies that evaluated targeted mass campaigns found financial costs per ITN delivered ranged from $2.47 to $4.67 for those integrated with vaccination campaigns (63, 68-69) and $7.08 for a stand-alone campaign (75). More detailed economic analyses were conducted for the stand-alone campaign in Uganda, giving an economic cost per ITN delivered of $3.55 at district scale (75).

It is important to note that these figures should be compared cautiously due to differences between studies, most importantly scale and strategy of the intervention delivery, and scale and perspective of the economic analysis. Economic costs are generally lower than financial costs due to annuitization of capital costs (in particular ITNs) which means that they cost less in any particular year. Similarly, the economic cost per TNY is often less than the cost per ITN delivered reflecting the higher number of re-treatment kits distributed than pre-treated nets.
Table 7: Costs for IPTp, ACT and ITN or LLIN programmes included in this review

<table>
<thead>
<tr>
<th>Country</th>
<th>Intervention</th>
<th>Level of scale up</th>
<th>Target group</th>
<th>Perspective</th>
<th>Time frame of analysis</th>
<th>Financial Costs</th>
<th>Economic Costs</th>
<th>Distribution of costs</th>
<th>Sensitivity Analyses</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>Tanzania (46)</td>
<td>ACT (AS-SP) District (n=1)</td>
<td>GP through government and mission health facilities</td>
<td>Provider</td>
<td>2003-05</td>
<td>Set-up costs (equipment, IEC activities, training), recurrent costs (drug purchase, repackaging &amp; distribution). Incremental costing approach excluded infrastructure, supervision &amp; staff costs as assumed these remain same with a new drug policy.</td>
<td>Capital costs annualised (Vehicles 10y; motorbikes 5y; office equipment 3y) and discounted (5%); All costs converted to 2003 US$. District costs extrapolated to national costs.</td>
<td>At district level (actual costs): Drug purchase 73%; Total set-up costs 20%. At national level (modelled costs): Drug purchase 69%; IEC 15%; Drug distribution 10%.</td>
<td>Staff costs; HF utilisation; Drug cost</td>
<td>At district level (actual costs): Average annual financial cost of $1.63 per capita. At national level (modelled costs): Annual financial cost of $1.29. Sensitivity analyses showed +39% change for increased facility use, -56% change for cheaper ACT.</td>
<td></td>
</tr>
<tr>
<td>Burkina Faso (65)</td>
<td>LLIN District (n=1)</td>
<td>GP via private retail sector (subsidised); PW via ANC (free)</td>
<td>Provider &amp; societal</td>
<td>2006-07</td>
<td>Private retail: Provider costs incurred by NGO, wholesalers, shopkeepers, incl transport, storage, labour &amp; profit, IEC materials. ANC: Provider costs for MoH, incl training &amp; supervision, transport of LLINs. Capital cost of LLINs same for each delivery strategy.</td>
<td>Capital costs annualized (LLINs over 5y, vehicles over 7y) and discounted (3%); All prices converted to US$; Detailed opportunity costs calculated for space and personnel on project; User contribution calculated as difference btw provider financial costs &amp; actual costs recovered</td>
<td>Private retail: ITNs 23%; Costs to wholesalers/private retailers 25%; Staff 22% ANC: ITNs 23%; Transport 15%; Staff 54%</td>
<td>Discount rate; LLIN lifespan; Costs of transport, personnel, rent, IEC materials; Leakage of LLINs</td>
<td>Financial cost per LLIN delivered (i) Private retail: $8.08; (ii) ANC: $7.21. Economic cost per LLIN delivered $4.81 for private retail &amp; ANC ($4.73 - $6.01); outcomes most sensitive to LLIN lifespan &amp; leakage</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>ITN Description</td>
<td>National Distribution</td>
<td>District</td>
<td>Provider</td>
<td>Year</td>
<td>Costs Included</td>
<td>Capital Costs</td>
<td>Discount Rate</td>
<td>Financial Cost</td>
<td>Economic Cost</td>
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<tr>
<td>Eritrea (59)</td>
<td>ITN (pre-treated)</td>
<td>GP via CHAs; PW via ANC (free), with re-treatment campaigns</td>
<td>National</td>
<td>Provider</td>
<td>2001-05</td>
<td>All direct costs to provider, incl commodities, delivery, IEC activities, staff, taxes</td>
<td>Capital costs annualised and discounted (3%); all prices converted to US$ and adjusted for inflation to 2005 prices; Shared costs for personnel &amp; space on project calculated.</td>
<td>ITNs &amp; insecticide 64%; Staff 21%</td>
<td>Discount rate; ITN cost, use, lifespan &amp; effectiveness; Proportion of shared costs</td>
<td>Financial cost per ITN delivered $4.72, per TNY $1.43; Economic cost per ITN delivered $3.98 [$3.29-$10.30], per TNY $1.21; most sensitive to ITN costs &amp; shared cost allocation. Cost per child death averted $1449 [$724 – $5795]; Cost per DALY averted $44 [$36-$176]; most sensitive to ITN effectiveness &amp; use.</td>
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<tr>
<td>Ghana (69)</td>
<td>ITN (pre-treated); LLIN (45%)</td>
<td>District (n=1)</td>
<td>Measles campaign</td>
<td>Provider</td>
<td>2002</td>
<td>ITNs, transportation, training, supervision, social mobilisation; Campaign costs that would have been incurred for measles vaccination without inclusion of ITNs excluded</td>
<td>NR</td>
<td>Financial costs only. ITNs 91%; Other elements of delivery 9%</td>
<td>NR</td>
<td>Financial cost per ITN delivered $3.74</td>
</tr>
<tr>
<td>Kenya (71)</td>
<td>ITN (pre-treated or bundled with treatment kit)</td>
<td>District (n=35)</td>
<td>PW through routine ANC</td>
<td>Provider</td>
<td>2001</td>
<td>ITNs &amp; transport (international, to district and to ANC facilities)</td>
<td>NR</td>
<td>NR</td>
<td>Financial cost per ITN delivered to ANCs $3.81; to pregnant women $5.26.</td>
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<tr>
<td>Malawi (9)</td>
<td>ITN bundled with treatment kit</td>
<td>National</td>
<td>GP via formal private retail (unsubsidised) and after 2003 via community-based groups, PW and &lt; 5yr children via MCH (subsidised)</td>
<td>Provider</td>
<td>1999-2003</td>
<td>Capital &amp; recurrent costs, incl ITNs, vehicles, staff, brand creation, advertising &amp; promotion. Capital costs annualised (ITNs 5y, brand 7y, vehicles 8y) and discounted (3%); All prices converted to US$</td>
<td>ITNs 55%; Staff 10%; Supplies/overheads 10%; Fuel 9%</td>
<td>NR</td>
<td>Average economic cost per ITN delivered: $2.63; decreased from $5.04 in 1999 to $1.92 in 2003 as no. ITNs distributed increased suggesting economies of scale. Average economic cost per TNY $4.41 (from $7.69 in 1999 to $3.44 in 2003)</td>
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<tr>
<td>Country</td>
<td>ITN bundled with treatment kit</td>
<td>Area</td>
<td>Target Group</td>
<td>Provider &amp; user</td>
<td>Year</td>
<td>Capital &amp; recurrent costs</td>
<td>Capital costs annualised (ITNs 3y, vehicles 8y) and discounted (3%); Opportunity costs for providers &amp; users (incl top-up paid for ITN); All prices converted to US$ and reported in 2006 US$</td>
<td>ITN costs: subsidy 20%, user 8%; Staff 25%; Promotion activities 16%</td>
<td>Discount rate; User top-up; ITN price, effective lifespan, re-treatment use; LLINs</td>
<td>Financial cost per ITN delivered</td>
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<tr>
<td>Tanzania (52)</td>
<td>ITN bundled with treatment kit</td>
<td>National</td>
<td>Children &lt; 5 yrs and PW through subsidised voucher exchanged at formal private retailers</td>
<td>Provider &amp; user</td>
<td>2004-06</td>
<td>Capital &amp; recurrent costs incl formative research, planning, training, vehicles, ITNs, IEC, personnel, overheads</td>
<td>Capital costs annualised (ITNs 3y, vehicles 8y) and discounted (3%); Opportunity costs for providers &amp; users (incl top-up paid for ITN); All prices converted to US$ and reported in 2006 US$</td>
<td>ITN costs: subsidy 20%, user 8%; Staff 25%; Promotion activities 16%</td>
<td>Discount rate; User top-up; ITN price, effective lifespan, re-treatment use; LLINs</td>
<td>Financial cost per ITN delivered $8.49; Economic cost per ITN delivered $7.57 [$7.40-$8.59], per TNY $4.23 [$4.13-$8.45]; Economic cost per child death averted $873 [$857-$1754]; most sensitive to ITN lifespan and use</td>
</tr>
<tr>
<td>Tanzania (72)</td>
<td>ITN bundled with treatment kit</td>
<td>District (n=2)</td>
<td>GP through private retail sector (unsubsidised)</td>
<td>Provider &amp; user</td>
<td>1996-2000</td>
<td>Capital and recurrent costs divided into set-up activities (branding, sensitisation) and ongoing supply of ITNs (ITNs, personnel, transport, training, promotional materials &amp; activities)</td>
<td>Capital costs annualised (ITNs 5y, brand 7y, vehicles 10y) and discounted (3%); Opportunity costs for providers &amp; users (incl price paid for ITN); All prices converted to US$ and reported in 2000 US$</td>
<td>ITNs &amp; insecticide 31%; Staff 28%; ‘Other’ recurrent costs 32%</td>
<td>Health measures (ITN coverage, inclusion of untreated nets, duration of effectiveness)</td>
<td>Economic cost per TNY $13.38/$6.70 if insecticide lasts 6/12 months; Economic cost per child death averted $1559 [$587-$1018]; Economic cost per DALY averted $57 [$22-$37]; sensitive to all outcome measure assumptions.</td>
</tr>
<tr>
<td>Tanzania (63)</td>
<td>ITN bundled with treatment kit</td>
<td>Regional</td>
<td>Children &lt; 5 yrs through Measles campaign</td>
<td>Provider</td>
<td>2005</td>
<td>ITNs, transport to district, IEC, NMCP staff</td>
<td>Not included</td>
<td>Financial costs only: ITNs 88%; Other elements of delivery 12%</td>
<td>NR</td>
<td>Financial cost per ITN delivered $2.47</td>
</tr>
<tr>
<td>Country</td>
<td>LLIN Description</td>
<td>District</td>
<td>Children &lt;5 yrs</td>
<td>Provider</td>
<td>Year</td>
<td>Detailed costs of LLINs, transport, storage, distribution, IEC activities, training, personnel; All separated by delivery strategy (campaign or ANC).</td>
<td>Capital costs annualised (ITNs 3y, vehicles 7.5y); Shared costs of personnel time &amp; overheads; All costs incurred in 2007 so no inflation adjustment; prices converted to 2007 US$.</td>
<td>Campaign: Distribution 30%; LLIN transport 15%; Registration 16%; IEC 13%.</td>
<td>Discount rate, LLIN lifespan &amp; cost; Net usage &amp; retention</td>
<td>Financial cost per LLIN delivered $6.19/$7.08 (campaigns in 2 districts) $6.59 (ANC); Economic cost per LLIN delivered $2.88/$3.55 [$2.17-$4.52] (campaign), $4.39 [$3.68-$5.28] (ANC); Economic cost per TNY $0.96/$1.18 (campaign), $1.46 (ANC). Cost estimates most sensitive to LLIN lifespan.</td>
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<tr>
<td>Uganda</td>
<td>LLIN (75)</td>
<td>District (n=2)</td>
<td>PW through routine ANC, and children &lt; 5yrs through campaign</td>
<td>Provider</td>
<td>2007</td>
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</table>
| Zambia   | LLIN in rural areas and voucher exchangeable for a pre-treated ITN at private retailers in urban areas (68) | District (n=4) | Children <5 yrs through Measles campaign | Provider | 2003 | ITNs, transport, training, IEC activities; Campaign costs that would have been incurred for measles vaccination without inclusion of ITNs excluded | Financial costs only: ITNs 94%; Other elements of delivery 6% | NR                                                                                   | Financial cost per ITN delivered $4.67 (rural) or $5.06 (urban) | Distribution of costs presented as the percentage of total economic costs; main costs reported only ** Distribution of costs reported as proportion of total costs excluding the LLINs. **

