Costs and Consequences of Malaria Control in sub-Saharan Africa: the economics of vector control and parasitological diagnosis

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Prof. Dr. Eberhard Parlow
Dekan

For Kate Macintyre, who graciously did not write this thesis, and who is probably happy about that.

Table of Contents

List of Figures

List of Equations

List of Tables

List of Acronyms

AC	Average Cost
ACT	Artemisinin Combination Therapy
AED	Academy for Educational Development
ALU	Artemether-Lumefantrine
ANC	Antenatal Care
BS	Blood Slide
CBO	Community-Based Organization
CDC	US Centers for Disease Control and Prevention
CE	Cost-Effectiveness
CHA	Community Health Agent
CHF	Swiss Franc
CHMT	Council Health Management Team
CI	Confidence Interval
CIF	Cost, Insurance and Freight Price
CMH	Commission on Macroeconomics and Health
CYP	Child Year of Protection
DALY	Disability-Adjusted Life Year
DCPP	Disease Control Priorities Project
DDT	Dichloro-Diphenyl-Triochloroethane
DHLY	Discounted Healthy Life Year
DHMT	District Health Management Team
DHS	Demographic and Health Surveys
DMO	District Medical Officer
EIR	Entomological Inoculation Rate
ESMG	Eritrea Social Marketing Group
FIFO	First In First Out Accounting
IMF	International Monetary Fund
IRK	Insecticide Re-treatment Kit
IVM	Integrated Vector Management
GDP	Gross Domestic Product
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GNI	Gross National Income
HAMSET	World Bank HIV/AIDS, Malaria, and TB Control Project
HF	Health Facility
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
HRP2	*Plasmodium* Histidine Rich Protein 2
IRS	Indoor Residual Spraying
ITN	Insecticide-Treated (Bed) Net
KZN	KwaZulu-Natal
LLIN	Long-Lasting Insecticidal Nets
LIFO	Last In First Out Accounting
LSDI	Lubombo Spatial Development Initiative
MARA/ARMA	Mapping Malaria Risk in Africa/*Atlas du Risque de la Malaria en Afrique*
MC	Marginal Cost
MCH	Maternal and Child Health
MDA	Mass Drug Administration
MEDA	Mennonite Economic Development Associates
MICS	Multi-Indicator Cluster Survey
MOH	Ministry of Health
MSH	Management Sciences for Health
NATNETS	Tanzanian National ITN Program
NGO	Non-Governmental Organization
NMCP	National Malaria Control Program
NSEO	National Statistics and Evaluation Office [Eritrea]

OPD	Out-Patient Department
PCR	Polymerase Chain Reaction
PMI	President's Malaria Initiative [United States]
PNLP	*Programme National de Lutte contre le Paludisme*
PPP	Purchasing Power Parity
PSI	Population Services International
PYP	Person Year of Protection
QALY	Quality Adjusted Life Year
RBM	Roll Back Malaria
RCH	Reproductive and Child Health
RDT	Rapid Diagnostic Test for Malaria
RHS	Residual House Spraying
SDC	Swiss Agency for Development and Cooperation
SE	Standard Error
SES	Socio-Economic Status
SI$	Solomon Islands Dollar
SSA	sub-Saharan Africa
STI	Swiss Tropical Institute
TNVS	Tanzanian National Voucher Scheme
TNY	Treated Net Years
TSH	Tanzanian Shilling
UNICEF	The United Nations Children's Fund
US	United States of America
US BEA	United States Bureau of Economic Analysis
USD	United States Dollar
USSR	Union of Soviet Socialist Republics
VAT	Value Added Tax
WHO	World Health Organization
WHO-CHOICE	World Health Organization – Choosing Interventions which are Cost-Effective
XOF	West African Franc CFA
ZMC	Zoba Malaria Coordinator

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Summary

Introduction

Economic evaluations of health intervention programs can provide decision makers with quantitative information on how to allocate the scare resources available for health investment. Malaria is the single most important parasitic infection in humans and accounts for a large proportion of the disease burden of sub-Saharan Africa. Currently many strategies are being employed for malaria prevention, and there is a need for evaluation of the various strategies being used. Additionally, routine malaria diagnosis in Africa often leads to mis-use of anti-malarial drugs and there is an urgent need to assess the cost implications of strategies for diagnostic improvement.

Costs and cost-effectiveness of vector control

Economic evaluations of ITNs (insecticide treated bednets) and IRS (indoor residual spraying) have been conducted in several settings but few of these evaluations relate to the scope and scale of interventions currently underway. Furthermore, few of these evaluations used comparable methodologies. We developed a standardized methodology for the economic evaluation of malaria vector control programs by reviewing and refining existing guidelines. Utilizing this methodology we collected new data from several settings (Eritrea, Malawi, Senegal, and Tanzania) and reanalyzed existing datasets from others (Togo, South Africa, and Mozambique). These sites were chosen to represent geographic variability as well as a diversity of implementation models for ITN delivery.

The goals of this thesis were threefold: (1) to evaluate the relative cost and cost-effectiveness of ITNs and IRS for vector control in sub-Saharan Africa, (2) to evaluate the relative cost and cost-effectiveness of different implementation strategies for ITN delivery, and (3) to estimate the costs of introducing RDTs and their effect on the cost of case management of febrile patients. The ITN programs which we evaluated were chosen to represent five different delivery strategies: (1) free delivery through integrated vaccination campaigns (Togo), (2) free delivery through routine services and community mechanisms (Eritrea), (3) highly subsidized delivery through routine services (Malawi), (4) subsidized delivery through the commercial sector utilizing vouchers aimed at pregnant women and infants (Tanzania), and (5) pure commercial sector subsidization (Senegal).

ITN/IRS Results

The results of the studies generally showed that both interventions remained attractive uses of health resources in a low income country context under almost any scenario. More

specifically, for conventional ITNs (targeted to children) the cost per treated net year of protection (TNY) and child death averted ranged from USD 1.21 to USD 6.05 and USD 438 to USD 2,199, respectively. Long-Lasting Insecticidal Net (LLIN) scenarios (also targeted to children) resulted generally in improved cost-effectiveness (USD 1.38 to USD 1.90 per TNY and USD 502 to USD 692 per death averted). IRS was more expensive in base scenarios, with a total cost per person year of protection of USD 3.27 in KwaZulu-Natal and USD 3.90 in Mozambique, this resulted in costs per death averted of USD 3,933 and USD 4,357.

ITN programs appeared to be a more efficient strategy for the prevention of child mortality in highly endemic sub-Saharan African settings. However, this was dependant on both effective use of nets and a preferential usage of nets by children. Generally, the cost effectiveness of either strategy was heavily dependant on the cost of the commodities and their effective lifetime (nets for ITN programs and insecticide for IRS programs). ITN programs benefited clearly from a shift to LLINs.

Under most scenarios free net delivery utilizing integrated campaigns appeared the most attractive method for short term "catch-up" in coverage levels for ITNs. The other strategies that were reviewed appeared to be better suited to the long term maintenance of coverage ("keep-up").

The data presented here provide a significant amount of new information collected and analyzed in a comparable manner to aid in decision making regarding vector control for malaria in sub-Saharan Africa.

Costs of introducing rapid diagnostic tests in Tanzania

We also conducted a study on the costs of implementation of Rapid Diagnostic Tests (RDTs) for malaria in Dar Es Salaam, Tanzania. Data were collected both at the level of individual patients and for entire health facilities.

RDTs significantly lowered patient expenditure on drugs (by USD 0.37; p=0.001) and provider drug costs (by USD 0.44; p=0.014), but did not significantly reduce patients' overall expenditures (USD 1.08 vs. USD 1.36) and have increased total provider costs (USD 3.62 vs. USD 2.31). Clinician's compliance with tests was higher in clinics with RDTs than in those with routine microscopy.

Use of the economic data in this thesis will hopefully help to provide a better evidence base for program managers to make more rational and efficient decisions about malaria control options and case management of febrile patients.

Zusamennfassung

Einleitung

Wirtschaftliche Evaluierungen von Interventionsprogrammen im Gesundheitswesen bieten Entscheidungeträgern quantitativ gestützte Informationen darüber, wie knappe Mittel sinnvoll für Investitionen im Gesundheitswesen eingesetzt werden können. Malaria ist die bedeutendste parasitäre Erkrankung des Menschen, und sie macht einen grossen Teil der Krankheitslast im subsaharischen Afrika aus. Derzeit werden viele Strategien zur Malariaprävention verfolgt. Diese müssen dringend evaluiert werden, um eine bestmögliche Ausschöpfung vorhandener Mittel zu erreichen. Ausserdem kommt es durch die routinemässige Diagnose von Malaria in Afrika häufig zu einem Missbrauch von Malariamedikamenten. Strategien zur Verbesserung der Diagnostik und die damit verbundenen Kosten müssen dringend beurteilt werden.

Kosten und Kostenwirksamkeit der Vektorkontrolle

Wirtschaftliche Evaluierungen des Einsatzes von ITNs (mit Insektizid behandeleten Mückennetzen) und IRS (das Besprühen von Hausinnenwänden mit Insektizid) wurden bereits durchgeführt. Nur wenige dieser Evaluierungen werden jedoch der Bandbreite und der Grössenordnung derzeit laufender Interventionen gerecht. Ausserdem stützen sich nur wenige dieser Evaluierungen auf eine vergleichbare Methodik. Wir haben eine standardisierte Methodik für die wirtschaftliche Evaluierung von Vektorkontrollprogrammen für Malaria entwickelt, indem wir bestehende Richtlinien weiterentwickelt haben. Diese Methodik wurde dann zum einen verwendet, um neue Daten an verschiedenen Standorten (Eritrea, Malawi, Senegal und Tansania) zu erheben, und andererseits um bereits vorliegende Daten aus dem Togo, Südafrika und Mosambik erneut zu analysieren. Die Standorte wurden so ausgewählt, dass die geographische Vielfalt der verschiedenen Modelle zur ITN- Abgabe abgedeckt wurde.

Die vorliegende Dissertation hat drei Ziele: (1) die Kosten und die Kostenwirksamkeit von ITNs und IRS zur Vektorkontrolle im Afrika zu vergleichen, (2) die Kosten und Kostenwirksamkeit von verschiedenen Implentierungsstrategien der Abgabe von ITNs zu evaluieren, und (3) die Kosten von Malariadiagnostik darzustellen. Die evaluierten ITN Programme wurden so ausgewählt, dass fünf verschiedene Strategien der ITN-Abgabe berücksichtigt wurden: (1) Gratisabgabe im Rahmen integrierter Impfkampagnien (Togo), (2) Gratisabgabe über Gesundheitsdienste und durch die Gemeinden gesteuert (Eritrea), (3) stark subventionierte Abgabe über Gesundheitsdienste (Malawi), (4) stark subventionierte Abgabe über den kommerziellen Sektor zussamen mit einem Gutscheinsystem für

schwangere Frauen und Kleinkinder (Tansania), sowie (5) eine ausschliessliche Subventionierung des kommerziellen Sektors (Senegal).

ITN/IRS Resultate

Die Studien ergaben im Allgemeinen, dass beide Interventionen unter fast allen Szenarios attraktive Investitionen im Gesundheitswesen in einkommenschwachen Ländern sind. Für herkömmliche ITNs, die an Kinder gingen, waren die Kosten pro behandeltes Netz und Jahr (TNY) zwischen 1.21 und 6.05 US Dollar und die Kosten für einen verhüteteten Tod eines Kindes von 428 bis 2199 US Dollar. Szenarios unter Verwendung von dauerhaft imprägnierten Mückennetzen (LLIN), verbesserten im Allgemeinen die Kostenwirksamkeit (1.38 bis 1.90 US Dollar pro TNY, und 502 bis 692 US-Dollar für einen verhüteten Todesfall). IRS erwies sich in Basisszenarien als teurer. Die Gesamtkosten pro Person und Jahr der Schutzwirkung beliefen sich auf 3.27 US Dollar in KwaZulu-Natal und auf 3.90 US Dollar in Mosambik und ergaben Kosten pro verhüteten Todesfall in der Höhe von 2,933 und 4357 US Dollar. ITN Programme stellten sich als wirksamere Strategie heraus, um der Kindersterblichkeit in hochendemischen Gebieten im subsaharischen Afrika vorzubeugen. Dies hing jedoch einerseits davon ab, ob die Netze tatsächlich benutzt wurden, und andererseits ob sie bevorzugt Kindern zu Gute kamen. Allgemein hing die Kostenwirksamkeit der jeweiligen Strategie stark von den Materialkosten ab und von der Wirksamkeitsdauer der Netze bei ITN Programmen und des Insektizids bei IRS Programmen. ITN Programme würden von einer Umstellung auf LLINs generell profitieren. Den meisten Szenarien gemäss erwiesen sich die integrierten Kampagnien, bei denen Netze gratis abgegeben werden als attraktivster Weg, einen höheren Deckungsgrad von ITNs innerhalb kurzer Zeit zu erreichen („Catch-up“). Die anderen Strategien, die untersucht wurden, schienen besser geeignet zu sein für ein „Keep-up“ des Deckungsgrades über längere Zeit. Mit den hier vorgestellten Daten, die auf vergleichende Weise erhoben und ausgewertet wurden, sind nun neue Informationen in beträchtlichem Umfang verfügbar, um Entscheidungen in der Malaria-Vektorkontrolle im subsaharischen Afrika zu treffen.

Kosten für die Einführung von Diagnostik-Schnelltests in Tansania

Wir führten weitherhin eine Studie durch, in der die Kosten der Einführung von Diagnostik-Schnelltests (RDTs) für Malaria in Dar Es Salaam, Tansania, untersucht wurden. Hierzu wurden mittels Umfragen Daten auf der Ebene der einzelnen Patienten und auf der Ebene von Gesundheitszentren erhoben. Es zeigte sich, dass RDTs die Ausgaben der Patienten für Medikamente signifikant verringerten (0.37 US Dollar, p=0.001), und ebenso die Ausgaben des Gesundheitssystems für Medikamente (0.44 US Dollar, p=0.014). Die für die Patienten entstehenden Gesamtausgaben wurden jedoch nicht deutlich gesenkt (USD 1.08 vs. USD

1.36) und die für die Verkäufer entstehenden Gesamtausgaben dürften sogar angestiegen sein (USD 3.62 vs. USD 2.31). Die Compliance des klinischen Personals mit Tests war in Kliniken, in denen RDTs eingesetzt wurden höher, als dort, wo Mikroskopie routinemässig eingesetzt wird.

Die Verwendung wirtschaftlicher Daten in der vorliegenden Dissertation kann als Grundlage dienen, auf der Manager von Malariakontrollprogrammen begründete und wirksame Entscheidungen in der Malariakontroll- und Behandlungsstratgie treffen können.

1. Introduction

1.1 Economics and Health

Economics has been defined as the study of "human behavior as a relationship between ends and scarce means which have alternative uses (Robbins, 1935)." Its techniques have been used in both their micro and macro formations to examine both the individual choices which help to understand the prices and quantities of goods consumed and produced in a market and the aggregate results of this activity in the formation and behavior of national or regional economies. Only more recently have the techniques developed in these fields been implemented or adapted to the specific features and nuances of human health and health care markets.

Much work has been carried out examining the relationships between macroeconomics and health. In total it shows that health and economic development are intertwined with causal relationships between the two often flowing in both directions (Rivera & Currais, 1999; CMH, 2001). Low socio-economic status populations are likely to bear the highest burden of disease, as well as to be the least likely to access medical care and preventive interventions. Consequently, their share of the disease burden is disproportionate (Marmot, *et al.*1987; Wagstaff, 2000; Schellenberg *et al.*, 2003; Victora *et al.*, 2003; Barat *et al.*, 2004). Furthermore, individuals and households with low socio-economic status are also most likely to have their economic prospects damaged by the costs of the health care or losses to productivity associated with disease states (Ettling *et al.*, 1994; Russell, 2004). It is clear that economic development and growth will be required for poor-countries to financially sustain improvements in health, but also that economic growth alone is not enough to ensure good health outcomes. The poor in middle and high income countries still have substantially worse health outcomes than those higher on the economic ladder within their own societies (CMH, 2001; Lynch *et al.*, 2000; Yusuf *et al.*, 2007). At the same time, it is clear that with outside support and resources substantial gains in health outcomes can be made for the poorest of the poor with interventions which can be delivered even in the absence of an ideal health system (Bryce *et al.*, 2003). Several diseases, including HIV/AIDS and malaria, have been shown to clearly slow the overall economic growth of countries with high burdens (Cuddington, 1993; Cuddington & Hancock, 1994; Gallup & Sachs, 2001; Sachs & Malaney, 2002; Jefferis *et al.*, 2008). The relationship has also been shown to run

from economic growth or stagnation to health impact (Gurfinkel *et al.*, 1996; Pritchett & Summers, 1996; Yusuf *et al.*, 2007; Preston, 2007).