ACT= Artemisinin combination therapy; AM= Anti-malarial; ANC= Antenatal care; DALY= Disability adjusted life year; GP= General population; HF= Health facility; IEC= Information education communication; ITN= Insecticide treated net; LLIN= Long lasting insecticide treated net; MCH= Maternal and child health; MoH= Ministry of health; NGO= Non-governmental organisation; NMCP= National malaria control programme; NR= Not reported; PW= Pregnant women; TNY= Treated net year
Facilitators and barriers to achieving delivery at scale

Health system ‘building blocks’ perspective

In order to understand and discuss the health system facilitators and barriers to implementing IPTp, ACT, and ITN or LLIN control programmes at scale, it is necessary to have some idea of the implementation process of each intervention. To this end, three “logic models”, one for IPTp, one for ACT, and one for ITNs or LLINs, were developed; these are presented from the user’s perspective and show the steps involved in achieving coverage of IPTp, ACT and ITN or LLIN interventions, illustrating the need for high and equitable coverage at all steps in order to reach universal coverage (figures 6, 7 and 8). For example, in the case of IPTp, if 90% clients attend clinic, 90% are eligible to receive IPTp, 90% attend clinics with SP available, and 90% receive SP on site as direct observed therapy, and these figures are repeated for the second dose, coverage will be \((0.90 \times 0.90 \times 0.90 \times 0.90) \times (0.90 \times 0.90 \times 0.90 \times 0.90) = 43\%\), which is inadequate. Furthermore, inequities at each step are likely to increase coverage gaps between most and least vulnerable groups.

Intermittent preventive treatment in pregnancy

Figure 6 illustrates that in order to receive IPTp according to policy, i.e. at least two doses of SP after 16 weeks gestation or ‘quickening’, a pregnant woman needs to attend the ANC clinic where she can be offered, accept and receive SP. Contraindications to receiving SP include gestational age less than 16 weeks, receipt of SP for IPTp or for malaria treatment within the previous month, and cotrimoxazole treatment for co-infection with HIV. Once a woman has been offered, accepted and received a dose of SP, guidelines recommend that direct observed therapy (DOT) is used, which means that the woman takes the dose on site in the presence of a health worker. This whole process is then repeated for the second DOT dose of SP during pregnancy. Where ANC attendance and IPTp are not provided free of charge, additional steps of payment (dashed arrows) are necessary.
Qualitative information on health system facilitators and barriers to delivering IPTp at scale was extracted from four papers (41-44). Hill et al. review the implementation of IPTp in five East African countries, and data was drawn from routine information and interviews with national malaria control programme (NMCP) staff, while information from Newman’s review of West African countries draws on data from national and regional meetings and conferences. In the national scale up of IPTp in Tanzania, Mubyazi et al. present information from qualitative work with health staff and other stakeholders from two districts. Qualitative data on the scale up of delivery of IPTp in two districts in Mozambique was obtained by Brentlinger et al. through site meetings and supervision visits.