While macro-economic relationships between health and economic growth are important. Investments in health can provide benefits not only in the realm of saved lives or averted episodes of disease, but also in terms of relieving drags on economic growth in the aggregate or perhaps stimulating economic growth themselves. Micro-economics also has tools which are highly relevant for decision makers in the health care sector both in developed and developing countries.

1.2 Disease Control Priority Setting and Welfare Analysis

Health policy makers are forced to allocate scarce resources to only a subset of the possible investments which might provide health benefits. In order to rationalize these choices and to improve the economic efficiency of the mix of health investments made, several types of economic analysis were developed or adapted to the health care sector.

Classically, an economic analysis might use cost-benefit analysis to evaluate an investment or policy decision. In such an analysis the potential costs of an approach are calculated and the potential monetarized gains which could be generated from this investment or policy change are summed. An analysis which indicated that there were net benefits from making the investment would indicate that the investment should be made. In a more complicated decision environment of several investment choices, the choice with the highest net benefits would be favored. There are substantial methodological problems with such analysis, including estimating levels of uncertainty in cost and benefit measurements or estimates, and insuring that the appropriate costs as well as benefits are included. When applied to the health arena these problems become even more substantial.

The foremost issue has to do with the fact that in many cases the benefits are not financial in nature but rather lives saved, or healthy lives extended. Unsurprisingly, the estimation of a monetary value for a year of human life raises issues both methodologically and ethically. For this reason welfare analysis in the health context typically uses specialized adaptations. Though estimates and benchmarks are

available for desirable levels of spending to gain a healthy year of human life in different settings, other types of analysis are more common. Among these the main groups are cost minimization and cost effectiveness analysis. Cost minimization analysis seeks to estimate the least costly way to achieve a fixed health outcome. For example: given that 1,000 new HIV infections occur in our district each year, what is the least costly way to reduce the number of new infections by 500? Cost-effectiveness analysis on the other hand asks what the unit cost of achieving a given health outcome is with a specific methodology. For example: what is the cost of saving a life by preventing malaria through the use of insecticide treated bed-nets or by immunizing children against measles? The results would indicate that the intervention which has a lower unit cost per health outcome measure would be the more cost-effective intervention, and would thus be a more efficient investment when allocating scarce health care resources.

In order to make comparisons across different interventions, specific measurements of disease burden which incorporate and quantify both morbidity and mortality due to disease have been developed. Measures such as the disability adjusted life year (DALY) or the quality adjusted life year (QALY) allow better comparisons between interventions which target very different diseases (*e.g.* childhood acute respiratory infections and traffic accidents) in different populations (*e.g.* elderly mortality vs. neonatal mortality).

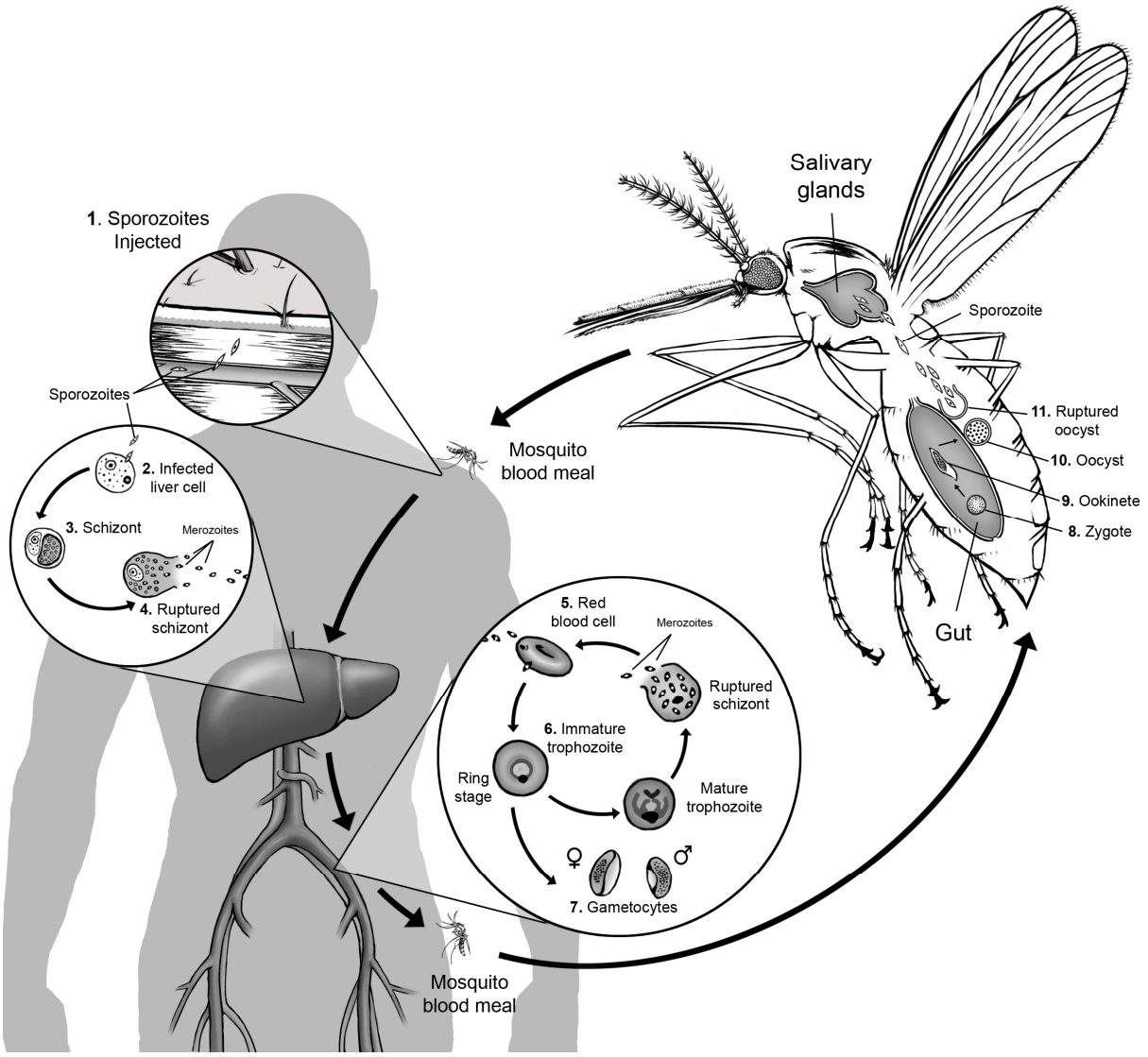
These techniques and measures offer powerful methods for evaluating health care investment decisions. This thesis examines the use of economic welfare analysis applied to the problem of prevention and treatment of malaria in sub-Saharan Africa.

1.3 Malaria

Malaria is a parasitic disease caused by one of four members of the genus *Plasmodium*. In addition, one species which has been typically held to be primate malaria (*P. knowlesi*) has recently been shown to be a source of zoonotic malaria (Gilles & Warrell, 1993; Singh *et al.*, 2004; Cox-Singh & Singh, 2008). Of the four human malaria species, (*P. malariae*, *P. ovale*, *P. vivax*, and *P. falciparum*) *P. falciparum* is both the most common in Africa and causes the most severe forms of disease. These protozoan parasites are transmitted exclusively by female *Anopheles*

mosquitoes. During the blood meal an infected mosquito injects sporozoites under the skin, which then pass to the bloodstream of its human host. These sporozoites travel through the bloodstream until they reach the liver where they infect liver cells, multiply and mature. The cells then rupture releasing merozoites back into the hosts' bloodstream. *P. vivax* and *P. ovale* also produce hypnozoites, dormant liver stages which can result in relapse of infection months or years later. The blood stage parasites go on to infect erythrocytes (human red blood cells) and continue to multiply and mature, eventually rupturing the erythrocytes and releasing more parasites (also called merozoites) to infect other cells. This part of the cycle is largely responsible for the clinical manifestations of human disease. Some blood stage parasites differentiate into male or female gametocytes, which can be ingested by a mosquito taking a blood meal on the host. When a mosquito ingests male and female gametocytes, the parasites undergo sexual reproduction in the mosquito mid-gut and differentiate into ookinetes, which then invade the mosquito's mid-gut wall and form oocysts. When these oocysts rupture, releasing sporozoites which subsequently migrate to the mosquito's salivary glands the mosquito is then competent to transmit the infection to further human hosts. The cycle of transmission and disease lasts for varying periods depending on the parasite species, as well as temperature conditions and the acquired immunity of the human host among other factors. Generally it requires from 10 to 18 days from the mosquito's ingestion of gametocytes to its ability to transfer the infection, and the human cycle typically requires at least seven days before clinical symptoms appear. Relapses may appear months or even years later, especially in the case of *P. vivax* or *P. ovale* which both produce dormant liver stages (Gilles & Warrell, 1993). Figure 1 illustrates the life cycle of *P. falciparum*.

Figure 1: Life cycle of *Plasmodium falciparum* malaria



1.4 Clinical Features of Malaria

Generally *P. falciparum* malaria is clinically classified in one of two categories, uncomplicated or severe, though there is a continuum of symptoms over this range. Uncomplicated disease is characterized by a myriad of symptoms, including but not limited to fever, malaise, fatigue and pain in the back and limbs, nausea and chills. Symptoms onset at least seven days after infection, though the incubation period can vary depending on both host and parasite factors. Disease can proceed very rapidly from uncomplicated to severe disease, especially among the non-immune. While severe disease may fall into an array of varied pathologies including cerebral malaria,

it is generally characterized by convulsions, malarial anemia, hyperpyrexia, hypoglycemia, renal failure, and other signs and symptoms. Cerebral malaria is a complication of malaria characterized by a loss of consciousness, generalized convulsions and persistent coma. It has a high case fatality rate, 10-15% if good hospital care is available, but much higher if treatment is unavailable or poor. Malaria anemia is also associated with a high potential for fatality in young children and in parts of Africa may be responsible for as many deaths in children as cerebral malaria. Severe and cerebral malaria also can leave lasting sequelae including mental and cognitive impairments (Gilles & Warrell, 1993).

In highly endemic areas in sub-Saharan Africa the vast majority of mortality occurs in children under five years of age. An individual who survives this high risk period is likely to have developed some level of clinical immunity and tolerance to the parasite. This dramatically reduces the probability of dying from a *P. falciparum* infection. While neonates and infants typically have reduced malaria specific mortality due to conferred maternal immunity, this quickly fades and between six months and three years of age children in highly endemic areas are at a high risk of mortality (Gilles & Warrell, 1993).

In highly endemic areas pregnant women also form a special high risk group; this is especially true of primagravidae. In areas with unstable or low transmission there is a high risk of maternal mortality, abortion or still birth as a result of malaria, while in higher transmission areas the complications of malaria in pregnancy are largely characterized by increased likelihood of low birth weight and the concomitant risks to child survival (Gilles & Warrell, 1993).

1.5 Mosquito Ecology and Malaria in Africa

Malaria is always transmitted by a mosquito from the *Anopheles* genus. However, despite there being several hundred Anopheline species recognized worldwide, only approximately 50 species are recognized as important vectors of malaria transmission in nature (Gilles & Warrell, 1993). Of these, the most important in sub-Saharan Africa are *An. gambiae* sensu lato and *An. funestus* (Gilles & Warrell, 1993).

Both the *gambiae* complex and the *funestus* species have slightly different behavior and ecological patters, but also have highly important similarities.

Both species are highly efficient vectors for malaria transmission and both tend to be anthropophilic and endophilic, and they preferentially feed between 10 pm and dawn on sleeping hosts. Both have similar geographic distributions, though typically choose different larval habitats and often are responsible for malaria transmission with different seasonal patterns (Gilles & Warrell, 1993).

1.6 Breaking the transmission cycle

Malaria transmission can be interrupted at various stages in both the mosquito and human cycles. Several interventions are available to do this, including insecticide treated bednets (ITNs), indoor residual spraying (IRS), mass drug administration (MDA), larviciding, integrated vector management (IVM) and the possible development of effective vaccines. Here we will focus only on the two most common prevention strategies, insecticide treated bed nets and indoor residual spraying.

1.7 Insecticide Treated Bednets (ITNs)

Insecticide treated bed nets are a modern adaptation of an age old technique for the prevention of biting by nuisance mosquitoes. In many areas of the world, including parts of sub-Saharan Africa, people have used netting over beds or sleeping areas to prevent nuisance mosquitoes from interfering with sleep, perhaps inadvertently or knowingly preventing malaria to some extent as well (Ross, 1910; Lindsay & Gibson, 1988). Though examples of their use in the USSR in the 1930s and by US and German militaries was available in the 1940's and 50s, it was not until the late 1980s and early 1990s that techniques were revived, developed and properly tested in many African settings. The trials indicated that the consistent use of polyester nets soaked in an emulsion of a synthetic pyrethroid insecticide could significantly reduce the incidence of clinical malaria as well as both malaria specific and all-cause mortality in under five children (Lindsay & Gibson, 1988; Lengeler, 2004). Concurrent and subsequent research indicated that this effect occurred for a combination of reasons. The primary being that malaria infected mosquitoes are prevented from biting human hosts using ITNs (direct protection), due simultaneously to the excito-repellency of the insecticide, the killing properties of the insecticide

impregnated into the net, and the physical barrier to the mosquito which an intact net presents (Curtis *et al.*, 1990). The second way in which ITNs prevent malaria infections happens is by massive mosquito mortality as the coverage and use of nets locally increases leading to reductions in parity of the local female *Anopheline* population and thereby to reductions in transmission of malaria even to those who are not directly protected. This effect has been termed variously the mass-, mass-killing- or community effect (Magesa *et al.*, 1991; Binka *et al.*, 1998; Howard *et al.*, 2000; Hawley *et al.*, 2003; Killeen *et al.*, 2007).

1.8 Indoor Residual Spraying (IRS)

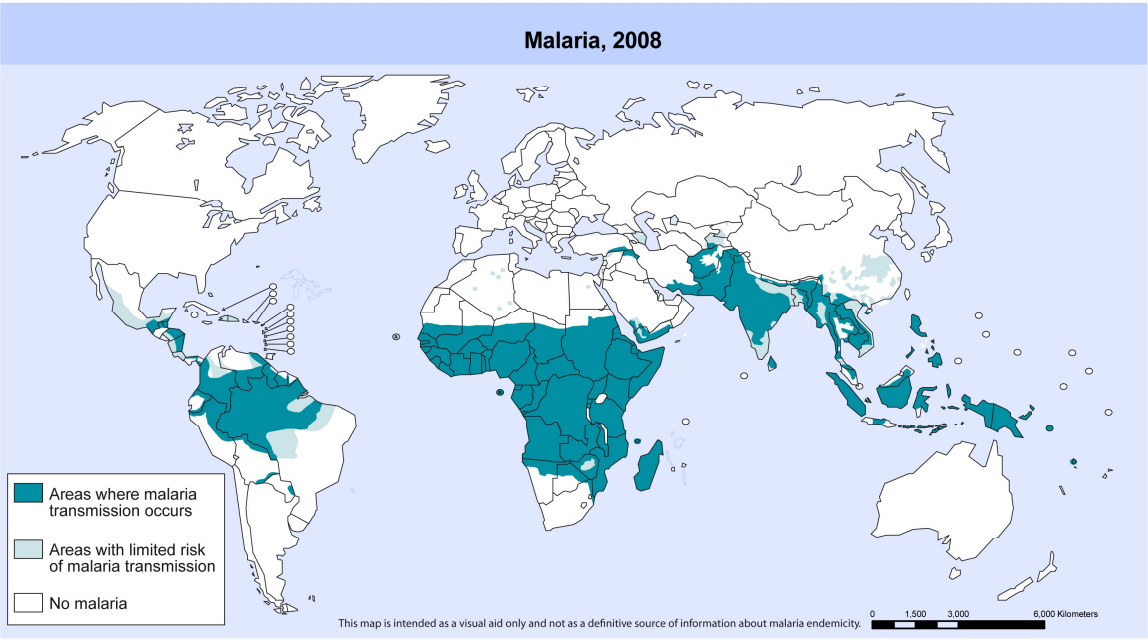
Indoor residual spraying involves coating the inside walls and ceilings of homes or other structures with an insecticide which clings to walls for an extended period. Because both *An. gambiae* and *An. funestus* tend to rest on vertical surfaces after taking a blood meal and tend to feed indoors (endophagy) they are thus exposed to the insecticide and killed after feeding. IRS breaks the malaria transmission cycle by preventing a mosquito from further transmitting its infection. This occurs by killing (hence reducing the longevity of) adult female *Anophelines* and thus reduces transmission intensity over time (Lengeler & Sharp, 2003). However, unlike in the case of ITNs, IRS does not typically directly protect individuals whose home has been sprayed from being bitten by an infected mosquito, except in the case where the insecticide used for spraying has a strong excito-repellent effect (Lengeler & Sharp, 2003).