- **Attending ANC**: Factors including long distances, waiting times, poor attitude of ANC staff and user fees were identified as barriers to ANC attendance by pregnant women (42-43).

- **Timing of initiating IPTp**: Challenges discussed included inaccuracy in estimates of gestational age (e.g. poor recall by pregnant women, lack of staff expertise, lack of technology such as ultrasound (41)); lack of clarity in guidelines around timing of initiating IPTp; and poor communication with the periphery about these guidelines (42-43).

- **Contraindications to SP**: All programmes mentioned the challenge of avoiding co-administration of SP for malaria treatment in addition to IPTp, timing of previous or subsequent doses of SP for IPTp and the need for communication with other departments and clinicians and good record keeping of SP treatment. Brentlinger’s study also discussed this in the context of high HIV prevalence and use of cotrimoxazole for prevention of opportunistic infections. SP was not approved for use during pregnancy in a number of settings; for example in Mozambique the national formulary had to amend their guidelines to allow the use of SP for IPTp (41).

- **Receiving SP**: SP availability and stock outs were mentioned by all programmes. Experiences from East Africa also described challenges in forecasting drug need, and in the logistics of drug supply and delivery (43).

- **DOT of SP**: The review of programmes from East Africa, and the Tanzania and Mozambique studies mentioned the lack of water and cups as a barrier to DOT of SP (41-43).

Important influences on the delivery of IPTp mentioned were those of staff shortages, absences, supervision and training (42-43). The need for adequate supervision also linked to issues of record keeping and health information; for example in Tanzania, Mubyazi et al. found that staff reported having too little time to keep good records and did not recognise the value of the information produced. In other settings strategies to overcome challenges in information were used, such as in Mozambique where ANC cards were altered to show SP doses administered and training and communication with other departments was put in place to ensure clinicians checked ANC cards before prescribing SP for non-IPTp purposes (41). The importance of integration between health departments, particularly between NMCP and reproductive health (RH) was emphasised in all studies.

Challenges identified included insufficient funds, delays in releasing funds to districts, and the lack of autonomy and flexibility for districts to spend according to their local situation (42, 44). The integration of policy into service providers other than those from the government or ministry of health was also highlighted as a challenge in Tanzania, where there was reported confusion in interpreting policy guidelines as to whether SP stock, staff training and funds were to be distributed to ANC clinics not under government control (42). Finally the reviews of IPTp in East and in West African countries also highlighted the importance of sharing experience between countries (43-44).
Artemisinin Combination Therapy

In order for 80% of malaria cases to be treated promptly with an appropriate anti-malarial, which in many cases is an ACT, a number of steps are necessary (figure 7). Patients must attend a dispensing point for ACT, where their infection is confirmed, and where ACT may be prescribed and dispensed. This depends on the availability of high quality diagnostics that are appropriately administered and which influence treatment behaviour, and the availability of high quality drugs, preferably co-formulated. Patients must then receive the appropriate dosing of ACT, as well as information to promote appropriate adherence with the prescription. Where diagnostics and ACT are not provided free of charge, additional steps of payment (dashed arrows) are necessary.

Figure 7: ACT logic framework

Of the three papers included in this review, only Alba et al.’s study of the influence of accredited drug dispensing outlets (ADDOs) in Kilombero and Ulanga districts of Tanzania provided some information on the implementation process of ACT (47). This paper aimed to report trends in treatment seeking and drug use, and factors influencing accessibility to treatment and did not have a specific focus on facilitators and barriers to delivering ACT at scale. Nonetheless it is a useful example as it included the private retail sector, an important source of anti-malarials in Tanzania, and describes the successful upgrading of drug outlets to ADDOs through training of private retailers, accreditation and regulation. The most important influence on access to treatment was presence of a drug dispensing outlet (health facility or ADDOs) in the village. Authors report that uptake of ALu remained low (39% of cases treated with ALu) despite its free availability from health facilities and at subsidised cost from ADDOs, however ADDOs frequently sold ALu at full cost and rarely took up the subsidy due to low profit margins and the long distance to the centralised wholesaler, therefore cost of ALu in the private sector may have remained an issue.

Insecticide treated nets and long lasting insecticidal nets:
In order for 80% of the population at risk to sleep under a treated ITN or LLIN, a number of steps are involved (figure 8). The target population needs to attend the distribution point for a net or voucher which may be a private retail outlet, an ANC or MCH clinic, other health facility contact point, or in the case of scale up implemented through campaign activities this may be a vaccination/ drug distribution point or the participant’s home. Attendance at the distribution point and eligibility to receive an ITN or LLIN or voucher may sometimes depend on some prior criteria such as attending a vaccination point, belonging to the target group, or living in a household registered during an campaign.

Once at a distribution point, participants may be offered, accept and receive the intervention. In the simplest case this may be an LLIN offered free of charge to the end user. If pre-treated ITNs are offered, these require pre-treatment at an earlier stage in the process. If ITNs bundled with treatment kits are offered, this requires treatment by the recipient. An additional step of payment is required if recipients receive a subsidised (as opposed to free) net (dashed arrows). If participants receive a voucher this leads to further intermediary steps in the process as they are required to exchange the voucher for a free (100% subsidy) or partially subsidised ITN or LLIN, often at a different geographic location. Once the ITN or LLIN is received, information on how to use, treat or re-treat may be necessary in order to promote retention and use. It is important to note that although it is beyond the scope of this review which focuses on strategies to delivery interventions at scale, the effectiveness of ITNs/LLINs depends on their regular use, which is frequently much lower than ownership and influenced by many factors.

Figure 8: ITN or LLIN logic model
Of 32 papers included in this review describing the delivery at scale of ITN or LLINs, 15 provided no information that addressed the qualitative question of this review. These were principally cross sectional, cost effective, or before and after studies, as well as a cluster RCT (50, 54, 56-57, 61, 63-64, 70, 72-74, 76-78, 80).

Eight other papers provided little data. These programmes related to free delivery (100% subsidy) to the general population through health facilities in Eritrea, delivery of free LLINs to pregnant women through ANC in Uganda, campaigns of free nets integrated with MDA for LF in Nigeria, measles campaigns in Zambia and Ghana, a national voucher scheme delivering subsidised ITNs through ANC in Tanzania, and delivery of subsidised ITNs in Malawi. These eight papers were cross sectional, cost effectiveness and case study designs (51-52, 59, 67-69, 75, 79).

Nine further papers provided more substantial qualitative data on facilitators and barriers to delivering ITNs/LLINs at scale. These nine studies related to delivery of ITN or LLINs that could be grouped into seven programmes as follows:

- LLINs at partially subsidised cost through private retailers and social marketing, and free of charge to pregnant women in the Nouna health district of Burkina Faso
- Pre-treated ITNs at partially subsidised cost through a voucher scheme in the Volta region of Ghana
- Pre-treated ITNs, or ITNs bundled with treatment kits at partially subsidised cost through the national routine ANC system in Kenya
- ITNs bundled with treatment kits at partially subsidised cost to pregnant women through ANC, and to the general population through private retailers in Kenya
- ITNs bundled with treatment kits at partially subsidised cost to pregnant women, nationally, through a voucher scheme in Tanzania
- LLINs free of charge for children aged less than five years, through a national campaign on Zanzibar
- LLINs free of charge to children aged less than five years, through a national campaign in Togo

These were qualitative studies, case studies, or papers dealing with economics or cost effectiveness (48, 53, 55, 58, 60, 62, 65-66, 71). In particular, information from four papers provided detail relevant to health system elements: Biersmann et al.’s report results from focus group discussion with local people concerning the delivery of LLINs through social marketing and ANC in Burkina Faso; Guyatt et al. discuss the implementation process of delivering ITNs through the ANC sector in 35 districts in Kenya; Kweku et al. report on interviews with private retailers, ANC staff and pregnant women on the district level voucher scheme in Ghana; and Magesa et al. discuss the development of a strategy for ITN delivery in Tanzania.

- **Eligibility to receive nets:** In some campaigns eligibility to receive a net at the distribution point depended on pre-registration e.g. during house to house visits in the Zanzibar national distribution campaign (48).
- **Attend distribution point:** Where distribution points were permanent health service delivery points such as ANC or MCH clinics, or health facilities, similar influences on attendance applied as described in IPTp studies (e.g. user fees, distance to facility). However where distribution points were formal private retail outlets or temporary campaign distribution points, community awareness played a large role in influencing attendance. Principal methods of increasing awareness included social marketing techniques, especially the use of radio broadcasts (59, 66), although more innovative methods such as plays in rural markets were also used (49). Awareness for campaigns was principally gained through social mobilisation and sensitisation by mass media, home visits or village criers (48, 55).
• **Receiving a voucher:** Important influences on whether or not a voucher was received included voucher stock outs (62), screening by health staff of recipients in terms of their perceived ability to pay the top-up fee (62), or perceived risk status of the recipient (71); this was influenced by the issue of limited net availability at private retailers as perceived by those giving the voucher (ANC nurses) in the voucher scheme in Volta region Ghana (62).

• **Exchanging the voucher for a subsidised net:** The main barrier reported in purchasing a subsidised net through a voucher scheme was the cost (62, 66).

• **Receiving an LLIN or pre-treated net:** Systems that deliver nets through a voucher scheme or by direct means both require the availability of nets. The stock out of nets at health facilities, campaign distribution points and private retailers was raised consistently as a barrier (48, 55). Important influences on the availability of nets included accurate forecasting of need (68), record keeping (65), clearly allocated responsibility at each health system level (65), finances for procurement (62), and logistical issues of delivery and transport (69).

• **Pre-treatment of net:** Health facility and campaign delivery systems identified barriers of lack of water and time to pre-treat sufficient nets to meet distribution demands (71).

Training and supervision were identified by numerous studies as important influences in the effective delivery of nets at scale (53, 58, 69, 75). As found for the delivery of IPTp, the importance of record keeping was also highlighted; for example child welfare cards in Kenya (58), ANC cards in Burkina Faso (65), and health passports in Malawi (53) were all amended and used to record receipt of a net.

Numerous studies identified the logistical challenges of delivering nets from central stores to districts and then distributing nets between peripheral health facilities or campaign distribution points (67, 69, 75). Studies also frequently raised the issue of insufficient funds for net procurement; Magesa *et al.* describe how a financial barrier was addressed and overcome in the TNVS by the removal of tax on nets (60).

Clarity of guidelines was raised by a number of the studies; for example, confusion over whether to give one net for each child or for each household in the national campaign in Togo was compounded by fear of insufficient net supplies (55) and resulted in inconsistency between distribution sites in the number of nets allocated per household. Guyatt *et al.* describe how in the absence of clear instructions on how to implement free ITNs to pregnant women through ANC clinics in Kenya, different districts made different choices, including different ways of forecasting need, differences in allocation of nets between facilities, and differences in the population targeted, with some districts choosing to target young children as well as pregnant women (71).

Finally, five of 17 studies highlighted the positive influence of cooperation between the NMCP, EPI, and reproductive health departments within the Ministry of Health (48, 52, 55, 69, 75), as well as strong partnerships (55), and involvement of other key stakeholders outside the health service such as WHO, UNICEF, national and international Red Cross societies and other NGOs and bilateral agencies (60, 71, 75).

**Health system elements:**

Table 9 shows a summary of important influences highlighted in the papers reviewed, categorised by WHO health system building block. Although the included papers describe a variety of delivery methods, through different sectors, to different target groups and at varying levels of cost to the end user, some cross cutting issues were identified, in particular staff training and supervision, well developed clear guidelines that are effectively communicated, and issues of supply stock outs, whether drugs or nets.
Table 8: Summary of important influences on scale up of delivery of IPTp and ITN or LLIN interventions categorised by health system building block

<table>
<thead>
<tr>
<th>Building blocks</th>
<th>Characteristics and priority areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health services</td>
<td>• User fees/ Top up fees; cost of products (nets, drugs)(42-43, 62, 66)</td>
</tr>
<tr>
<td></td>
<td>• Distance to point of care(42-43)</td>
</tr>
<tr>
<td></td>
<td>• Integrated services (NMCP, ANC, MCH, EPI) &amp; communication between departments (41-44, 48, 52, 55, 69, 75)</td>
</tr>
<tr>
<td></td>
<td>• Infrastructure and logistics (e.g. water for DOT SP and pre-treatment of ITNs)(41-43, 71)</td>
</tr>
<tr>
<td></td>
<td>• Clarity of guidelines at regional or district level(41-43, 55, 71)</td>
</tr>
<tr>
<td>Health workforce</td>
<td>• Training, supervision(41-44, 53, 58, 62, 69, 71, 75)</td>
</tr>
<tr>
<td>Health information</td>
<td>• Record keeping, cross health department records(41-42, 53, 58, 65)</td>
</tr>
<tr>
<td>Medical products, vaccines and technologies</td>
<td>• Procurement, storage, supply, distribution(67, 69, 75)</td>
</tr>
<tr>
<td></td>
<td>• stock outs(41-44)</td>
</tr>
<tr>
<td></td>
<td>• Guidelines on use and safety(41-44)</td>
</tr>
<tr>
<td>Health financing</td>
<td>• Sources of funding and availability of funds (44)</td>
</tr>
<tr>
<td>Leadership and governance</td>
<td>• Co-operation with stakeholders (60, 71, 75)</td>
</tr>
<tr>
<td></td>
<td>• Co-operation with other government departments (e.g. treasury on taxes on nets) (60)</td>
</tr>
<tr>
<td></td>
<td>• Sharing experience with other districts, regions and countries(43-44)</td>
</tr>
</tbody>
</table>

ANC= Antenatal care; DOT= Directly observed therapy; EPI= Expanded programme on immunization; ITN= Insecticide treated net; MCH= Maternal and child health; NMCP= National malaria control programme; SP= Sulphadoxine Pyrimethamine

Discussion

Gaps in the evidence base

Thirty-nine papers have been reviewed on the delivery of IPTp (n=4), ACT (n=3) and ITNs or LLINs (n=32) at scale. The evidence base for scaling up ITN/ LLIN interventions in the published literature is wider than that for other malaria control interventions, in particular than that for the treatment of malaria, where there is a particular knowledge gap. Specifically there is a need to know what works in scaling up the delivery of appropriate treatment, which in many settings is artemisinin combination therapy:

i. through different providers whose personnel may have different levels of training and expertise, e.g. routine government health system, private not for profit health facilities, private retail (general shops, drug shops, accredited outlets), and community sources

ii. in a variety of malaria transmission settings; all three studies included in the review were conducted in Tanzania so knowledge is needed about ACT delivery in a variety of contexts where health service access and usage may differ. In addition, there is an increasing need in many contexts to manage non-malaria causes of febrile illness as well as malaria fevers.