IRS is a relatively old intervention, the first experiments with the technique in Africa date back to the 1930s. By the 1950s large scale operations were under way using DDT in a number of settings (De Meillon, 1936; Park Ross, 1936; Kouznetsov, 1977; Mabaso *et al.*, 2004). By the mid-1950s a global effort to eradicate malaria using IRS with DDT and mass drug administration was under way, though little of the programs efforts were focused in Africa (Kouznetsov, 1977). The ultimate failure of this program to eradicate malaria globally, despite many local successes, led to the subsequent neglect of malaria control (Scholten *et al.*, 1972). Subsequently IRS has continued to be used, albeit infrequently, in Africa until recent increases in funding for malaria control have led to large expansions (Lengeler *et al.*, 2003; Sadasivaiah *et al.*, 2007).

1.9 P. falciparum and the distribution of malaria globally and locally

Sub-Saharan Africa, by any measure bears the largest burden of malaria of any region on the globe (Hay *et al.*, 2004). While large numbers of people are at risk in both South East Asia and South Asia, those at risk are often from specific sub-groups, as with forest malaria in South East Asia. In many areas individuals are mainly exposed to *P. vivax* malaria, which carries a far lower mortality risk than does *falciparum* malaria, the dominant species in sub-Saharan Africa (SSA) (Gilles & Warrell, 1993; Mendis *et al.*, 2001). Best estimates are that around one million deaths occur due to malaria globally and that, of these, 80% occur in children in SSA (WHO 2008). While vast areas of Asia, the Indian sub-Continent, Latin America, and Central Asia appear in global risk maps for malaria, nowhere but in sub-Saharan Africa is the combination of *falciparum* malaria, highly competent vectors and ideal climactic conditions for malaria transmission so pervasive. Figure 2 shows the global distribution of malaria risk according to the WHO.

Figure 2: Worldwide risk of malaria transmission. (http://www.who.int/globalatlas)



Even within Africa there is a large heterogeneity of malaria transmission patterns, seasonality, specific dominant vector species and both at the country level and lower (Gilles & Warrell, 1993). Evidence also indicates that within cities heterogeneity of

transmission occurs on very small scales (Robert *et al.*, 2003; Keiser *et al.*, 2004). All of this indicates that while some vector control strategies may be appropriate in very large areas, significant consideration of the national, regional or local situation should be incorporated into the decision making process for malaria control. Some strategies may be inappropriate for certain climatic conditions, local living conditions or vector species.

1.10 Distribution strategies for Insecticide Treated Nets

Given that ITNs are now a proven technology African Heads of State and international organizations have made several declarations of the intent to provide protection for populations with ITNs and other suitable vector control measures. These include the Abuja declarations and Roll Back Malaria strategic goals among others (African Heads of State and Government, 2000; RBM Partnership, 2005). However, a diversity of implementation methods for the delivery of ITNs have been proposed or implemented and relatively little evidence has been generated on which to base decisions as to the most appropriate delivery methods. The main proposed and implemented strategic delivery options are: support and development of a commercial sector for the retail sale of ITNs -- pure social marketing (in which an organization develops and sells a branded, usually subsidized, product) -- delivery, either free or subsidized, through existing health care services (including especially ante-natal care clinics or other health facilities) -- community interventions (Community based organizations (CBOs)) -- free delivery through campaigns (often integrated with vaccination campaigns) -- and the use of vouchers to subsidize sales through the commercial sector (Webster *et al.*, 2007).

Each of these strategies have unique features which may help or hinder their ability to provide ITNs and have them used. For example, commercial strategies risk failing to supply ITNs to areas where markets are limited or excluding those on the bottom end of the socio-economic ladder (Curtis *et al.*, 2003). Social marketing faces some of the same risks, though by subsidizing the price of ITNs price exclusion of low income groups might be reduced (Guyatt *et al.*, 2002). Delivering nets through existing health services can potentially add burden to those services which in many African settings are already under-staffed, under-trained and under-funded, and is further dependant on access and equity of access to services in order to deliver nets

(Hongoro & McPake, 2004). CBOs are unlikely to have the funding to finance large capital purchases on their own, and though they may be far reaching, they also have a potential to be highly uncoordinated resulting in a myriad of different implementation strategies and varying levels of access (Wacira *et al.*, 2007). Free net delivery campaigns can be far reaching in scope but are temporally very limited and may leave gaps in access to ITNs during the long time periods between campaigns (Lengeler *et al.*, 2007). Finally, voucher systems potentially help with the price based exclusion which can occur in pure commercial systems while reducing the logistic burden on health facilities and systems, but they typically also rely on individuals having access to both health services and private ITN markets and the expansion of both (Lengeler *et al.*, 2007).

ITNs can be classified in economic terms as a "mixed good," meaning that they possess attributes of both private and public goods. Given their public good aspects the socially desirable level of ITN usage is unlikely to be achieved without subsides (Hanson, 2004; Stevens, 2005). How, where, when and whom should receive these subsidies are essentially the main elements of the debate around ITN implementation in Africa.

1.11 Cost and cost-effectiveness studies of ITNs

When compared to most other malaria control interventions, ITNs have been more thoroughly investigated from a cost and cost-effectiveness perspective - though most studies were associated with trials or small scale projects and programs. Extensive trials were conducted in the Gambia (Picard *et al.*, 1993; Aikins *et al.*, 1993; Aikins *et al.*, 1998).

While these two studies both used rigorous methodology to establish effectiveness and cost data they are illustrative of the problems associated with comparing CE ratios, even from within the same country. Picard *et al.* (1993) established cost and included the cost to households but reported gross costs as opposed to Aikins *et al.* (1998), who reported net costs (which include savings from reduced treatment). Furthermore, the study populations covered different age ranges. Their comparability suffers further when one considers the differences in the methodology of establishment of effect measures. Finally, the Gambia already had a high level of

bednet usage, meaning that in both of these interventions, only insecticide for treating the nets needed to be supplied. This significantly reduced the cost of implementation, improved the CE ratio and possibly, due to already prevalent usage, improved adherence compared to an area with little experience with ITNs.

Another important ITN study, carried out in Ghana by Binka *et al.* (1997), reported gross CE ratios of $2,003 per death averted and $74 per DHLY (Discounted Healthy Life Year) gained (1993/1994 USD). This controlled trial was carried out in an area with low net usage pre-intervention thus the costs of purchasing and distributing nets were included, significantly increasing the costs and shifting CE ratios. Further, sensitivity analysis from this study suggested that program implementation and delivery mechanism may have significant effects on the cost-effectiveness ratio for ITN programs (Binka *et al.*, 1997).

Other cost and cost effectiveness studies of ITNs have been conducted in the Gambia, Kenya, Ghana, Benin, Tanzania, Malawi, the Solomon Islands, Thailand, Vietnam, India, Afghanistan, Colombia and South Africa (Maccormack *et al.*, 1989; Kere & Kere, 1992; Rashed *et al.*, 1997; Curtis *et al.*, 1998; Rowland *et al.*, 1999; Verle *et al.*, 1999; Goodman *et al.*, 2001; Kamolratanakul *et al.*, 2001; Guyatt *et al.*, 2002b; Guyatt & Snow, 2002; Kroeger *et al.*, 2002; Hanson *et al.*, 2003; Wiseman *et al.*, 2003; Bhatia *et al.*, 2004; Ngugi *et al.*, 2004; Grabowsky *et al.*, 2005; Stevens *et al.*, 2005; Mulligan *et al.*, 2008). A 2002 study conducted by Guyatt *et al* performed a cost analysis of programs for Residual House Spraying (RHS) and ITNs during a 1999 malaria epidemic. The study used the output indicator of cost per person protected as its outcome measure and therefore was not directly comparable to other studies of ITNs which used impact indicators such as cost per death averted. They found a cost per person protected with ITNs of $2.34 per year and $0.88 with IRS per year (one round of spraying) (2000 USD)(Guyatt *et al.*, 2002a). Wiseman *et al*'s 2003 report on permethrin impregnated ITNs in western Kenya is interesting because it attempts to incorporate positive externalities of ITN usage i.e. the possibility of a "mass-killing" or neighborhood effect on vector densities. This would indicate the extension of protection to households in a community or near to areas with high ITN usage. While there is incomplete quantitative evidence of phenomenon's size and importance in varied settings (Binka *et al.*, 1998; Hawley *et al.*, 2003; Killeen *et al.*,

2007; Gosoniu *et al.*, 2008) its existence may be an important factor in determining the CE of ITNs in operational settings and furthermore, justification for considering them partially as public goods thereby providing impetus for including them in publicly funded malaria control programs (Wiseman *et al.*, 2003; Hanson, 2004; Stevens, 2005). Wiseman *et al.* (2003) found significant decreases in both the CE ratios for DALY saved and all cause sick child clinic visits when the community effect was included in their study, from $65 to $49, and $49 to $38 respectively (1996 USD).

Several issues are of importance to expanding the scope of the ITN CE literature, one is the relative effect on CE ratios of extending the interventions to areas of low malaria mortality. A community randomized control trial conducted in India by Misra *et al.* compared IRS to ITNs in the Surat district of Gujarat State, India, a highly malarious area for India, but one where malaria mortality is low (Misra *et al.*, 1999; Bhatia *et al.*, 2004). The authors of the subsequent costing study reported net costs as $50 and gross costs $52 both per case averted (1997 USD), mortality being too low in the district to measure (Bhatia *et al.*, 2004).

One other area of importance which has been little explored is the delivery method for ITNs. One study from Tanzania conducted by Hanson *et al.* described a social marketing program for ITNs. They found CE ratios of $1560 per death averted and $57 per DALY saved which consequently fell to $1018 and $37 when the costs and effects of untreated nets were included (2000 USD) (Hanson *et al.*, 2003).

Recently a review of existing cost and cost effectiveness literature on ITNs was conducted by Kolaczinski and Hanson. The authors found that there were major difficulties in comparing cost assessments due to large variations in the methodologies used (Kolaczinski & Hanson, 2006). More recently information on the costs of large scale implementation of ITNs has become available, Mueller *et al.* reported on the costs of a national scale ITN campaign in Togo, Stevens *et al.* produced cost estimates for large scale ITN distribution in Malawi, and several other studies of ITN delivery at large scales are included in this thesis (Stevens *et al.*, 2005; Mueller *et al.*, 2008; Mulligan *et al.*, 2008; Yukich *et al.*, 2008; Yukich *et al.*, 2009).

1.12 Cost and cost-effectiveness studies of IRS

Most studies identified which performed cost-effectiveness analyises of IRS programs were done in comparison with ITN programs. This may be a consequence of the perceived need to make a policy decision between the two interventions, as well as the relatively sparse application of IRS in Africa in recent years (Pluess *et al. in press*; Sadasivaiah *et al.*, 2007). Currently the effect of combining ITNs and IRS is poorly understood and considerable debate remains as to how much additional benefit can be gained by adding one intervention to the other; some evidence of an additive (non-interactive) effect does exist (Kleinschmidt *et al.*, 2006). No studies of the cost or cost effectiveness of combining the two interventions have been identified in the present work.

The first identified report of CE analysis of IRS was done in 1979 by Walsh & Warren (Walsh & Warren, 1979). Many reports from the era of malaria eradication also included cost measurements but given the large gap in time between those studies and more current data, refinements in costing methodology, as well as the development of new insecticides we decided not to include such information here. Their paper estimated effectiveness and cost for IRS with DDT twice per year using data from trials in the 1950s and 60s showing 40-50% reductions in crude death rate and infant mortality to estimate a cost of $584 per adult death averted and $1,402 per infant death averted (1995 USD) (Walsh & Warren, 1979; Goodman & Mills, 1999b).

By 1986 Barlow & Grobar had estimated the cost per case averted by residual house spraying at $342 (1995 USD). But their study, based on data from the Garki project in Nigeria, included substantial research costs (Molineaux & Gramiccia, 1980; Barlow & Grobar, 1986; Goodman & Mills, 1999b).

Anne Mills' Nepal study analyzed a program containing both passive case detection, active case detection and indoor spraying with DDT, Malathion or Bendiocarb but was unable to determine outcome level effectiveness and therefore used the process indicator of spraying cycle cost per capita which varied from $0.61 when DDT was used to over $1.05 when Ficam was used (USD 1984) (Mills, 1992).

Bhatia *et al.* (Bhatia *et al.*, 2004) found that IRS in a randomized control trial in India

had a gross CE ratio of $87 per case averted (1997 USD). Goodman *et al.* (Goodman *et al.*, 2001), examined the provision of ITNs and IRS in KwaZulu-Natal, South Africa where a significant IRS program, already running, was the base-case or control scenario. Because IRS was already in place they could not calculate average cost-effectiveness versus do-nothing approach but they did show that the cost of IRS per capita using pyrethroids was approximately $2.30 to $2.40 (1999 USD) (Goodman *et al.*, 2001).

Guyatt *et al.*(Guyatt *et al.*, 2002b) studied an IRS campaign in the highlands of Kenya found an economic cost of $0.88 per capita when a pyrethroid insecticide was sprayed, the research did not measure effectiveness of the two intervention and thus could not estimate a cost-effectiveness measure (Guyatt *et al.*, 2002b).

A detailed study of a large IRS program in Southern Africa conducted as part of the Lubombo Spatial Development Initiative was conducted by Conteh *et al.* (Conteh *et al.*, 2004). The program was an internationally supported attempt to reduce malaria burden and transmission in southern Mozambique and thereby also reduce the number of introduced cases of malaria into South Africa. Where two rounds of spraying with carbamate insecticides were conducted, they found that the economic cost of spraying per capita was $3.48 and $2.16 for the rural (LSDI) and peri-urban areas respectively when both project management costs and monitoring and surveillance costs were excluded. When these costs were included the cost per capita for the two rounds of spraying increased to $4.82 and $2.83 per capita (2000 USD). Conteh *et al.* (Conteh *et al.*, 2004) also estimated a cost per infection averted based on the monitoring data generated by an associated intervention assessment of $20-$30 per infection/case averted assuming that all the averted infections in a before and after assessment were due to the spraying program; the raw data produced by this study were reanalyzed as part of this thesis (Conteh *et al.*, 2004).

Several other studies conducted in assorted settings examined various aspects of IRS implementation with respect to costs. Walker (Walker, 2000) examined the relationship between the various aspects of insecticide choice and the insecticide costs of IRS programs based on a simple model of house size, duration and application rates. The model confirmed the commonly held tenet that DDT is the

lowest cost insecticide when residual lifetime is considered and that the carbamate insecticides group is at the higher end of the cost scale due to their shorter residual lifetimes and high prices (Walker, 2000).

Kroeger *et al.* (2002) examined the relative unit costs of malaria vector control in Colombia and found a mean cost per house sprayed and person protected per year with two spraying rounds of $37-$48 and $7-$10; the ranges varied depending on how far the communities to be sprayed were from district centers (2001 USD).

Curtis *et al.* (1998) used the framework of a comparative trial between ITN and IRS in Tanzania to estimate a cost of $2.3 per person protected per year using one round of pyrethroid insecticides, not including spray pumps and protective clothing which could continue to be used for multiple years.

In western Thailand Kamolratanakul *et al.* (2001) examined the relative cost and cost effectiveness of ITNs and IRS in the frame of a trial. They estimated a cost per person protected by one round of spraying with DDT of $1.87 (1994 USD).

Rowland (1999) published the results of an economic analysis of an IRS campaign in the North West Frontier Province of Pakistan, which showed a cost per person protected per year of $0.63 using one round per annum of malathion or lambda-cyhalothrin, and a cost per infection averted of $20. It was not clear if or to what year costs were standardized, though the program analysis covered the years 1990-1995 (Rowland, 1999).

Verlé *et al.* (1999) estimated the costs per person protected with one round of spraying of a pyrethroid insecticide (lambda-cyhalothrin) in Hoa Binh Province of Vietnam and found a cost of $0.47 USD per year (1996 USD). This cost did not include program management costs. They also compared insecticide usage based on national guidelines and observed usage rates based on activity reports and found that usage rates based on activity reports was much lower per capita than national guidelines indicated.