Knowledge gaps remain relating to the scale up of other treatment strategies, particularly home or community based management of malaria, and to the scale up of diagnostics. No papers were identified on the delivery of malaria diagnostics at scale, and only one was identified on home based management of malaria, which was excluded as it was delivered at sub-district level (81).

In comparison to the global distribution of malaria (see figure 1), studies included in the review are drawn from a condensed geographical area, clustered in East Africa and part of West Africa. Some
high burden countries, responsible for large numbers of malaria-related deaths, including the DRC and Ethiopia, are not represented at all. Of the 19 countries which contributed information, all are African, and the majority of information on delivering IPTp, ACT and ITNs or LLINs at scale is drawn from district level experience.

**Strategies for delivering IPTp, ACT and ITNs/ LLINs at scale**

As expected, there was no evidence to suggest that one single delivery strategy was appropriate for scaling up delivery of all malaria control interventions included in the review, and ITN/ LLIN interventions showed more variety in the strategies used. All four IPTp papers delivered SP to pregnant women for free through ANC clinics. Two of three ACT papers delivered treatment free to the general population through health facilities, and one delivered treatment at cost through accredited drug dispensing outlets (private retail sector)\(^1\). Methods of delivering ITNs/ LLINs, or vouchers for these varied over the 21 programmes included in the review. Fifteen programmes delivered to a targeted population (children (n=8) or pregnant women (n=3) or both (n=4)). Campaigns were a popular strategy (nine programmes), while 10 programmes used routine health system delivery on its own (n=3) or in combination with private retail, campaigns or community delivery (n=7). Most programmes (n=11) delivered ITNs/ LLINs at no cost (100% subsidy) to the end user.

Direct comparison of different delivery strategies was possible for only one study, a cluster randomised control trail comparing delivery of LLINs using social marketing alone, to that using routine delivery through ANC in addition (76), although from the information published this analysis does not appear to have been adjusted for the cluster design. This study was in Burkina Faso and the increase in household ownership of ITNs one year following the study was greater in districts with the sale of subsidised nets (social marketing) occurred together with free delivery to pregnant women through ANC clinics (22% increase), than in districts where social marketing alone was implemented (5%).

**Coverage and Equity**

Almost none of the papers included had study designs that provided good evidence that a change in coverage was attributable to the delivery at scale of the malaria control intervention described. Only five were before and after studies providing baseline pre-intervention estimates using the same methodology to estimate coverage at two time points, and fewer still (n=3) included concurrent comparison groups, and only one of which provided high quality evidence as categorised using the GRADE criteria.

Findings from the three papers discussing IPTp show inadequate coverage (≥2 doses of SP) in pregnant women, ranging from 4%-47% despite high ANC attendance; for example the highest coverage of 47% was reported from Mozambique where around 90% of women attend ANC.

Two of the three papers on the delivery of ACT at scale reported associated reductions in parasitaemia (decline of 4%), or increases in prompt and effective treatment for children (increase of 15% to 88% of children <5 yrs), the latter reaching the RBM target of >80% coverage for this indicator. Conclusions are limited however, as all studies were from Tanzania or Zanzibar and strategies for delivery included health facilities or accredited private retailers only.

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\(^1\) ACTs were available from a central wholesaler for delivery to the end user at partially subsidised cost; however most sales recorded were at full cost.
In contrast, most studies describing delivery of ITN/LLIN interventions at scale provided at least one standard measure of coverage, although as outlined above baseline levels of coverage were frequently not collected, and the study designs did not often allow for the change in coverage to be attributed to a specific delivery strategy. Post intervention household ownership of ITNs/LLINs ranged from very low (e.g. 13% in Zambia) to very high (e.g. 94% in Ghana). The most common strategy reported in papers showing low coverage (<40%) was delivery at partially subsidised cost to the end user. Nine programmes reached the 2000 Abuja targets of ≥60% household ownership, most by delivering free (100% subsidy) nets to children using a campaign strategy. Two programmes reached the current RBM target of ≥80% ownership through distribution integrated with measles campaigns targeting children in Zambia and Ghana. A notable exception to the pattern of campaign delivery was the national ITN/LLIN distribution in Eritrea which delivered free ITNs to the population at large using antenatal care clinic and routine community-based health worker distribution strategies.

If targets of universal coverage (≥80%) are to be achieved, malaria control interventions must reach low socio-economic groups since large proportions of the populations of these countries fall into these categories. Stratification of coverage by socio-economic status was not frequently presented and none of the studies addressing delivery of IPTp or ACT reported findings that allowed comparison of socio-economic equity. In contrast, two thirds of papers on ITN/LLIN interventions included information on socio-economic equity; in general those that were pro-poor or achieved similar coverage across socio-economic strata were delivered free to the end user through campaigns, although some campaigns were inequitable. Only two programmes distributed free nets through the routine health system alone, one of which achieved socio-economic equity, and the other did not report coverage by socio-economic status.

**Costs**

It is difficult to present a comprehensive estimate for the costs or cost effectiveness due to variations in economic analysis methods used in the 11 eligible studies (10 ITNs/LLINs, 1 ACT) included in the review, as emphasised previously by Kolaczinski & Hanson (82).

The results of studies which evaluated delivery of nets through the private retail sector in Burkina Faso, Malawi and Tanzania suggest some degree of economies of scale. Comparing between different delivery strategies to try and make recommendations is possible to some degree using the data from the Burkina Faso and Uganda studies, which each compared routine ANC with private retail sector and a mass campaign. In the case of Burkina Faso, the economic costs per ITN delivered were the same regardless of delivery strategy at $4.81. In Uganda, the cost per ITN delivered via routine ANC was $4.39 versus $3.55 for the mass campaign. The authors comment that this is largely due to the greater project management inputs for routine ANC distribution.

All except one of the economic evaluation studies conducted sensitivity analyses around the major cost and outcome parameters. The common elements to which the cost or cost-effectiveness estimates were most sensitive were effective ITN/LLIN lifespan and proportion of ITNs actually used (leakage). Estimates for LLINs in those studies that involved ITNs/re-treatment generally showed similar results to conventional ITNs as the increased cost of the LLIN was offset by improved length of effectiveness and reduced costs due to removal of re-treatment activities.

Similarly, for all of the included studies, the main cost associated with ITN delivery programmes was the ITNs/LLINs themselves, most often followed by staff costs and then transport; overheads and other shared costs were generally relatively low as a proportion of the total programme cost. This has implications for sustainability of ITN programmes which tend to rely on donor funding for these major costs.
Further costing and cost effectiveness studies of national level ITN distribution programmes are still needed to add to this body of evidence. However, perhaps more importantly, further economic evaluation studies are needed for the delivery of prompt and effective case management of malaria with appropriate diagnosis and ACT in different settings to assist decision making on different delivery strategies and financial forecasting. The single study included here presents a cost analysis of implementation of a new ACT drug policy at the district level. Without other studies for comparison, it is difficult to comment on the annual per capita financial cost estimate of $1.63. However, as the authors discuss, the financial projections for implementation of ACT at national scale in Tanzania suggest that donor support will be necessary for this to be affordable since the expenditure on non ACT anti-malarials by the Ministry of Health in 2005 would only cover 15% of the annual expected ACT drug cost estimates.

Facilitators and barriers to delivering interventions at scale: health system perspective

In general, few studies included in the review recorded facilitators and barriers to delivering malaria control interventions at scale. The evidence base on this objective was drawn from all four papers relating to the delivery of IPTp (which addressed this topic well); one paper addressing the scale up of ACT (facilitators and barriers were not the main focus of this publication); and four papers on ITNs/ LLINs that described the implementation process in detail.

Facilitators to delivering these interventions at scale included good access to control interventions, in particular for treatment, and high awareness of distribution activities for ITN/ LLIN programmes; amended record keeping methods also aided implementation of ITN/ LLIN programmes. Integration between malaria control programmes and other departments (e.g. ANC and reproductive health for IPTp, EPI for ITN/ LLINs), both within and outside the MoH; the involvement of stakeholders in planning stages; and sharing experience were also highlighted as facilitators.

Barriers included lack of infrastructure, especially water for directly observed therapy of IPTp-SP or pre-treatment of ITNs; the negative impact of stock outs of SP, nets and vouchers; the costs of ACTs and lack up uptake of subsidies for ACTs by private retailers; and challenges in funding intervention distribution activities. The lack of well-developed guidelines that are clearly communicated to all parties, and effective staff training and supervision to implement these guidelines were highlighted by many IPTp and ITN/ LLIN programmes as important barriers to delivery of these interventions at scale.

Identification of which health system elements were essential or which to strengthen was not elucidated conclusively from this review. However, it can be concluded that since no single health system element was clearly identified as a priority target for strengthening, and because the contribution of different building blocks varied between settings, contextual factors and analysis of a specific setting’s needs are important elements of the analysis when deciding how best to scale up a particular malaria control intervention.

Limitations

Scaling up is a relatively new term and there is no single accepted definition. This may have led to our search strategy missing some reports of scale up. However, unless any missed papers describe very different scale up strategies, or highlight different facilitators and barriers, then this bias shouldn’t be systematic.

We attempted to review available published and grey literature, however the majority of studies included were from the published literature, and this review may be subject to publication bias as
experts were not contacted directly to obtain unpublished or recent work that may have been relevant (83). Other sources of bias in the review process are unlikely as only two papers were excluded on the basis of language, and all titles and abstracts were double reviewed, and all full papers also double reviewed for inclusion criteria and where there was disagreement, a third reviewer was used.

The extraction of qualitative data is subject to interpretation. This process was guided by an extraction form and the WHO health system building blocks framework. For about half of the papers, qualitative data was extracted by two reviewers working independently and similar information was obtained. With more time we would have used double extraction throughout as well as having more discussion and clearer consensus between co-authors, which would have further strengthened this methodology (40).

Findings of this review are not generalisable beyond the interventions reviewed; seven papers that covered integrated management of vector control and multiple interventions were unfortunately excluded due to time constraints. Findings may also not be relevant to excluded populations, including migrants, internally displaced populations, and international refugees. A similar review of effective strategies to deliver malaria interventions to these specific populations would be worthwhile.

**Methodology**

This systematic review has highlighted gaps in the evidence base concerning the delivery at scale of IPTp, ITN/LLIN, and in particular, ACT interventions. It has provided a summary of strategies to deliver these interventions, coverage and equity that may be associated with these strategies, and costs of these strategies, as highlighted in the published literature. Disappointingly, the outputs of this systematic review were not well-aligned with the qualitative question of identifying important influences from a health systems perspective and providing guidance on what elements of the health system are essential to achieving delivery at scale, or which elements to prioritise for strengthening interventions. Inclusion of details from process evaluations in published papers and reports would improve the ability to address this question by the process of systematic review. Additional methodologies may be appropriate to supplement information from systematic reviews, in order to address this question. These may include primary qualitative data collection from key informants working in the delivery of malaria control interventions at scale, a systems approach, and potentially the prospective and systematic collection of process evaluation and monitoring data from ongoing and future implementation studies in parallel with scale up activities.
REFERENCES


49. CHAVASSE D, KOLWICZ C, SMITH B. Preventing malaria in Malawi Essential Drugs Monitor 2001;30.


### Abbreviations and Glossary

#### Abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACT</td>
<td>Artemisinin combination therapy</td>
</tr>
<tr>
<td>ADDO</td>
<td>Accredited drug dispensing outlet</td>
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<tr>
<td>AM</td>
<td>Anti-malarial</td>
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<td>ANC</td>
<td>Antenatal care</td>
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<tr>
<td>CHA</td>
<td>Community Health Assistant</td>
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<tr>
<td>DALY</td>
<td>Disability adjusted life year</td>
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<tr>
<td>DHS</td>
<td>Demographic and Health survey</td>
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<tr>
<td>DOT</td>
<td>Directly observed therapy</td>
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<tr>
<td>EPI</td>
<td>Expanded programme on immunization</td>
</tr>
<tr>
<td>GRADE</td>
<td>Grading of Recommendations Assessment, Development and Evaluation</td>
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<tr>
<td>GP</td>
<td>General population</td>
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<tr>
<td>HF</td>
<td>Health facility</td>
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<tr>
<td>HH</td>
<td>Household</td>
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<tr>
<td>HMIS</td>
<td>Health Management Information System</td>
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<tr>
<td>IEC</td>
<td>Information, education, communication</td>
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<tr>
<td>IPTp</td>
<td>Intermittent preventive treatment in pregnancy</td>
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<tr>
<td>IPTi</td>
<td>Intermittent preventive treatment in infants</td>
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<tr>
<td>IRS</td>
<td>Indoor residual spraying</td>
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<tr>
<td>ITN</td>
<td>Insecticide treated net</td>
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<tr>
<td>LF</td>
<td>Lymphatic Filariasis</td>
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<tr>
<td>LLIN</td>
<td>Long lasting insecticidal net</td>
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<tr>
<td>MAP</td>
<td>Malaria Atlas Project</td>
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<tr>
<td>MCH</td>
<td>Maternal and child health</td>
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<tr>
<td>MoH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>NA</td>
<td>Not applicable</td>
</tr>
<tr>
<td>NGO</td>
<td>Non governmental organisation</td>
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<tr>
<td>NMCP</td>
<td>National Malaria Control Programme</td>
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<tr>
<td>PRISMA</td>
<td>Preferred Reporting Items for Systematic reviews and Meta-Analyses</td>
</tr>
<tr>
<td>PSI</td>
<td>Population Services International</td>
</tr>
<tr>
<td>PW</td>
<td>Pregnant women</td>
</tr>
<tr>
<td>RDT</td>
<td>Rapid diagnostic test</td>
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<tr>
<td>RBM</td>
<td>Roll Back Malaria</td>
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<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
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<tr>
<td>SM</td>
<td>Social marketing</td>
</tr>
<tr>
<td>SP</td>
<td>Sulphadoxine Pyrimethamine</td>
</tr>
<tr>
<td>TNVS</td>
<td>Tanzania National Voucher Scheme</td>
</tr>
<tr>
<td>TNY</td>
<td>Treated net year</td>
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<td>WHO</td>
<td>World Health Organization</td>
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</table>

#### Glossary

**Scaling up**
We define scaling up as ‘increase in coverage of health interventions that have been tested in pilot and experimental projects in order to benefit more people and support policy and programme development at a large or national scale’(84). This definition focuses on the increase in coverage beyond the initial pilot population, and expansion in geographical area, rather than simply an increase in inputs such as finances, health system or human resources. The emphasis is on scale up as a process as well as an objective in itself.

**At scale**
In this review “at scale” refers to delivery of an intervention in at least one district (first administrative level).

**Universal coverage**
We use the definitions of RBM and WHO, of 80% of at risk population having access to malaria control interventions (31).