Cost and cost-effectiveness for IRS appears to be sensitive primarily to the price of insecticide and the number of rounds of spraying per year (Guyatt *et al.*, 2002b; Conteh *et al.*, 2004). Additionally, compliance in operational settings and perhaps resistance to insecticides may also play a role in cost and cost-effectiveness of the intervention either directly or by driving insecticide choice towards more expensive alternatives (Mnzava *et al.*, 1998; Goodman *et al.*, 2001; Conteh *et al.*, 2004; N'Guessan, *et al.*, 2007).

Indoor residual spraying remains an important component of the prevention strategies of some African countries especially in southern Africa, including South Africa where it has remained the primary preventative measure since its large-scale inception in the 1940s (Mabaso *et al.*, 2004). Currently IRS has received dramatically increased interest with the large expansion of malaria control funding available due the Global Fund for AIDS Tuberculosis and Malaria, and the U.S. President's Malaria Initiative (Sadasivaiah *et al.*, 2007).

Ultimately, the studies discussed here together range in estimates of cost per person protected annually range from USD 0.47 to USD 10, greater than an order of magnitude. These estimates reflect differences in choices as to which costs to include, choices of different insecticides, different timing of studies and many other sources of methodological variation. Overall the costing literature on IRS programs shows the same type of heterogeneity of methods, assumptions, quality and clarity as is shown by Kolaczinski and Hanson (2006) for the economic analysis of ITN programs. Because of this large variation in time, type of data collection, clarity, completeness of reporting of data and conclusions it is difficult to asses either the comparability of the various studies or their potential for portability or predictive value in other settings.

1.13 Comparing ITNs and IRS: which strategy is more cost-effective?

Understanding the tradeoffs between ITNs and IRS in terms of both cost and effectiveness is currently of the utmost importance. For ITNs and IRS there is an existing, but limited body of literature on the relative effectiveness of the two interventions, which was reviewed by (Lengeler & Sharp, 2003) and by a recent Cochrane Review on IRS (Pluess *et al.* submitted). Both reviews found that there

was not a consistent and significant difference in the two interventions in settings where they were applied effectively. The Lengeler and Sharp review covered several studies with locations in Africa, Asia, the Solomon Islands and India (Kere *et al.*, 1996; Curtis *et al.*, 1998; Misra *et al.*, 1999; Mnzava *et al.*, 1999; Rowland, 1999; Kamolratanakul *et al.*, 2001; Guyatt *et al.*, 2002a).

Curtis and Mnzava (2000) compared historical IRS trials and modern ITN trials as well as modern IRS trials and found that in modern trials the effectiveness of the two intervention systems was comparable on all outcome measures. In the historical comparisons IRS performed better, however, the settings of the trials were, due to the large gap in time, undertaken in very different populations, with differing availability of effective drugs and vastly altered socio-economic status making such comparisons difficult at best and of questionable validity (Lengeler, 2001).

Mnzava *et al.* (1999) conducted a cluster randomized trial comparing ITNs and IRS in South Africa. The trial showed that ITNs were significantly more effective in preventing malaria cases than an established IRS program, though subsequent economic analysis showed that ITNs were also significantly more expensive (Goodman *et al.*, 2001).

In Tanzania a comparative trial using lambda-cyhalothrin for either IRS or bednet impregnation was conducted by Curtis *et al.* (1998). They demonstrated significant effects on the vector population with both interventions and strongly reduced the probability of re-infection after a parasite clearing treatment among children, but were not able to detect meaningful differences between the effectiveness of the two interventions.

A comparison of ITNs and IRS in highland area of Kenya where there was operational targeting of communities to receive either intervention was conducted by Guyatt *et al.* (2002a). Their study found that among randomly selected households, the presence or use of the intervention at the household level was protective against infection, however IRS appeared significantly more protective, and a subsequent cost analysis showed an economic cost per infection averted of $9 with IRS as compared to $29 with ITNs (Guyatt *et al.*, 2002b).

Outside of Africa, trials or other investigations into the comparative effects and cost-effectiveness of the two interventions were conducted in several settings including India, Pakistan, Thailand and the Solomon Islands (Kere *et al.*, 1996; Misra *et al.*, 1999; Rowland, 1999; Kamolratanakul *et al.*, 2001; Over *et al.*, 2004) Implications for cost and cost-effectiveness where built upon these studies or examined separately in other areas (Kere *et al.*, 1992; Rowland, 1999; Verlé *et al.*, 1999; Kamolratanakul *et al.*, 2001; Kroeger *et al.*, 2002; Bhatia *et al.*, 2004). Generally the studies found differences in both costs and effectiveness of the two interventions but the results did not show consistency in either direction or size of the effect. Nor were the differences easily attributable to the vastly different malaria epidemiology present in the various study areas.

Additionally, comparisons between ITNs and IRS have been conducted through and extensive modeling study, the results of which were reported by Goodman *et al.* (1999a). Using data from published studies as well as cost data collected from program managers, they estimated that in a very low income country with high malaria transmission ITNs and IRS would be likely to overlap in cost effectiveness, while ITNs would be likely to be more cost effective if only insecticide treatment was required (*e.g.* the nets already exist in the community) but that these estimates were sensitive to factors which include the length of the transmission season (which has an effect by increasing cost due to need for extra spray rounds), cost of commodities (Nets, ITNs, LLINs and insecticide) as well as usage and compliance factors.

Based on the existing evidence it seems clear that no universal conclusion regarding the relative cost or cost-effectiveness of these two interventions is possible at present. While this thesis does not attempt to provide new comparative data for effectiveness, it will attempt to produce standardized cost estimates for the two interventions.

1.14 Improving Malaria Diagnosis

The expansion of artemisinin combination therapy (ACT) in Africa has driven an increased need for the improvement and evaluation of malaria diagnostic methods (Guerin *et al.*, 2002). Typically in African public health facilities malaria has been

diagnosed either clinically or microscopically. However, due to the high costs of ACTs as compared to past first line treatments, as well as concerns about the development of drug resistance due to drug overuse, many donors and health system managers are searching for ways to improve the rational use of drugs for malaria treatment. Additionally, mistreatment of other febrile disease in the context of falling incidences of clinical malaria, both due to urbanization and vast expansion of vector control, has further enhanced the need for new diagnostic strategies (Bell *et al.*, 2006; d'Acremont *et al.*, 2009). The modern generation of HRP2 antigen based rapid diagnostic tests (RDTs) have been shown in trials to have high sensitivity and specificity for the diagnosis of *P. falciparum* infection among clinical patients in Africa (Bell *et al.*, 2006; Abeku *et al.*, 2008; D'Acremont *et al.*, 2008). When the standard use of microscopy in many health facilities is poor, RDTs may produce more accurate diagnostic results in many settings despite expert microscopy being regarded as the gold standard for research purposes (Mundy *et al.*, 2000; Reyburn *et al.*, 2007; Abeku *et al.*, 2008).

More accurate parasitological diagnosis may help to rationalize anti-malarial drug use at health facilities in Africa and might be expected to significantly reduce the usage of anti-malarial drugs in some situations (Reyburn *et al.*, 2007; Hume *et al.*, 2008). However, any cost-savings made from the reduction of anti-malarial prescriptions may be outweighed by increases in prescription of antibiotics or other drugs to treat the non-malarious patients. Additionally, RDTs add cost to diagnosis which is not inversely proportional to throughput, as is likely to be the case is for microscopy (Lubell *et al.*, 2007). Furthermore, the effects of diagnostic changes will depend not only on the sensitivity and specificity of the RDT as compared to routine microscopy but also on the adherence of clinicians to the diagnostic result, the frequency with which they request a test, and the prevalence of parasitaemia among the clinical population (Zurovac *et al.*, 2006; Lubell *et al.*, 2008b).

There is a sizable body of literature which has examined the implications of improving and changing malaria diagnostic methods, including both empirical and modeling studies. The results of the empirical studies have shown that there is a possibility to reduce average cost per patient and household costs through improving malaria diagnosis and that such interventions could be highly cost-effective (Jonkman *et al.*,

1995; Hume *et al.*, 2008; Lubell *et al.*, 2008b). However, whether there would be cost saving or improvement in treatment outcomes depended on the prices of the RDTs and the first line drug regimen, but also on situational factors such as prevalence of malaria among patients and the effectiveness of the alternative diagnostic method (Lubell *et al.*, 2008a; Zikusooka *et al.*, 2008).

Modeling studies have helped to confirm and highlight the myriad factors which could influence both the cost-effectiveness of improving diagnosis as well as the overall cost-saving potential of implementing parasitological diagnostic improvements including RDTs. The main factors which influence the desirability of one testing mechanism over another relate to the proportion of febrile cases which are parasite positive, the sensitivity and specificity of the new methods and their alternatives, and the costs of both the tests themselves and the drug regimens prescribed to parasite positive patients vs. parasite negative patients (Jonkman *et al.*, 1995; Lubell *et al.*, 2007; Hume *et al.*, 2008; Lubell *et al.*, 2008a; Lubell *et al.*, 2008b; Shillcutt *et al.*, 2008; Zikusooka *et al.*, 2008).

Because the potential for improvement in outcomes and cost savings appear to be highly situation dependant it is necessary to evaluate the decision to shift to rapid diagnostic test locally and at specific levels of the health care system. Useful models have been developed to aid in decision making (Lubell *et al.*, 2008a). However, it is still necessary to evaluate the decision empirically in representative settings, especially before embarking on large national programs. The final section of this thesis examines the economic implications of implementing parasitological diagnosis with RDTs in an urban African setting, Dar Es Salaam, Tanzania.

1.15 Goals and Objectives

The goal of this thesis is generally to improve the knowledge of allocatively effeicient strategies in malaria control for Africa. More specifically it aims to do so by improving the current evidence base on the costs and cost-effectiveness of vector control for malaria using ITNs and IRS, and examining the cost implications of the introduction of antigen based diagnosis for malaria in primary health care facilities in Tanzania.

Specific Objectives:

1. To measure the costs and estimate the cost-effectiveness of large scale vector control programs utilizing ITNs or IRS in sub-Saharan Africa.

2. To compare different delivery strategies for ITNs on the basis of cost and cost-effectiveness.

3. To develop operational descriptions of each vector control intervention strategy for the comparison of the operational feasibility and the prospects for financial and operational sustainability of each intervention.

4. To measure the cost implications of the introduction of rapid diagnostic test based malaria diagnosis in six primary health care facilities in Dar es Salaam, Tanzania.

2. Methods

As the general aim of this thesis is to produce comparable cost estimates of the implementation of ITN and IRS programs on large scales in sub-Saharan Africa, and to analyze this data in a comparable manner, the following chapter outlines the general methodology which is used to measure and value costs and activities as well as to estimate health effects. Sections 2.1 and 2.2 cover the methods used in the vector control studies, while section 2.3 covers the methods used in the malaria diagnostic study.

2.1 Costing Methodology

2.1.1 Time frame

The time frames of the costing studies in this thesis vary due to constraints both in data collection and due to the varied timing of implementation of the programs. In general it was intended to collect data over a time period which encompassed both the start-up of the program until it had been running at scale for a reasonable period, however, because either some programs were implemented over relatively short periods, *e.g.* Togo, and others were begun long before data collection was possible, *e.g.* Eritrea and KwaZulu-Natal, this was not always possible.

Attempts have been made to follow existing guidelines for the cost evaluation of ITN programs, as well as to use methodologies comparable to past studies in order to maximize comparability (Phillips *et al.*, 1993; Creese & Parker, 1994; Drummond *et al.*, 2005; Stevens *et al.*, 2005; Kolaczinski & Hanson, 2006).

2.1.2 Perspective and types of costs included

These studies generally use what could be termed a “modified provider perspective,” or alternatively a “limited societal perspective.” Travel or time costs to users, or other household-level costs or cost savings have not been measured or included. All identified direct and shared costs of the ITN or IRS program to the provider, including those of the commodities and their delivery, health promotion, social mobilization, and international overheads of implementing agencies as listed in Table 1 are included. Additionally where it was applicable we have included the direct costs to the

user of ITN purchases, this is especially relevant where there is a cost sharing or commercial sector approach to ITN delivery.

Costs generally represent the marginal cost of adding an ITN or IRS intervention onto an existing malaria control program and health system. These expenses include the cost of training health workers, or spraymen, health promotion and social mobilization, use of facilities, transportation, payment of personnel, and the commodities themselves. Costs that were required to build and train networks of community health workers or to develop a network of health facilities have not been included. Additionally these costs represent gross costs, and do not incorporate any savings which might arise due to reduced in- or out-patient health care demand.

2.1.3 Cost collection

Costs were generally collected retrospectively from financial and operational records kept by the various implementing agencies. This included examining agencies' financial records, including budgets, expenditure records, receipts, and invoices, but also included activity reports and conducting semi-structured interviews with key stakeholders and managers. Cost and activity information were collected through stakeholder interviews and direct observation where costs were not reflected in the financial records. Identification of costs was guided by thorough operational descriptions which were compiled using Monitoring and Evaluation documentation, agencies' internal and external reports, existing literature and semi-structured interviews with stakeholders.

Where possible, the ingredients approach has been used, meaning that unit activities were first determined and then a unit cost was determined for these activities, allowing for the establishment of a total cost. Where this approach was not possible, either because the information was deemed too sensitive or was not available in adequate detail, aggregated expenditure was generally used.

Some costs have been estimated using the WHO Choosing Interventions which are cost-effective (WHO-CHOICE) unit cost and activity database (WHO-CHOICE 2006a). WHO-CHOICE database costs are reported in 2000 International Dollars and have been converted to their equivalent in 2000 US dollars (USD) for the country of

interest, using implied purchasing power parity (PPP) ratios from the International Monetary Fund (IMF, 2006). These costs were then been adjusted into prices for the appropriate year of the input using the US gross domestic product (GDP) deflator index published by the US Bureau for Economic Analysis (US BEA, 2007). Following adjustment, these costs were treated identically to all other costs included in the study.

Table 1: Costs included in the following studies

	ITN Programmes	**IRS Programmes**
Capital cost	Buildings	Buildings
	Vehicles	Vehicles
	ITNs (retail cost & subsidies)1	Sprayers
	Other equipment	Other equipment
	Start-up costs2	
Recurrent cost	Insecticide (when separable from nets)	Insecticide
	Personnel	Personnel
	Fuel/maintenance	Fuel/maintenance
	Management cost/training & meetings	Management cost/training & meetings
	Office/warehouse rental	Office/warehouse rental
	Supplies/overheads	Supplies/overheads
	Recurrent building costs	Recurrent building costs
	Basic evaluation and monitoring (excluding specific research costs)	Basic evaluation and monitoring (excluding specific research costs)
	Advertising and promotion (or related)	

Resource use was generally valued at multiple levels depending on the structure of the program: centrally (within the MOH and the NMCP), at regional warehouses or coordinating sites and at peripheral health facilities or implementing sites. Where unit activities were available resources were valued according to their financial and economic costs as appropriate to the activity, more details for country specific instances are available directly in those country specific studies included in this thesis or in an unpublished report (Yukich *et al.*, 2007).

2.1.4 Cost classification and adjustments

Costs have been divided into *capital* and *recurrent* costs based mainly on the lifetime of the goods being purchased. As stated above, it was not possible in all cases to collect start-up costs. Capital costs have been discounted in the economic analysis using lifetimes and discount rates determined through stakeholder interviews, expert information, and past literature. Varying discount rates and lifetimes were generally examined in the sensitivity analysis. Both financial and economic analyses were conducted, in order to show (1) what the actual expenses of running a program would be, as well as (2) the level of all resources used. In the financial analysis, taxes were included where they applied though most implementing agencies had tax exempt status, while in the economic analysis they have been treated as transfer payments and have therefore been excluded. In the financial analysis, capital costs have not been discounted and are instead incurred in full at the time of the purchase.

Most costs were collected in either local currencies or USD, though some were collected in Swiss Francs (CHF). Costs collected in local currencies or CHF were converted to USD based on official yearly average exchange rates for the period during which the costs were incurred, and all costs were adjusted for inflation to 2005 prices using the US GDP deflator produced by the US Bureau for Economic Analysis (US BEA, 2007).

2.1.5 Outputs

Generally, two main output measures were used: (1) *number of nets delivered* and (2) *number of re-treatments performed*. Though methods for measuring these indicators varied across settings, more details on the specifics of output measurements are available in the country specific chapters or in the previously mentioned report (Yukich *et al.*, 2007).