**Social marketing**
We use the definition of Andreason (1995) “...the application of marketing technologies developed in the commercial sector to the solution of social problems where the bottom line is behaviour change” (30).
APPENDIX

Search strategy
We searched ten bibliographic databases in May 2010 (table 9):

- MEDLINE (Database including all aspects of clinical medicine, biomedicine, nursing, dentistry, allied health, health policy, genetics including more journals from North America) (Search from 2000 to May 2010, limit humans).
- EMBASE (Database including all aspects of clinical medicine, biomedicine, nursing, dentistry, allied health, health policy, genetics including more journals from Europe) (Search from 2000 to May 2010, limit humans).
- CAB Abstracts (Database providing information on the applied life sciences) (Search from 2000 to May 2010).
- Global Health (Database covering all aspects of international Public Health including information from conference proceedings, books and grey literature) (Search from 2000 to May 2010).
- ELDIS (Database including freely available full text documents from a variety of sources (i.e. resource guides; dossiers; country profiles) in development policy, practice and research (Search May 2010).
- Africa Wide (Database including all aspects of African life, culture, development and health) (Search from 2000 to May 2010).
- WHO Global Health Library
  - AIM (African Index Medicus) (Database covering Medical topics from journals published in the WHO African region) (Search May 2010).
  - IMEMR (Index Medicus of the Eastern Mediterranean Region) (Database covering Medical topics from journals published in the WHO Eastern Mediterranean region) (Search May 2010).
  - LILACS (Database covering Health Sciences literature from and relevant to Latin America and the Caribbean) (Search May 2010).
  - WPRIM (Western Pacific Region Index Medicus) (Database covering Medicine and health articles published in the WHO Western Pacific region) (Search May 2010).

Table 9: Search results by source

<table>
<thead>
<tr>
<th>Databases</th>
<th>Search terms</th>
<th>Results</th>
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<tbody>
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<td>MEDLINE</td>
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<td>EMBASE</td>
<td>Figure 10</td>
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<td>CAB Abstracts</td>
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<td>Global Health</td>
<td>Figure 11</td>
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<td>Africa Wide</td>
<td>Figure 12</td>
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<tr>
<td>ELDIS</td>
<td>Browsed all titles under ‘Malaria’ and ‘health systems/priority diseases/malaria’ index headings</td>
<td>23</td>
</tr>
<tr>
<td>WHO Global Health Library</td>
<td>Browsed all titles under ‘Malaria’ index heading</td>
<td>66</td>
</tr>
<tr>
<td>Other</td>
<td>Websites and email alerts</td>
<td>29</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1324</strong></td>
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</table>
Figure 9: Ovid Medline search

1. (malaria* or severe malaria or plasmodium or plasmodium falciparum or plasmodium vivax).ot, tw, ab, fs, kw, ti, hw, nm.
2. Malaria/ or exp Malaria, Falciparum/ or Malaria, Cerebral/ or Malaria, Vivax/
3. Plasmodium ovale/ or Plasmodium falciparum/ or Plasmodium/ or Plasmodium malariae/ or Plasmodium vivax/
4. exp Anopheles/
5. 1 or 2 or 3 or 4
6. Mosquito Control/
7. Insect Vectors/
8. "Bedding and Linens"/
9. Mosquito Nets/
10. Insecticide-Treated Bednets/
11. exp Insecticides/
12. exp Pyrethrins/
13. DDT/
14. Housing/
15. Larva/
16. exp Anopheles/
17. exp Chemoprevention/
18. Sulfadoxine/
19. Pyrimethamine/
20. pregnancy complications, infectious/ or pregnancy complications, parasitic/
21. Infant/
22. exp Anti-malarials/
23. Diagnosis/
24. exp Microscopy/
25. exp Laboratoires/
26. Diagnostic Tests, Routine/
27. Point-of-Care Systems/
28. exp Therapeutics/
29. exp Drug Therapy/
30. Artemisinins/
31. Amodiaquine/
32. Mefloquine/
33. exp Chloroquine/
34. Primaquine/
35. Insect Repellents/
36. Community Health Aides/
37. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38. (LLIN* or long-last* net or (long-lasting adj 5 net)).ot, tw, ab, fs, kw, ti, hw, nm.
39. (ITN* or insecticide-treat* net or insecticidal-treat* net or insecticide-net or insecticidal-net or bed-net or bednet or treated-net or mosquito-net).ot, tw, ab, fs, kw, ti, hw, nm.
40. (IRS or indoor-residual spray* or indoor-spray*).ot, tw, ab, fs, kw, ti, hw, nm.
41. (larvicid* or larval control or larvi* fish or environment* management or environment* control* or drain* or house-screen* or (mosquito-proof* adj 5 house) or repellent* or insecticide-treat* veil or insecticide-treat* hammock or insecticide-treat* blanket or insecticide-treat* cloth*).ot, tw, ab, fs, kw, ti, hw, nm.
42. (IPT or IPTp or IPTC or intermittent preventive treatment*).ot, tw, ab, fs, kw, ti, hw, nm.
43. (diagnosis or RDT* or rapid diagnos* test* or rapid test* or microscop* or laborator*).ot, tw, ab, fs, kw, ti, hw, nm.
44. (treatment or antimalaria* or artemisinin-combination treat* or artemisinin-combination therap* or artemether lumefantrine or artesunate or amodiaquine or mefloquine orchloroquine or primaquine).ot, tw, ab, fs, kw, ti, hw, nm.
45. (malaria control or malaria intervention* or vector control* or vector management).ot, tw, ab, fs, kw, ti, hw, nm.
46. (community health worker* or village health worker* or (home manag* adj 5 malaria)).ot, tw, ab, fs, kw, ti, hw, nm.
47. 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48. 37 or 47
49. (scale-up or scaling-up or at-scale or go* to-scale or large-scale or roll-out or universal coverage).ot, tw, ab, fs, kw, ti, hw, nm.
50. 5 and 48 and 49
51. limit 50 to (humans and yr="2000 -Current")

Text word search fields: ot = original title, tw= title word, ab=abstract, fs=floating sub heading, kw=keyword, ti=title, hw=heading word, nm= name of substance word, * = Truncation, exp = explode subject heading term
Figure 10: Embase search strategy

1. (scale-up or scaling-up or at-scale or go* to-scale or large-scale or roll-out or universal coverage).ot,tw,ab,fs,kw,ti,hw,nm.
2. (malaria* or severe malaria or plasmodium or plasmodium falciparum or plasmodium vivax).ot,tw,ab,fs,kw,ti,hw,nm.
3. malaria/ or brain malaria/ or plasmodium/ or plasmodium falciparum/ or plasmodium malariae/ or plasmodium ovale/ or plasmodium vivax/
4. 2 or 3
5. Malaria control/ or Vector control/ or Bed net/ or Mosquito anopheles/ or exp Pyrethroid/ or exp Insect repellent/ or Larvicidal agent/ or Larva/ or Environmental management/ or exp anti-malarial agent/ or Sulfadoxine/ or Pyrimethamine/ or Diagnosis/ or Diagnostic test/ or Laboratory test/ or exp Microscopy/ or exp Laboratory/ or Health auxiliary.sh.
6. (LLIN* or long-last* net or (long-lasting adj5 net)).ot,tw,ab,fs,kw,ti,hw,nm.
7. (ITN* or insecticide-treat* net or insecticidal-treat* net or insecticide-net or insecticidal-net or bed-net or bednet or treated-net or mosquito-net).ot,tw,ab,fs,kw,ti,hw,nm.
8. (IRS or indoor-residual spray* or indoor-spray*).ot,tw,ab,fs,kw,ti,hw,nm.
9. larvicid* or larval control or larvi* fish or environment* management or environment* control* or drain* or house-screen* or (mosquito-proof* adj5 house) or repellent* or insecticide-treat* veil or insecticide-treat* hammock or insecticide-treat* blanket or insecticide-treat* cloth*).ot,tw,ab,fs,kw,ti,hw,nm.
10. (IPT or IPTp or IPTi or IPTc or intermittent preventive treatment*).ot,tw,ab,fs,kw,ti,hw,nm.
11. (diagnosis or RDT* or rapid diagnosis* test* or rapid test* or microscop* or laborator*).ot,tw,ab,fs,kw,ti,hw,nm.
12. (treatment or antimalaria* or artemisinin-combination treat* or artemisinin-combination therap* or artether lumefantrine or artesunate or amodiaquine or mefloquine or chloroquine or primaquine).ot,tw,ab,fs,kw,ti,hw,nm.
13. (malaria control or malaria intervention* or vector control* or vector management).ot,tw,ab,fs,kw,ti,hw,nm.
14. (community health worker* or village health worker* or (home manag* adj5 malaria)).ot,tw,ab,fs,kw,ti,hw,nm.
15. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. 1 and 4 and 15

Text word search fields: ot = original title, tw= title word, ab=abstract, fs=floating sub heading, kw=keyword, ti=title, hw=heading word, nm= name of substance word; * = Truncation; exp = explode subject heading term

Figure 11: Search strategy for CAB Abstracts and Global Health databases

1. (scale-up or scaling-up or at-scale or go* to-scale or large-scale or roll-out or universal coverage).ot,tw,ab,fs,kw,ti,hw,nm.
2. (malaria* or severe malaria or plasmodium or plasmodium falciparum or plasmodium vivax).ot,tw,ab,fs,kw,ti,hw,nm.
3. malaria/ or cerebral malaria/ or plasmodium/ or plasmodium falciparum/ or plasmodium malariae/ or plasmodium ovale/ or plasmodium vivax/
4. 2 or 3
5. (LLIN* or long-last* net or (long-lasting adj5 net)).ot,tw,ab,fs,kw,ti,hw,nm.
6. (ITN* or insecticide-treat* net or insecticidal-treat* net or insecticide-net or insecticidal-net or bed-net or bednet or treated-net or mosquito-net).ot,tw,ab,fs,kw,ti,hw,nm.
7. (IRS or indoor-residual spray* or indoor-spray*).ot,tw,ab,fs,kw,ti,hw,nm.
8. (larvicid* or larval control or larvi* fish or environment* management or environment* control* or drain* or house-screen* or (mosquito-proof* adj5 house) or repellent* or insecticide-treat* veil or insecticide-treat* hammock or insecticide-treat* blanket or insecticide-treat* cloth*).ot,tw,ab,fs,kw,ti,hw,nm.
9. (IPT or IPTp or IPTi or IPTc or intermittent preventive treatment*).ot,tw,ab,fs,kw,ti,hw,nm.
10. (diagnosis or RDT* or rapid diagnosis* test* or rapid test* or microscop* or laborator*).ot,tw,ab,fs,kw,ti,hw,nm.
11. (treatment or antimalaria* or artemisinin-combination treat* or artemisinin-combination therap* or artether lumefantrine or artesunate or amodiaquine or mefloquine or chloroquine or primaquine).ot,tw,ab,fs,kw,ti,hw,nm.
12. (malaria control or malaria intervention* or vector control* or vector management).ot,tw,ab,fs,kw,ti,hw,nm.
13. (community health worker* or village health worker* or (home manag* adj5 malaria)).ot,tw,ab,fs,kw,ti,hw,nm.
14. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15. Vector control/ or Bed nets/ or Mosquito nets/ or exp Insecticides/ or Impregnated fabrics/ or Anopheles/ or exp Pyrethroids/ or DDT/ or exp Insect repellents/ or "ovicides and larvicides"/ or Insectivorous fishes/ or exp Drainage/ or Environmental management/ or Sulfadoxine/ or Pyrimethamine/ or exp Anti-malarials/ or Chemoprophylaxis/ or Multiple drug therapy/ or Laboratory diagnosis/ or Amodiaquine/ or Chloroquine/ or Primaquine/ or Artemesinin/ or Medical auxiliaries/
16. 14 or 15
17. 1 and 4 and 15

Text word search fields: ot = original title, tw= title word, ab=abstract, fs=floating sub heading, kw=keyword, ti=title, hw=heading word, nm= name of substance word; * = Truncation; exp = explode subject heading term
Figure 12: Africa Wide search (EBSCOhost interface)

1. Malaria* or Plasmodium falciparum or Plasmodium vivax
2. ITN* or Insecticide-treat* net or Insecticidal-treat* net or Insecticide-net or Insecticidal-net or Bed-net or Bednet or Treated-net or Mosquito-net or LLIN* or Long-last* net
3. Indoor-residual spray* or Indoor-spray*
4. Repellent* or Insecticide-treated veil* or Insecticide-treated hammock* or Insecticide-treated or blanket* or Insecticide-treated clothing
5. Larvicid* or Larval control or Larvi* fish or Environmental management or House-screening
6. Intermittent preventive treatment or IPTp or IPTi or IPTc
7. RDT* or Rapid diagnostic test or Microscopy
8. Antimalaria* or Artemisinin-combination or Artemether lumefantrine or Artesunate or Amodiaquine or Mefloquine or Chloroquine or Primaquine
9. Community health worker* or Village health worker* or Home management malaria
10. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. Scale-up or Scaling-up or Roll*-out or Universal coverage
12. 1 and 10 and 11

Text word search fields: ot = original title, tw= title word, ab=abstract, fs=floating sub heading, kw=keyword, ti=title, hw=heading word, nm= name of substance word. * = Truncation, exp = explode subject heading term

Screening of titles and abstracts
Initially 100 records were randomly selected to assess inter-reviewer agreement and refine selection criteria. Inter-reviewer agreement was assessed using Cohen’s Kappa score (85). Agreement on these randomly selected 100 titles and abstracts was moderate (Kappa score 0.52, and 76% agreement). Following this piloting exercise, selection criteria were discussed and clarified, and double screening of the remaining 483 titles and abstracts was done (table 10 in Appendix). Agreement was excellent for these papers (Kappa score 0.83, and 69% agreement).

Table 10: Exclusion reasons applied to title and abstract screening, before and following piloting of 100 titles and abstracts

<table>
<thead>
<tr>
<th>Criteria established prior to pilot of 100 titles/ abstracts</th>
<th>Criteria added following pilot and inter-reviewer discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irrelevant to scale up</td>
<td>Other disease</td>
</tr>
<tr>
<td>Population</td>
<td>Non-human malaria</td>
</tr>
<tr>
<td>Non endemic countries</td>
<td>Description of an intervention, but no practical insight into how to scale-up</td>
</tr>
<tr>
<td>Travellers</td>
<td></td>
</tr>
<tr>
<td>Displaced populations/ conflict/ complex emergencies</td>
<td></td>
</tr>
<tr>
<td>Military</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>Not malaria intervention</td>
</tr>
<tr>
<td>Insecticide coils/ heated dispensers</td>
<td></td>
</tr>
<tr>
<td>Insecticide treated wall matting</td>
<td></td>
</tr>
<tr>
<td>Vaccines</td>
<td>Herbal remedy intervention</td>
</tr>
<tr>
<td>Civil engineering</td>
<td></td>
</tr>
<tr>
<td>Non-English language</td>
<td>Too small scale</td>
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<tr>
<td>Paper discussing Polymerase chain reaction methods</td>
<td>Too historic</td>
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<tr>
<td>Supply chain</td>
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<tr>
<td>News Item</td>
<td></td>
</tr>
<tr>
<td>More appropriate original data paper already included</td>
<td></td>
</tr>
<tr>
<td>Review</td>
<td></td>
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</table>
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