The two output indicators above were used to calculate a third combined output measure: *treated net years (TNY)*, which blend the results of both outputs by assuming that either a re-treatment or a new ITN provides 1 year of full protection for

any individual using that net. This combined indicator is useful because it allows the inclusion of re-treatments of existing nets as part of the outcome measure, while the calculation of the cost per ITN delivered does not. Though in some programs a significant portion of all nets delivered (all nets in Togo) were LLINs, all nets have been treated as conventional nets for the calculation of outputs in the base scenario of this analysis. The number of TNYs delivered through an LLIN would be theoretically higher — approximately 3-5 years per net — and the inclusion of the extended benefits of using these nets would be expected to significantly lower the cost per TNY or the cost per health impact. In the sensitivity analysis, outputs were also calculated using the assumption that all nets delivered were LLINs.

2.1.6 Base scenario

In these studies, a base scenario was used to increase the comparability across interventions; generally, this scenario relies on the following set of assumptions. A discount rate of 3% has been applied to both DALYs (see below) and to economic capital costs. Shared costs have been attributed to the interventions based on the actual value of the indicator chosen to allocate them. Nets have been assumed to last for 3 years and, as noted above, treated nets and re-treatments to provide 1 year of protection each. Fifty percent of the nets delivered were assumed to be used by children and only one child was assumed to sleep under each of these nets. Additional assumptions specific to each country program were necessary in certain cases, these are detailed in the country specific studies or in an unpublished report (Yukich *et al.*, 2007).

2.2 Benefit Methodology

2.2.1 How benefits are calculated

Many of our methodological choices were guided by the overarching need to ensure comparability between the settings. As a result, our estimates differ from previously published costing studies for the programs in Malawi (Stevens *et al.*, 2005), Tanzania (Mulligan *et al.*, 2008) and Togo (Mueller *et al.*, 2008), but we believe these differences are minimal and important to maintain comparability.

DALYs and death averted

Generally, DALYs averted are calculated by adding years of life lost due to cause-specific mortality and years lived with disability (resulting from the specific disease or risk factor). In our calculations we have excluded (1) the disability DALYs and (2) DALYs lost in persons over five years of age. The burden of malaria in highly endemic areas (i.e., most of sub-Saharan Africa) is highly concentrated in under-five children (Breman *et al.*, 2006) and the large majority of lost DALYs are years of life lost rather than disability-related (WHO-DALY). Fortunately, the effects of vector control by either approach are likely to be similar and hence our approach is unlikely to bias our comparisons, as long as the settings are highly endemic for malaria (nearly 75% of the population of sub-Saharan Africa) (MARA/ARMA, 2004).

In accordance with the WHO Global Burden of Disease Project, we used a standardized life table for DALY calculations (WHO-DALY, 2006b). We made this decision in order to apply the same value to each life lost, regardless of the country investigated. Choosing country-specific life tables would have made comparisons between different vector control approaches in part dependent on different life expectancies and this was not desirable in the present study. As a result we have chosen to treat all child deaths as infant deaths and assign a value of 33 DALYs lost for each death (WHO-DALY, 2006b). This is conservative, since allowing for deaths among older children would have yielded higher numbers of DALYs averted, due to both slightly longer life expectancies for older children and age weighting.

We have also ignored the effect of vector control on pregnant women. Pregnant women form a relatively small fraction of the population, typically 4–5%, but their share of malaria mortality and morbidity is higher than average. Unfortunately, this risk is not properly quantified at present. At least we believe that the important effect of reduced infections in pregnant women on low birth weight and anemia in children has been taken into account in our estimates of child mortality.

Finally, significant increases in risk of malaria infection and severe disease due to HIV have been identified for all age groups (Hewitt *et al.*, 2006). Due to the high HIV prevalence levels in southern Africa, as well as the generally lower malaria transmission levels, there is likely to be a significant burden of increased malaria mortality and morbidity among adults. One modeling study estimated that deaths

from malaria in southern Africa could increase by as much as 114% due to the interaction of HIV and malaria, largely due to adult mortality (Korenromp *et al.*, 2005). Again, we decided not take this into account for lack of sufficient data.

Our decisions with regard to outcome assessment are unlikely to lead to a bias in our comparisons as long as the age profile of lost DALYs is similar in all programs. Where this is not the case, as perhaps in areas of low malaria transmission or epidemic prone areas, the comparisons shown here should be reconsidered in light of the differing distribution of burden of disease.

2.2.2 Impact data for ITNs and IRS

Another problem we were confronted with was the paucity of bias-free estimates of IRS efficacy and effectiveness in sub-Saharan Africa. While there are many descriptive studies that showed the significant health impact of IRS programs over time (Mabaso *et al.*, 2004; Lengeler & Sharp, 2003) there are only two randomized controlled trials that provided unbiased quantitative values of this impact (in Tanzania and South Africa, see above). A Cochrane review on IRS impact has been conducted (Pluess *et al. in press*) but it did not identify quality quantitative evidence on the effect of IRS and showed that past trials cannot be used to quantitatively estimate the impact of IRS. Fortunately, good impact estimates are available for ITNs from an existing Cochrane review (Lengeler, 2004): the regular use of ITNs in a high coverage situation averted 5.5 child deaths per 1,000 child-years of ITN use. In the absence of a better data set for IRS, and in the light of the fact that the impact of ITNs and IRS seemed to be similar, we decided to apply the same estimate of impact for IRS. We believe this is a reasonable assumption on the basis of our current knowledge (Lengeler & Sharp, 2003).

2.2.3 Targeting risk groups versus general coverage in the population

There was one important aspect in our calculations of cost per person protected and cost per death/DALY averted that presented a challenge for standardized comparisons: ITNs can be targeted at age specific high-risk groups, while IRS can not - either a high percentage of houses is sprayed or the effect is lost. This has obvious practical implications which are shown in this thesis (Yukich *et al.*, 2008). Protecting everyone in the population (either by ITNs or IRS) has obvious benefits,

for users and even more for non-users (Killeen *et al.*, 2007). However, this obviously bears a much higher cost (since children and pregnant women represent together only around 20% of the population) and it is unclear *a priori* how cost-effective this marginal increase in protection would be.

This point is important because of a recent shift in global targets for malaria vector control to increase coverage levels to 80% in the total population on the basis of at least two LLINs per household (Roll Back Malaria Partnership, 2005). With this goal, ITNs would be deployed in a way very similar to IRS, with no targeting and a high coverage level in all age groups. This approach is meant to maximize the vector control effects for the whole population. Since neither the cost nor the effects of this strategy are quantified at present, we will not further discuss this point here. Our cost estimates could provide a basis to estimate the total cost of such strategies on the basis of the cost per person-year protection, and the operational experience presented in the five ITN case studies might also prove useful.

2.3 Malaria Diagnostics

2.3.1 Study area

Twelve public health facilities in Dar Es Salaam, Tanzania were selected for inclusion in a trial of RDT rollout at the facility level. Of these six primary health care facilities were included in the costing exercise. Four primary care facilities were experimental facilities in which RDTs replaced routine microscopy for the parasitological diagnosis of malaria. Two primary care health facilities remained as controls. Dar Es Salaam is a large urban area (pop. approx. 3 million) in sub-Saharan Africa composed of highly heterogeneous developed areas including commercial districts, industrial districts, residential districts, urban slums, and areas with high levels of urban agriculture. Consequently there is a high variability in the availability of *Anopheline* breeding sites and mosquito densities. Generally, however, it is considered a low but stable malaria transmission area (EIR ≈ 1.3) with low parasitaemia prevalence (~10% in the general population) (Geissbuhler *et al.*, 2009). All of the health facilities included in the costing exercise are located in densely populated low-income urban areas, though one facility's catchment area also includes some peri-urban and higher income areas.

2.3.2 Collection of patient and facility costs and resource use

Costing was conducted both from the patient and provider perspectives. A larger survey examining the effects of RDT on health workers and patients was used as a platform for collecting patient specific and facility costs. Within the six selected facilities patients were selected who fit the inclusion criteria for potential non-severe malaria, namely: first consultation for the present complaint (not a follow-up visit), absence of severe disease, and main complain not trauma related. Patients or caretakers of young patients who fit the inclusion criteria and gave oral informed consent had their consultation passively observed by a survey worker with clinical training. These patients or caretakers were then selected for an exit interview which included questions relating to both their perceptions of the clinical and laboratory consultation as well as expenditures, and any previous treatment seeking. All patients or caretakers who participated in the exit interview, which included the costing questions, were requested to return to the same health facility one week later for a follow-up interview and were provided with a small incentive to cover transportation costs. At follow up all patients or caretakers were administered a questionnaire which solicited information on their current health status and any treatment seeking activity or expenditure which occurred in the intervening week, they were also asked about the previous consultation and any associated expenditures, mainly as a check on consistency. All returning patients were tested with an HRP2 based RDT in order to check for missed infections as well as to identify false negatives or positives in the control facilities given the persistence of the HRP2 antigen even in treated patients. For all patients testing positive by RDT during follow-up it was ascertained if they had received appropriate first line treatment and if their condition had improved, if they had not improved or received appropriate treatment it was ensured that they were subsequently treated at the health facility. In order to assess treatment costs to the provider a health facility survey was conducted in the six facilities participating in the cost study to identify per patient resource use at the facility level.

2.3.3 Valuation of Resource use

Costs of resource inputs were determined for the provider costs based on the Tanzania pharmaceutical and supply price list for 2007, and interviews with the appropriate financial managers of the Dar Es Salaam City Medical Office of Health. Information on drug prices was obtained from the International Drug Price Indicator Guide database published by Management Sciences for Health (MSH) or from the WHO-AFRO drug price indicator database (MSH, 2009; WHO-AFRO, 2008). Patient costs were valued by patients reported expenditure.

Costs for the initial implementation of RDTs, training in their use, and quarterly supervisory visits were calculated based on the reported expenditure and or activities tracked during the project, excluding specific research related costs. Costs were reported in the local currency (TSH), U.S. Dollars (USD), or Swiss Francs (CHF). All costs were converted to USD using official exchange rates and adjusted into a common year (2008) using the U.S. GDP deflator (US BEA, 2009). Capital costs were discounted and annualized using a 3% discount rate and assumed lifetimes for equipment based on expert opinion and past literature. All costs attributable to RDT implementation were then divided by the estimated total number of RDT tests performed in the nine experimental health facilities (328,000 – 435,000) over the duration of the project (approximately two years) to calculate an implementation cost per test.

Statistical methods are discussed in more detail in Chapter 7, where the full RDT study ispresented. Data was entered in EpiInfo 3.4.1 (U.S. Centers for Disease Control and Prevention, Atlanta, GA), and analyzed in STATA 9.2 (Stata Corporation, College Station, TX).

3. Costs and cost-effectiveness of vector control in Eritrea using insecticide-treated bed nets

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3.1 Abstract

Background

While insecticide-treated nets (ITNs) are a recognized effective method for preventing malaria, there has been an extensive debate in recent years about the best large-scale implementation strategy. Implementation costs and cost-effectiveness are important elements to consider when planning ITN programmes, but so far little information on these aspects is available form national programmes.

Methods

This study uses a standardized methodology, as part of a larger comparative study, to collect cost data and cost-effectiveness estimates from a large programme providing ITNs at the community level and ante-natal care facilities in Eritrea. This is a unique model of ITN implementation fully integrated into the public health system.

Results

Base case analysis results indicated that the average annual cost of ITN delivery (2005 USD 3.98) was very attractive when compared with past ITN delivery studies at different scales. Financing was largely from donor sources though the Eritrean government and net users also contributed funding. The intervention's cost-effectiveness was in a highly attractive range for sub-Saharan Africa. The cost per DALY averted was USD 13 - 44. The cost per death averted was USD 438-1449. Distribution of nets coincided with significant increases in coverage and usage of nets nationwide, approaching or exceeding international targets in some areas.

Conclusions

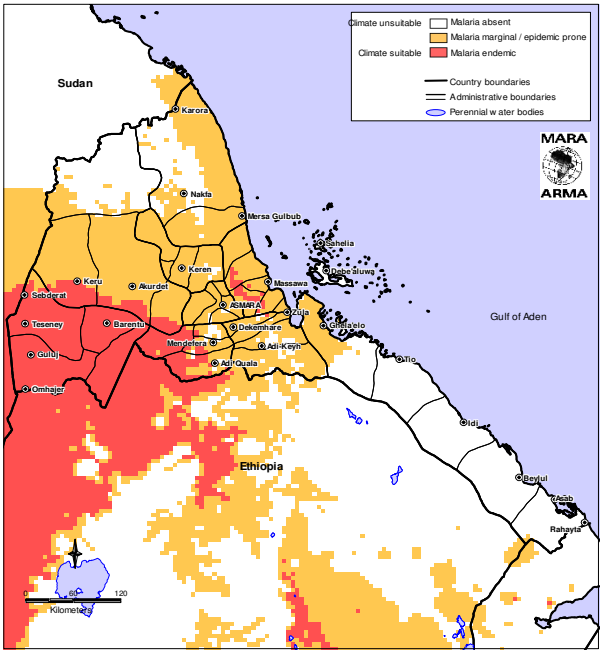
ITNs can be cost-effectively delivered at a large scale in sub-Saharan Africa through a distribution system that is highly integrated into the health system. Operating and sustaining such a system still requires strong donor funding and support as well as a functional and extensive system of health facilities and community health workers already in place.

3.2 Background

Vector control generally and insecticide-treated nets (ITNs) specifically have been identified as effective and cost effective methods for the prevention of malaria related mortality and morbidity in sub-Saharan Africa (SSA) (WHO, 2008). Despite the vast expansion of vector control implementation, relatively few studies have examined the key economic characteristics of programmes operating on a large scale (Aikins *et al*., 1998; Stevens *et al*., 2005; Mueller *et al*., 2008; Mulligan *et al*., 2008). Considerable debate still remains as to the most appropriate strategy for delivering ITNs on a national scale (Lengeler *et al*., 2007). Further, the relative merits of ITNs versus Indoor Residual Spraying (IRS) are also insufficiently documented. This study provides data on the operations, costs and estimates of the cost effectiveness of the national ITN programme in Eritrea. This analysis is part of larger multi-country analysis of the main strategies used by ITN and IRS programmes in SSA (Yukich *et al*., 2008).

Eritrea is divided into three zones of malaria risk based on epidemiology and geography. In the western lowlands, where the malaria burden is most severe, transmission is highly seasonal and most intense along water bodies or irrigation projects. The transmission season lasts from September until November. In the highlands there is generally little risk of malaria transmission, but due to the low immunity of the population there is a risk of epidemic malaria. Finally, in the coastal plains along the Red Sea, highly seasonal malaria transmission occurs which peaks between January and March, though transmission in this zone is generally low due to low levels of precipitation. A recent study estimated that two-thirds of the Eritrean population are considered at risk of malaria, either epidemic or endemic (Sintasath *et al*., 2005), and the Mapping Malaria Risk in Africa (MARA) project estimates that approximately 92% of the population is at risk for malaria, with approximately 51% at risk of endemic malaria (MARA/ARMA)(Figure 3). The population of Eritrea in the year 2005 was estimated to be 4.3 million (MARA/ARMA). Of this number, approximately 760,000 were children under five years of age. Using an assumption that 5% of the population is made up of currently pregnant women, there are approximately 215,000 such women in the country, while a total population of 2.9 million lives in malaria-endemic areas.

Figure 3: Climatic suitability for malaria transmission in Eritrea (source: Mapping Malaria Risk in Africa, www.mara.org.za).



The Eritrean ITN programme is part of a broader malaria control programme which includes environmental modification, larviciding, IRS and the provision of prompt and effective treatment. The mix of interventions used varies depending on the area of the country, with IRS being used more extensively in the highest burden areas and environmental management and larviciding used in all malarious regions, but most extensively in moderate to low burden areas (Nyarango *et al.*, 2006; Ceccato *et al.*, 2007; Graves *et al.*, 2008). The ITN programme currently utilizes free distribution of ITNs to high-risk groups through ante-natal care (ANC) clinics, and to the general population in malarious areas through community health agents (CHA) and local administrations. This has provided a "catch-up"strategy in Eritrea, increasing ITN coverage rapidly among households and vulnerable groups by providing a large number of free and low-cost nets. Recent coverage data are shown in Table 2. It has also maintained a more continuous pipeline and thereby helped to "keep-up" coverage in the longer term as well (Nyarango *et al.*, 2006; NSEO & ORC Macro 2003; Eisele *et al.*, 2006). Generally the programme has achieved relatively high ITN coverage and usage results including reaching household possession over 80%, and meeting Abuja Target usage levels in some regions and high coverage and usage overall

(Nyarango *et al*., 2006; Eisele *et al*., 2006; Macintyre *et al*., 2006). Several studies have found that ITN distribution has been effective in reducing the incidence of clinical malaria in Eritrea (Nyarango *et al*., 2006; Graves *et al*., 2008; Mufunda *et al*., 2007). Malaria specific mortality and case fatality rates also fell during the period of dramatic increases in ITN coverage in Eritrea (Nyarango *et al*., 2006; NMCP [Eritrea] 2002; NMCP [Eritrea] 2003; NMCP [Eritrea] 2004; NMCP [Eritrea] 2005; NMCP [Eritrea] 2006). As of 2008, the Eritrean programme still represents the only national-scale ITN interventions in SSA that relies almost entirely on routine public sector implementation. While overall results of this study have been published in a multi-country comparative study (Yukich *et al*., 2008), this paper provides an opportunity (1) to show the unique features of the Eritrea programme, (2) present in much more detail the data used for the comparative study, and (3) illustrate the ways in which average cost-effectiveness results can be confounded by issues of scale and timing of measurement.

Table 2: Net coverage and usage in Eritrea according to latest available statistics.

		2002 DHS*		2002 DHS**		2003 NMCP/Tulane**		2004 NMCP/RBM***	
		Any net	**ITN**	**Any net**	**ITN**	**Any net**	**ITN**	**Any net**	**ITN**
Children under nets last night	**All**	12.1%	4.2%		7.3%		76.6%		58.6%
	Urban	14.3%	4.8%						
	Rural	11.0%	4.0%						
Pregnant women under nets last night	**All**	6.6%	2.9%		4.7%		52.6%		50.4%
	Urban	8.7%	4.5%						
	Rural	5.5%	2.1%						
Household possession	**All**	33.8%		47.8%		92.3%	82.9%	79%	62%
	Urban	28.3%							
	Rural	37.3%							

NMCP=National Malaria Control Programme; RBM=Roll Back Malaria.
*ITN defined as a net treated within the last 6 months.
**ITN defined as any net treated within the last 12 months, surveys restricted to Gash-Barka and Anseba zobas for purposes of comparison. DHS survey is dry season, while the Tulane survey was conducted during the rainy season.
***ITN defined as any net treated within the last 6 months, survey conducted in Gash-Barka, Anseba, Debub and the Northern Red Sea zobas, where malaria control measures are active (data from (Nyarango *et al.*, 2006)).

3.3 Methods

ITN programme: operational description

ITN distribution began in 1995 as a pilot project in Gash-Barka, in the western lowlands. ITNs were delivered through health facilities and local administrations, with assistance from CHAs. The programme was gradually scaled up from a few villages to cover all malarious areas of the country. Families were charged 30 Nakfa (USD 2–3) per ITN before the 2003 distribution. Local administrations could make exceptions for those families deemed too poor to pay. In 2001, free

distribution to women at ANC and maternal and child health (MCH) clinics began, and from 2003, nets were also given freely to the general population living in malarious areas. Since 2001, over 900,000 ITNs have been delivered and two million re-treatments have been conducted through community campaigns and health facilities (NMCP [Eritrea] 2002; NMCP [Eritrea] 2003; NMCP [Eritrea] 2004; NMCP [Eritrea] 2005; NMCP [Eritrea] 2006).

Re-impregnation campaigns are conducted once a year, one to two months prior to the malaria transmission season, at health facilities and community re-treatment points. Supervision is ensured by health facility staff with the support of CHAs and with the collaboration of community members.

Administratively the country is divided into six regions, called Zobas, and further into sub-Zobas (districts) and Kebabis (agglomerations of ~3-10 villages). Four of the Zobas are considered to be at significant malaria risk, with the highest risk Zobas being Debub and Gash Barka and the lowest risk in the Northern Red Sea Zoba (Macintyre *et al.*, 2006). Operationally, the ITN programme functions similarly in all malarious regions with the caveat that some areas considered at higher risk were targeted for earlier distributions of ITNs. A full description of the Eritrean ITN programme is available in an unpublished report (Yukich *et al.*, 2007). The structure of the programme is shown schematically in Figure 4.

Figure 4: Structure of the Eritrean national ITN programme.

The ITN distribution system in Eritrea was highly successful in raising the level of coverage to Abuja target levels and survey evidence that the country had met the 60% coverage targets set under that agreement within specific regions became available in 2003 (See Table 2) (Eisele *et al.*, 2006). Given that success, the National Malaria Control Programme (NMCP) set higher targets at its annual meeting in Tesseney in 2004 (80% household ownership and pregnant women/under five usage by 2006) (NMCP [Eritrea] 2004). These targets are in line with current RBM international policy (WHO 2008). Unfortunately, there is no available survey data to provide evidence as to the expansion or maintenance of the success of the Eritrea programme after 2004, however, a NMCP/Tulane survey undertaken in 2003 showed that when ITNs were defined as nets treated within 12 months nearly 80% of households in the most highly malarious areas of the country already owned ITNs (Table 2 shows selected results of ITN coverage and usage surveys in Eritrea). Distribution of nets in Eritrea has continued since the last survey was conducted.

Time frame and perspective for costing exercise

Costs and outputs collected for this study cover a time period which extended from 2001, when nets were first given freely though ANC facilities, through the end of 2005, after three full years of community-wide distribution. This time interval covered a period of large scale up in ITN coverage, although it did not include the initial expansion of the programme to all malarious areas of the country (NSEO & ORC Macro 2003; Eisele *et al*., 2006). Hence, it was not possible to include the start-up costs of the programme.

Attempts were made to follow existing guidelines for the cost evaluation of ITN programmes, as well as to use methodologies similar to past studies in order to maximize comparability (Creese & Parker 1994; Stevens *et al*., 2005; Kolaczinski & Hanson 2006). On this basis all costing methods were standardized with six other national programme assessments that were conducted concurrently (Yukich *et al*., 2007; Yukich *et al*., 2008).

Types of costs included

The study generally used the provider perspective. Travel or time costs to users, or other household-level costs or cost savings have not been measured or included, however, user charges from the early years of the program were included when calculating sources of financing. All direct and shared costs of the ITN programme to the provider were included, including those of the commodities and their delivery, health promotion, and social mobilization, as listed in Table 3. Costs represent the marginal cost of adding Eritrea's ITN intervention onto an existing malaria control programme and health system. These expenses include the cost of training health workers in ITN use and re-treatment, health promotion and social mobilization, use of facilities, transportation, payment of personnel, and the commodities themselves. Costs required to build and train a network of Community Health Agents (CHAs) or to develop a network of health facilities have not been included.

Table 3: Types of costs included in the Eritrea analysis

Capital	Buildings
	Vehicles
	Equipment and furniture
	ITNs
Recurrent	Insecticide
	Personnel
	Training and meetings
	Fuel/maintenance of vehicles
	Office/warehouse rental
	Advertising and promotion
	Supplies/overheads
	Patients' expenditures (excluding cost of ITN)
	Management cost
	Basic evaluation and monitoring (excluding specific research cost)

Cost collection

Costs were collected retrospectively from financial and operational records kept by the NMCP, zonal offices in the four main malarious zobas of Eritrea, the Eritrean Social Marketing Group (ESMG), the World Bank-funded HAMSET project, and the Global Fund to Fight AIDS, TB and Malaria (GFATM). Cost and activity information collection occurred during two periods, from May to June 2005 and from May to June 2006. Costs were collected by examining agencies' financial records, including budgets, expenditure records, reports, receipts and invoices. In addition, cost and activity information were collected through stakeholder interviews and direct observation where costs were not reflected in the financial records.

Where possible, the ingredients approach was used, meaning that unit activities were first determined and then a unit cost was determined for these activities, allowing for the establishment of a total cost. Where this approach was not possible, either because the information was deemed too sensitive or was not available in adequate detail, aggregated expenditure was generally used.

Resource use was valued at three levels: centrally (within the MOH and the NMCP), at the Zoba level, and peripherally including health workers, health facilities, and CHAs. Direct costs to Kebabi administrators have not been included since they are believed to be small and no reliable information about these activities could be acquired within the framework of this study.

Resources were valued based on the reported expenditures or budgets, and in the case of shared personnel, on salary plus any fringe benefits. Capital goods were valued based on their procurement costs or alternatively, in the case of building rents, on an average market value of similar properties as reported by the Eritrean government.

Cost classification and adjustments

Costs have been divided into *capital* and *recurrent* costs based mainly on the lifetime of the goods being purchased. As stated above, it was not possible to collect start-up costs. Because of the long and gradual build-up to a full national scale programme, the start-up costs were likely to be large but also difficult to define as they were spread over a long time period and involved pilot programmes which would not be replicated if the strategy were used elsewhere. Due to the long development period, these costs would have little effect on the current running costs of the programme, but failure to capture them reduces the stated costs. Capital costs have been discounted in the economic analysis using lifetimes and discount rates determined through stakeholder interviews, expert information, and past literature. Varying discount rates and lifetimes were examined in the sensitivity analysis. Both financial and economic analyses were conducted, in order to show (1) what the actual expenses of running a programme would be, as well as (2) the level of all resources used. In the financial analysis, taxes on nets and insecticide have been included, while in the economic analysis, they have been treated as transfer payments and have therefore been excluded. In the financial analysis, capital costs have not been discounted and are instead incurred in full at the time of the purchase.

Costs were collected in either Eritrean Nakfa or United States Dollars (USD). Costs collected in Nakfa were converted to USD based on official yearly average exchange rates for the period during which the costs were incurred, and all costs were adjusted

for inflation to 2005 prices using the US Gross Domestic Product deflator produced by the US Bureau for Economic Analysis (US BEA).

Outputs

Generally, two main output measures were used: (1) *number of nets delivered* and (2) *number of re-treatments performed*. Both figures were reported by the NMCP annually, and reflect nets and re-treatments delivered at the primary health care facility level or community level. In the years 2001 and 2002, care was taken to disaggregate nets delivered via ANC clinics and community mechanisms, as nets delivered through community mechanisms involved a user fee, while nets delivered through ANC clinics did not. The number of re-treatments performed during annual re-treatment campaigns were reported by the Eritrea NMCP (NMCP [Eritrea] 2002; NMCP [Eritrea] 2003; NMCP [Eritrea] 2004; NMCP [Eritrea] 2005; NMCP [Eritrea] 2006).

The two output indicators above were used to calculate a third combined output measure: *treated net years (TNY)*, which blends the results of both outputs by assuming that either a re-treatment or a new ITN provides one year of full protection for any individual using that net. This combined indicator is useful because it allows the inclusion of re-treatments of existing nets as part of the outcome measure, while the calculation of the cost per ITN delivered does not. Though some nets in the year 2005 were LLINs, all nets have been treated as conventional nets for the calculation of outputs in the base scenario of this analysis. The number of TNYs delivered through an LLIN will be higher — approximately 3-5 years per net. In the sensitivity analysis, outputs were also calculated using the assumption that all nets delivered were LLINs.

Cost-effectiveness calculations

Two separate cost-effectiveness ratios were measured: (1) *cost per child death averted* and (1) *cost per disability-adjusted life year (DALY) averted*. Each of these ratios has been calculated using both the cost and effects of ITNs delivered and TNYs achieved. Only the effects of ITN use and possession by children were included in either calculation, thus ignoring potential benefits to older individuals. While this calculation underestimates the morbidity burden averted by ITN use, it

would be difficult to include other effects, which are not well quantified at present (Breman *et al*., 2007). It is also consistent with the fact that the DALY burden in malaria-endemic countries is largely driven by child deaths (Snow *et al*., 2004). The effects of untreated nets were excluded in the analysis because (1) it would have been difficult to obtain information on both numbers of such nets and their effect, and (2) the effects of long-lasting insecticidal nets (LLIN) were included in the sensitivity analysis, a more relevant scenario for the future.

Cost results were coupled with standard health impact indicators derived from (1) the Cochrane review on ITNs (Lengeler 2004), and (2) WHO methodology for the calculation of DALYs averted (WHO-DALY). Estimates from the Cochrane review show that approximately 5.5 child deaths are prevented for every 1,000 children who are protected by a net for one year, or approximately 33 DALYs per death if all deaths are treated as infant deaths. This output has been combined with both cost outputs (cost per ITN delivered and cost per TNY delivered) to produce the final cost-effectiveness ratios.

Base scenario

In this analysis, the base case scenario relies on the following set of assumptions. A discount rate of 3% has been applied to both DALYs (see below) and to economic capital costs. Shared costs have been attributed to the interventions based on the actual value of the indicator chosen to allocate them. Nets have been assumed to last for 3 years and, as noted above, treated nets and re-treatments are set to provide 1 year of protection each. Fifty percent of the nets delivered were assumed to be used by children and only one child was assumed to sleep under each of these nets. The cost of nets was based on the commodity, insurance and freight (c.i.f.) price of the nets; for the portion of nets delivered with user fees through community mechanisms the user fee was included for the purpose of calculating sources of funding (the proportion of nets delivered this way was assumed to be 50% in the early years of the programme). Clearly, these are conservative estimates, mainly chosen in order to make a cross-country comparison easier and more meaningful (Yukich *et al*., 2008).

3.4 Results and Discussion

The Eritrean national ITN programme delivered over 900,000 ITNs and over two million re-treatments during the period 2001-2005, at a total economic cost of USD 3.7 million, or a financial cost of just under USD 4.4 million USD (Table 4). The cost composition (Table 4 and Figure 5) of the programme was quite similar to that of other programmes which have been examined (Yukich *et al*., 2008). In economic terms, about 50% of the costs of the programme were capital costs, which were accounted for almost entirely by the cost of the nets. The commodity costs (nets and insecticide) represented 63% of the total economic cost of the programme. Other major costs were staff (21%), and vehicle costs (approximately 7%).

Table 4: Cost composition of the Eritrean national ITN programme (2005 USD).

Line item	Economic		Financial	
	Total cost	**%**	**Total cost**	**%**
Recurrent				
Insecticide	442,213	12%	473,698	11%
Staff	787,638	21%	787,638	18%
Overheads	125,309	3%	125,309	3%
Fuel and maintenance	111,284	3%	111,284	3%
Health promotion and marketing	73,850	2%	73,850	2%
Rented-vehicle costs	229,984	6%	229,984	5%
Subtotal recurrent	**1,770,278**	**48%**	**1,801,764**	**41%**
Capital				
Nets	1,901,729	51%	2,519,343	58%
Vehicles	18,527	1%	39,294	1%
Furniture and equipment	7,704	<1%	19,614	<1%
Subtotal capital	**1,927,960**	**52%**	**2,578,251**	**59%**
Grand total	**3,698,238**	**100%**	**4,380,015**	**100%**

In financial terms, the cost composition of the programme appeared somewhat differently. The largest differences were due to the removal of annualization for nets, which significantly increased their costs in any given year, as well as their share of the total cost of the programme. Secondly, there was a small increase in the costs of nets and insecticide due to the inclusion of import taxes. Other capital costs also increased significantly, but their overall contribution to the cost of the programme was generally low, so these increases had little effect on overall spending patterns.

Figure 5: Economic and financial cost composition of the Eritrean ITN programme

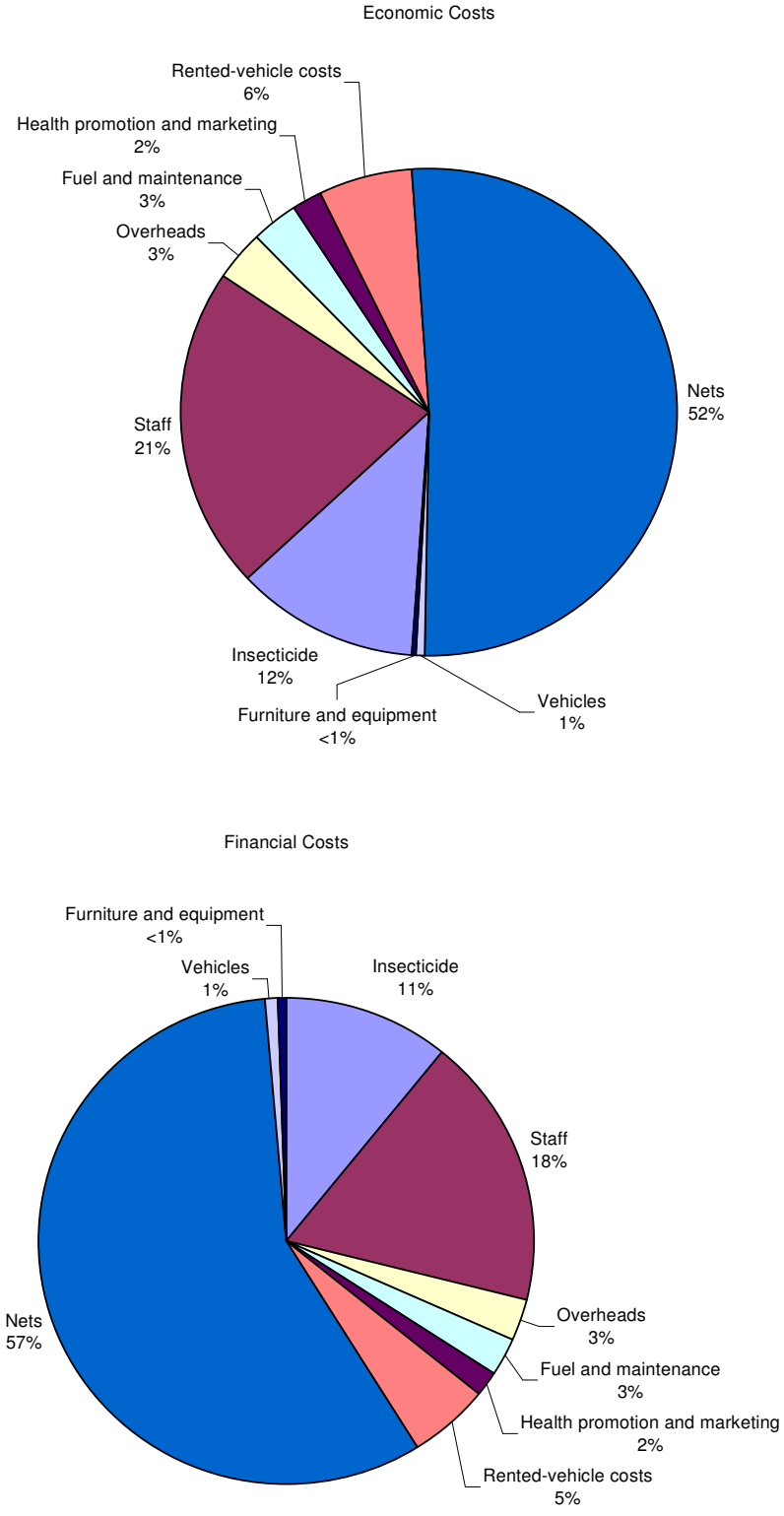


Table 5 summarizes the results of the costing analysis in terms of cost per ITN and TNY delivered. The results indicate an economic cost of approximately USD 3.98 per ITN delivered over the period 2001-2005 and a financial cost of USD 4.72. The cost per ITN delivered excluding the commodity cost (ITNs and re-treatments) was about USD 1.50. Costs per TNY were significantly lower due to the large numbers of re-treatments conducted during annual re-treatment campaigns, which increased the denominator in the TNY ratio significantly. When the commodity costs were excluded, the Eritrean programme delivered a year of protection for an approximate economic cost of USD 0.44.

Table 5: Annual costs per ITN and Treated Net-Year (TNY) delivered in Eritrea (2005 USD).

Year	2001	2002	2003	2004	2005	Average/Total
Financial cost (per ITN)	4.98	3.56	3.87	4.43	9.39	**4.72**
Economic cost (per ITN)	3.15	2.47	4.14	4.07	8.51	**3.98**
Economic cost (per ITN) less commodities	2.02	1.03	1.23	1.23	2.68	**1.46**
Financial cost (per TNY)	2.55	1.95	1.06	1.25	1.20	**1.43**
Economic cost (per TNY)	1.61	1.35	1.14	1.15	1.09	**1.21**
Economic cost (per TNY) less commodities	1.03	0.57	0.34	0.35	0.34	**0.44**
ITNs delivered	141,766	276,038	187,709	214,752	108,011	**928,276**
Re-treatments	135,290	227,750	497,117	544,464	734,154	**2,138,775**

The Eritrean national ITN programme was largely funded through donor contributions. However, in the early stages of the Eritrean national ITN programme (before 2003), user charges were collected for nets delivered through community mechanisms. Unfortunately, it was not possible to determine the specific number of

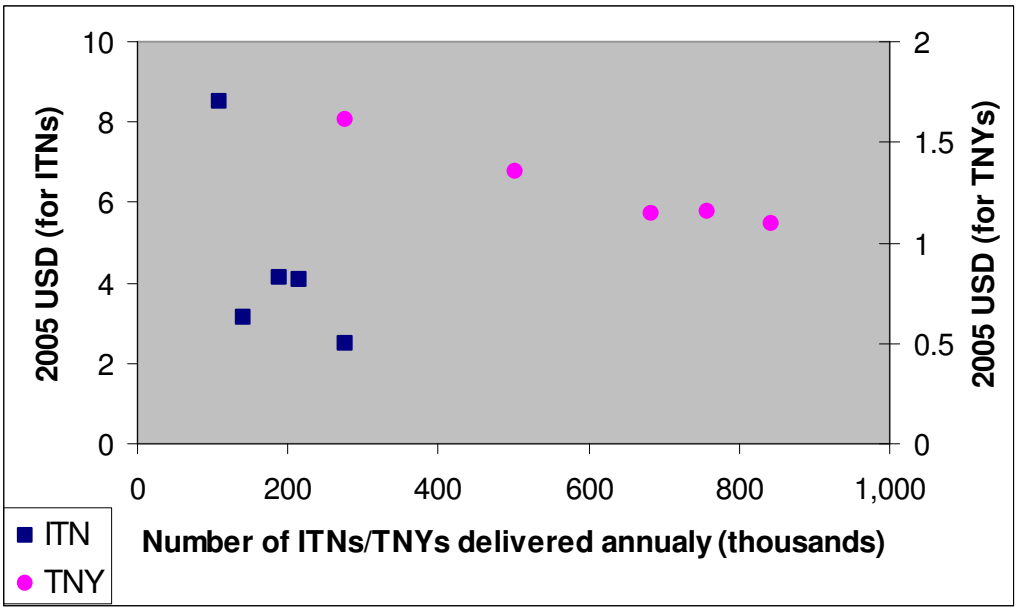
nets for which user charges were applied. As these charges were used to fund the programme, an assumption that 50% of nets delivered before 2003 included user fees when estimating the contribution to the program from each sector was used. In this scenario, donors contributed 69% of funding, users contributed 14% and the MoH contributed 17%. As the practice of charging user fees was discontinued after 2002, the programme relied much more heavily on donor and governmental financing from 2003 onward. Investment from the government of Eritrea was largely in terms of salaries, building space, and vehicles.

Returns to scale

When the costs were disaggregated by year (Table 5), several interesting findings emerged. One was that the cost of ITN delivery did not fall over time, partly because there was no trend toward an increase in scale over the time period analysed. In fact, the number of nets delivered fluctuated over time and the figures were substantially lower in 2005 compared to previous years.

Evidence of the increasing returns to scale is more apparent in these results due to the large increases in TNYs delivered as compared to the ITNs delivered. However, some of this effect was mitigated after 2003 by rising costs for net procurement. If, however, the analysis took into account the fact that some of the nets delivered in 2005 were LLINs and thus provide more than one TNY, the costs per TNY would have fallen despite the real increase in the cost per ITN delivered (*data not shown*).

Figure 6: **Annual economic costs vs. total output (period 2001–2005).**



Annual economic cost per ITN or Treated Net-Year (TNY) delivered vs. total annual number of ITNs or TNYs delivered in Eritrea (period 2001–2005).

Figure 6 and Table 6 illustrate the scale efficiency savings due to increases in the number of TNYs of protection and the numbers of ITNs delivered. In Eritrea's programme it is relatively straightforward to segregate procurement costs from distribution costs, and the former may be a good proxy for savings due to changes in the price of the inputs versus the latter. This can be used to examine changes due to efficiencies of delivery (or economies of scale in distribution). Separating these costs and analyzing their annual fluctuations shows that the programme achieved a savings of over 60% in terms of TNY distribution by its final year. These savings are largely attributable to the increasing share of re-treatments in the input mix, which significantly reduced the average cost of delivering one TNY of protection. The programme also showed approximately a 30% reduction in the total unit cost per TNY over the study period, indicating significant returns to scale in the system, despite procurement costs which increased. These results argue strongly for operating on a larger scale, as well as for the desirability of delivering re-treatments for nets when the use of LLINs is not generalized. Evidence that providing re-treatments to existing nets can be more cost-effective than delivering new nets has been developed previously in the literature (Goodman *et al.*, 1999). Figure 3 shows

how with increasing scale, the costs of distribution fell significantly in Eritrea both for TNYs and ITN delivery. As there is no trend of increasing scale over time in the Eritrean programme, the figure shows the cost versus annual delivery of nets and helps to better illustrate the scale efficiencies in the system.

Table 6: Scale efficiency savings in the Eritrean national ITN programme

Year	**2001**	**2002**	**2003**	**2004**	**2005**	**Total / average**
Output growth (actual)		113,366	90,519	37,195	311,502	1,665,025
Output growth (%)		82%	36%	11%	82%	53%
Total cost						
TNY unit cost	1.61	1.35	1.14	1.15	1.09	1.21
TNY unit cost savings		0.26	0.22	-0.02	0.06	0.52
TNY unit cost savings (%)		16%	16%	-1%	5%	32%
Procurement only						
TNY Unit Cost	0.58	0.79	0.80	0.80	0.75	0.76
TNY Unit Cost Savings		-0.21	-0.01	-0.01	0.05	-0.17
TNY Unit Cost Savings (%)		-36%	-1%	-1%	7%	-29%
Distribution only						
TNY Unit Cost	1.03	0.57	0.34	0.35	0.34	0.44
TNY Unit Cost Savings		0.47	0.23	-0.01	0.00	0.69
TNY Unit Cost Savings (%)		45%	40%	-3%	1%	67%

TNY=Treated Net Year

However, it should be pointed out that while there might be a significant amount of spare capacity within the Eritrean ITN programme, at least in low net delivery years, the integrated nature of the programme means that this spare capacity is likely to have been used for other productive activities.

Cost-effectiveness

Cost-effectiveness calculations began with the base case cost analysis and were derived using either cost per ITN or cost per TNY, as shown in Table 5. Table 7

shows the predicted health impacts of the intervention in a base scenario analysis. Using the total TNY measure of protection, it can be seen that significantly more deaths and thus DALYs were predicted to have been averted by the intervention due to the addition of protection through re-treatment delivery. By contrast, when only conventional ITNs, without re-treatment, were included in the calculation, the predicted health impact was much lower. These data illustrate again the urgent need to introduce LLINs instead of conventional nets.

Table 7 also illustrates the overall cost-effectiveness ratios that were derived in the base analysis. Overall, cost per death and DALY averted were generally low in terms of previously published WHO criteria for assessing interventions and research (Ad Hoc Committee 1996), but vary markedly depended on the output measure used. As expected, TNYs yielded significantly lower costs per death averted and DALY averted due to the large number of re-treatments provided by the programme.

Table 7: Estimated cost-effectiveness of the Eritrean national ITN programme (2005 USD).

	Using cost per ITN	**Using cost per TNY**
Deaths averted (2001–2005)	2,553	8,434
DALYs averted (2001–2005)	84,241	278,335
Cost per death averted (USD)	1,449	438
Cost per DALY averted (USD)	44	13

TNY=Treated Net-Year DALY=Disability-Adjusted Life Year

Sensitivity analysis

Sensitivity analysis was conducted to examine the effects of key assumptions on the cost per output and on cost-effectiveness ratios. The parameters examined included: lifetime of nets, discount rate, allocation of shared costs, the costs of nets and insecticide, and two scenarios corresponding to the use of Long-Lasting Insecticidal Nets (LLINs). The parameters have been varied to the extremes of their potential ranges, as determined by reviews of the literature or expert opinion.

Sensitivity analysis was also applied to the main assumptions about the connection between the cost output ratios and the cost-effectiveness calculations. Parameters

examined included the usage rates of the nets delivered, the percentage of nets used by children, the length of time during which a net or re-treatment offers protection, including the extended protection offered by LLINs, and the cost-to-output parameters which affect the overall cost of delivering a net or re-treatment.

The LLIN scenarios were calculated by assuming a nominal price and lifetime for types of LLINs: USD 5.00 and 3 years of protection or USD 7.00 and 5 years of protection. These scenarios were expected to bracket the cost-effectiveness ratios which would have been generated by assuming that some protection was offered by untreated conventional nets, an effect which was ignored in our base scenario. Table 8 shows the results of a sensitivity analysis for the cost per ITN and TNY delivered. Table 9 shows the results of the analysis for the other outputs and outcomes: deaths averted and DALYs averted.

Table 8: Results of sensitivity analysis: cost per ITN and Treated Net Year (TNY) delivered in Eritrea (2005 USD).

Parameter	Values assumed	Range (USD) per ITN	Range (USD) per TNY
Discount rate	1–10%	3.90–4.27	1.18–1.29
Cost of nets	1.50–5.00–7.00	3.62–6.88–8.75	1.09–2.08–2.65
Lifetime of nets	1 year–5 years	4.49–3.47	1.36–1.05
Cost of insecticide/liter	6.00–12.00	3.80–4.10	1.15–1.24
Shared costs	0–100%	3.29–10.30	1.00–3.12
LLIN use*	Base – 3 years, USD 5 – 5 years, USD 7	3.98–7.75–10.08 (NA - 7.28 - 9.60)	1.43–1.46–1.38 (NA - 2.43 – 1.92)
Length of protection offered by ITN or re-treatment	3 months – 6 months – 1 year	N/A	5.73–2.87–1.43

LLIN=Long-Lasting Insecticidal Net.
*numbers in brackets represent exclusion of re-treatment commodity costs and benefits

The overall range of results for the cost per ITN delivered is quite wide, ranging from USD 3.29 to 10.30, indicating that there are significant uncertainties in the cost measurements. However, there are several reasons to believe that the actual

variance is less than that suggested by the extremes of the sensitivity analysis. The upper values only exceed approximately USD 5.00 in the case of two variables: the cost of the nets and the allocation of shared costs. In terms of the cost of nets, USD 7 per net is an unlikely figure since the Eritrean programme was able to procure LLINs in 2005 for an average cost of USD 4.85. The other variable which gives rise to the most extreme value in the sensitivity analysis is the allocation of shared costs. In most cases, the personnel involved in the Eritrean ITN programme are involved with ITN activities for only a portion of the year, and even during that time, they are typically not fully dedicated to the programme. Most allocation measures, which were based on either the days of per diem paid to employees, or the amount of space used in offices and buildings, indicated that less than one-third of a given shared resource was being used for ITNs.

Table 9: Results of sensitivity analysis: cost per death and Disability-Adjusted Life Year (DALY) averted in Eritrea (2005 USD).

Parameter	Values assumed	ITN range (USD) per death averted	TNY range (USD) per death averted	ITN range (USD) per DALY averted	TNY range (USD) per DALY averted
Discount rate	1–10%	1,420–1,554	430–470	43–47	13–14
Cost of nets	1.50–5.00–7.00	1,315–2,503–3,183	398–758–963	40–76–96	12–23–29
Lifetime of nets	1 year – 5 years	1,634–1,263	495–382	50–38	15–12
Cost of insecticide/liter	6.00–12.00	1,383–1,490	419–451	42–45	13–14
Shared costs	0–100%	1,196–3,745	362–1,134	36–113	11–34
Length of protection offered by ITN or re-treatment	3 months – 6 months – 1 year	5,795–2,897–1,449	1,754–877–438	176–88–44	53–27–13
Usage of nets	25–50–100%	2,897–1,449–724	877–438–219	88–44–22	27–13–7
Children protected per net	1–2	1,449–724	438–219	44–22	13–7
LLIN use (TNY)*	Base – 3 years, USD 5 – 5 years, USD 7	438–531–502 (NA – 882 - 698)		13–16–15 (NA – 27 – 21)	

TNY = Treated Net Year; LLIN=Long-Lasting Insecticidal Net.
*numbers in brackets represent exclusion of re-treatment commodity costs and benefits

For the calculation of deaths averted and DALYs averted, the assumptions regarding (1) the length of protection provided by an ITN or re-treatment, and (2) assumptions concerning the usage of these nets among children had a dramatic impact on the results. While published information suggests that usage rates for children in net-owning households were high (on the order of 80%, meaning that 80% of households with nets had at least some children using them), the link between the actual number of nets delivered by the programme and usage is less certain (Macintyre *et al*., 2006). As a matter of course, some of the nets will be lost, damaged or misused. Hence, even if usage among households owning nets is high, the actual relationship between household ownership and nets delivered will yield lower rates of usage per net delivered. It was not possible to explicitly quantify this effect. However, usage rates were varied to include expected wastage rates in the sensitivity analysis (from 25% of nets used by children to 100%). Our assumptions were generally conservative, but it is clear that if usage of nets was worse and/or wastage higher, the cost effectiveness results presented here would overestimate the values presented for Eritrea. Additionally it should be noted that while we calculated health impacts in a manner intended to be consistent with the other studies in a large multi-country comparison, this scenario is reflective of a highly endemic malaria situation (Yukich *et al*., 2008). In a country with malaria epidemiology as varied as Eritrea's these results may not be reflective of the true epidemiological impact of the intervention in all settings.

When the scenarios using different LLIN assumptions were calculated, the cost-effectiveness ratios in all cases approached the result obtained by delivering inexpensive conventional nets and large numbers of re-treatments through campaigns. As it was not possible to disaggregate all re-treatment campaign costs from the analysis, it would be expected that the true LLIN cost-effectiveness ratios would improve slightly compared to those shown here.

3.5 Conclusions

Under the base case scenario the cost per DALY averted was as low as 13 USD. Considering that this is a conservative scenario, the result is clearly within the acceptable range for interventions in low-income countries as defined in previous WHO publications (Ad Hoc Committee 1996). The results of the sensitivity analysis

clearly showed that some parameters, such as the usage of the nets, their cost, and the length of protection delivered had important effects on cost per output and cost-effectiveness. Scenarios which incorporated LLINs showed only small changes in cost-effectiveness over the delivery of conventional nets and re-treatments but did so despite substantial increases in the upfront cost of ITN procurement. Since the use of LLINs would eliminate the need for re-treatment campaigns it appears that a full shift to LLIN technology would be beneficial in Eritrea and this has been adopted as the current national policy.

The Eritrean National ITN programme has increased ITN coverage dramatically to the point that it has essentially met the Abuja targets for ITN coverage in vulnerable groups within at least some areas of the country (Nyarango *et al*., 2006; Eisele *et al*., 2006). The new target of 80% protection in high-risk groups (WHO 2008; NMCP [Eritrea] 2004) should also be within reach of the programme. Two studies used regression analysis to demonstrate that ITNs had a measurable effect on clinical malaria incidence (Nyarango *et al*., 2006; Graves *et al*., 2008). The cost-effectiveness results presented here indicate that Eritrea has achieved this goal in an efficient manner and that it is possible to distribute ITNs at no charge to users through a system fully integrated into the existing health system. This is currently a unique model in SSA and worth investigating for other countries. It must be stressed, however, that such a system relies (1) on an adequately functioning health system, and (2) on a good outreach system, in the case of Eritrea in the form of CHAs. If these two conditions are not met, such a public sector approach might not be an effective way to distribute ITNs.

Similarly to the four other ITN programmes reviewed in a larger comparative study (Yukich *et al*., 2008), the Eritrean ITN programme is largely dependent on external financing, underscoring the importance of reliable and predictable funding for vector control activities. Ultimately, the Eritrean programme has been both successful in providing wide reaching high ITN coverage and sustaining it over a period of some years. Furthermore it has done so in a cost-effective manner, thus providing an example for other SSA countries, whether they still need “catch-up” ITN activities or need to “keep-up” already high ITN coverage.

4. Costs and effects of the Tanzanian national voucher scheme for insecticide treated nets

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4.1 Abstract

Background

The cost-effectiveness of insecticide-treated nets (ITNs) in reducing morbidity and mortality is well established. International focus has now moved on to how best to scale up coverage and what financing mechanisms might be used to achieve this. The approach in Tanzania has been to deliver a targeted subsidy for those most vulnerable to the effects of malaria while at the same time providing support to the development of the commercial ITN distribution system. In October 2004, with funds from the Global Fund to Fight AIDS Tuberculosis and Malaria, the government launched the Tanzania National Voucher Scheme (TNVS), a nationwide discounted voucher scheme for ITNs for pregnant women and their infants. This paper analyses the costs and effects of the scheme and compares it with other approaches to distribution.

Methods

Economic costs were estimated using the ingredients approach whereby all resources required in the delivery of the intervention (including the user contribution) are quantified and valued. Effects were measured in terms of number of vouchers used (and therefore nets delivered) and treated nets years. Estimates were also made for the cost per malaria case and death averted.

Results and Conclusion

The total financial cost of the programme represents around 5% of the Ministry of Health's total budget. The average economic cost of delivering an ITN using the voucher scheme, including the user contribution, was $7.57. The cost-effectiveness results are within the benchmarks set by other malaria prevention studies. The Government of Tanzania's approach to scaling up ITNs uses both the public and private sectors in order to achieve and sustain the level of coverage required to meet the Abuja targets. The results presented here suggest that the TNVS is a cost-effective strategy for delivering subsidized ITNs to targeted vulnerable groups.

4.2 Background

The cost-effectiveness of insecticide-treated nets (ITNs) in reducing morbidity and mortality is now well established (Wiseman *et al*., 2003; Picard *et al*., 1993). It is considered to be one of the most cost-effective ways of reducing the burden of malaria with an estimated cost per Disability Adjusted Life Year (DALY) averted of between $19 and $85 (1995 prices) (Goodman *et al*., 1999). International focus has now moved on how best to deliver ITNs to achieve a high level of coverage and what financing mechanisms might be used to achieve this. Recent debates have centred on the trade-off between the need for immediate impact and the long-term sustainability of increased coverage. Proponents of free distribution emphasize the urgency for immediate results, whereas those who favour a more pluralistic approach, including the development of domestic markets for ITNs, are keen to ensure the long term sustainability of delivery of ITNs (Muller & Jahn 2003; Stevens 2005; Curtis *et al*., 2003; Lines *et al*., 2003).

The WHO Position Statement on ITNs recommends implementation of strategies to sustain high levels of long-lasting insecticidal net (LLIN) coverage ("keep up" strategies) in parallel with strategies for achieving rapid scale- up ("catch up" strategies) with an overall aim of achieving full LLIN coverage (WHO 2007). However, the statement also recognizes that commercial markets are a valuable source of nets and recommends that where strong commercial markets exist or are developing they should be encouraged. The benefits of this are identified as ensuring longer-term access to nets and enhancing management of logistics and education efforts. The statement argues that separating the delivery of a targeted subsidy and the ITNs through distribution of vouchers or coupons to a target population makes it possible to stimulate local trade by building and maintaining a countrywide network of outlets. In this way "commercial demand and the commercial market are strengthened while the burden on the public health system of the logistics and distribution of ITNs, including long lasting nets, and of the associated management functions, is reduced" (WHO 2007). Importantly, the WHO statement recognizes that a decision to use vouchers should be considered in light of local experience.

The policy in Tanzania has been to combine the approaches of a targeted subsidy for those most vulnerable to the effects of malaria while at the same time providing support to the development of the commercial ITN distribution system using a social

marketing programme (Magesa *et al*., 2005). Social marketing in this context refers to a range of activities including improving the impact of locally manufactured nets by bundling them with long lasting insecticide and improving availability at the retail level. In 2008, this "keep up" approach will be reinforced by a massive "catch up" campaign for children aged between one and five who are not beneficiaries of the voucher programme.

In October 2004, with funds from the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM), the government launched the Tanzania National Voucher Scheme (TNVS), a nationwide discounted voucher scheme for ITNs for pregnant women and their subsequently new born infants. Table 10 shows the key events in the development of the scheme. Under the scheme, every pregnant woman who attends an antenatal clinic (ANC) is eligible to receive a voucher which can be used as part-payment for an ITN (defined as a conventional net bundled with a package of insecticide). The vouchers carry a fixed value: this was set at Tsh 2750 (around US$ 2) from October 2004 to December 2006, and was raised to Tsh 3250 from January 2007. Upon production of the voucher and her ANC card a woman can purchase any size of net using her voucher. This means that the value of the top-up amount is variable but in 2006 was around Tsh 1019 around 20% of the cost of a standard 4 × 6 net.

Table 10: **Timeline of key events**

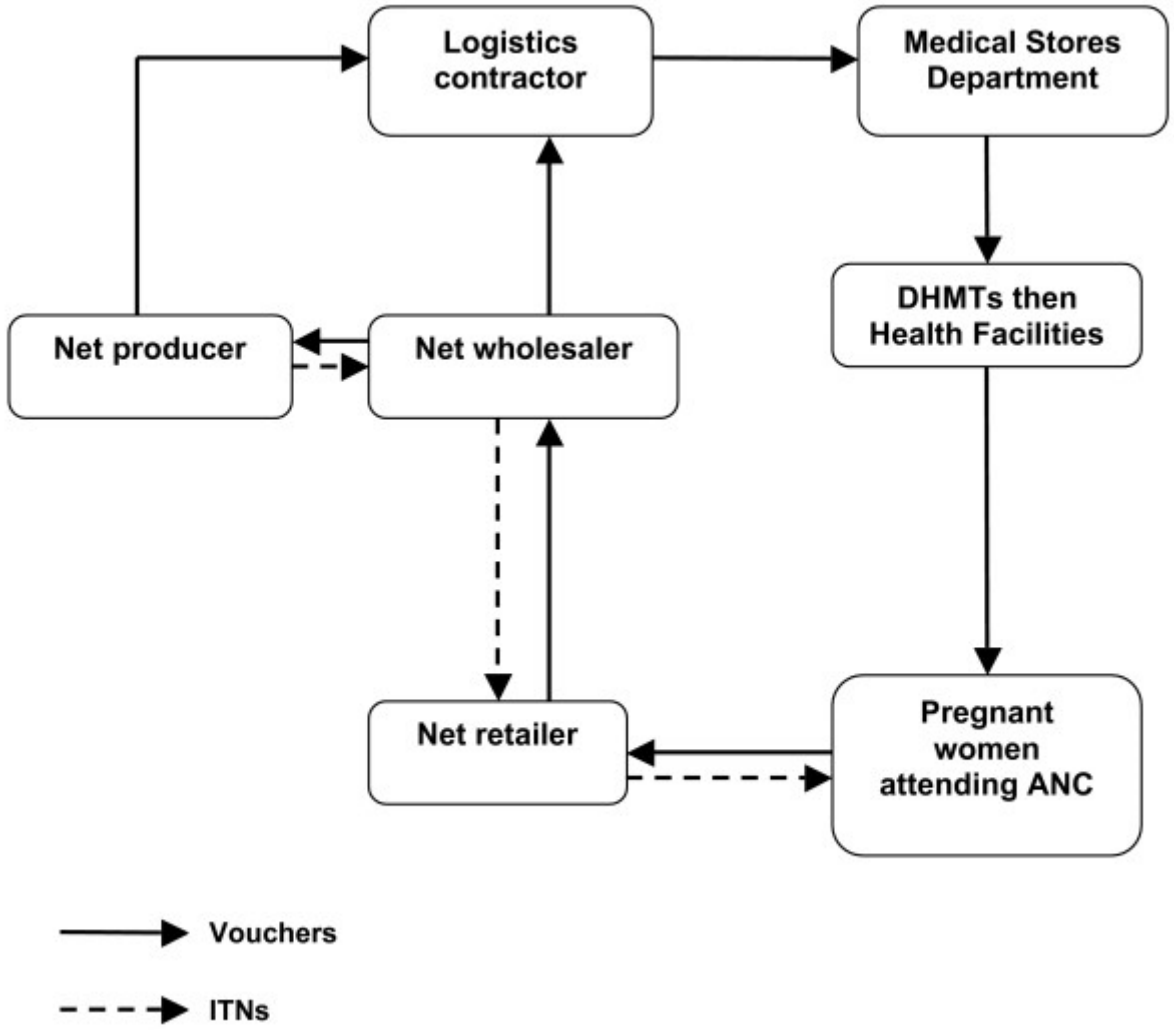
Time	Activity
Mar 2002	Contract signed with GFATM
Nov 2002	Agreement signed between MoH and GFATM
Mar 2003	GFATM Funds arrive
Apr 2003	ITN cell leader appointed with funds and technical assistance from Swiss Development Corporation and Swiss Tropical Institute
Oct 2003	Programme Assistant and advisor appointed
May 2004	Tender for contractors issued
June 2004	Contract issued to logistics and training contractors
Jul 2004	Roll out planning begins
Sep 2004	Rollout training begins Regional training begins for voucher redemption
Oct 2004	Contracts issued to auditors and monitoring and evaluation contractors
Oct 2004	TNVS scheme formally launched Voucher distribution begins phased roll-out by district
May 2006	100% nationwide coverage achieved

The TNVS was expanded from October 2006 onwards with funding from the President's Malaria Initiative (PMI) to provide a further voucher to the mothers and caretakers of infants aged nine months issued at the time of the measles vaccination, in order to provide continued protection for the child when it sleeps alone or with other siblings.

Implementation of the TNVS is through a public private partnership between the National Malaria Control Programme (NMCP), the district Council Health Management Teams (CHMTs), Reproductive and Child Health (RCH) facilities, private net manufacturers, over two hundred wholesalers, more than six thousand retailers and three non-governmental organisations (NGOs) contracted to the Ministry of Health. RCH staff and CHMTs are trained by World Vision Tanzania staff under a contract with the Ministry of Health and Social Welfare. Responsibility for voucher supply, distribution and redemption lies with the logistics contractor, Mennonite Economic Development Associates (MEDA), which procures vouchers and delivers

them to district level. District Medical Officers (DMOs) are responsible for delivering vouchers to RCH facilities. RCH facilities distribute them to pregnant women who then redeem the vouchers for ITNs at local retailers (Figure 7). Redeemed vouchers are returned to wholesalers and then to manufacturers in exchange for new stock. Cash is provided against vouchers only at the very top of the system, to any of the four local manufacturers or a limited number of large wholesalers. This is to minimize the misuse of vouchers for products other than ITNs. A parallel system is used to supply free insecticide re-treatment kits to children attending vaccination clinics at three months and nine months, to encourage regular re-treatment of nets. The Medical Stores Department (an autonomous agency of the Ministry of Health) supplies insecticide re-treatment kits (IRK) directly to the districts through the distribution channels used for drugs and other medical supplies. A phased roll-out of the TNVS was launched in the first districts in October 2004, and all districts on the mainland were covered by May 2006.

Figure 7: Structure of the Tanzanian National Voucher Scheme



The Ifakara Health Research and Development Centre and the London School of Hygiene and Tropical Medicine were contracted to undertake the monitoring and evaluation of the TNVS. The aim of this paper is to analyse the costs and effects of the scheme and to compare with other approaches to distribution. The perspective of the analysis is of both the provider and users whereby all costs and consequences attributable to the donors, the MOH and users were estimated.

4.3 Methods

Data collection

To ensure that this costing is comparable with future evaluations the analysis followed standardized guidelines recommended for costing ITN distribution systems (Kolaczinski & Hanson 2006). Economic costs were estimated using the ingredients approach whereby all resources required in the delivery of an intervention are quantified and valued. This involved collecting actual line item expenditure and activity data wherever possible. In other instances, budget data were used to estimate expenditure. Project cost data were collected retrospectively from accounting records held by NMCP and the implementing partners. Data on the costs incurred by users were derived from the TNVS household survey and retail audit (Hanson *et al.*, 2006; Stephen *et al.*, 2006). Household survey data also provided information on the mean number of children protected by a net bought with a voucher. Semi-structured interviews were held with key stakeholders and project staff to identify activities not recorded in project documentation and information on programme outputs. Estimates of ITN effectiveness (in terms of averted deaths and malaria cases) were derived from the literature (Lengeler 2004).

Categorization and analysis of costs

Economic costs or opportunity costs represent the value of resources in their next best alternative use. In this analysis economic costs differ from accounting financial costs in two main ways: first an equivalent annual capital cost is calculated for those items which are deemed to last more than one year and second any donated or subsidized goods and services (e.g. time of users to collect nets) are valued at their estimated market cost.

Cost identification was done by tracking the financial and economic costs associated with each activity. The time-frame for identifying costs ran from the first planning workshop held in early 2004 through to July 2006. The scheme involved four areas of activity: central management, training of key stakeholders, promotion activities and the logistics associated with the distribution, redemption and accounting for vouchers (see Table 11). Shared costs such as office equipment, office rent and office furniture and utilities were grouped as overheads. Budget estimates provided by the

implementing partners were used to assign values to these items. Fixed asset registers were also used to identify and value capital equipment.

Table 11: Contributors to the intervention

Contributor	**Role**
Global Fund to Fight AIDS, Tuberculosis and Malaria	• Funder of TNVS main activities
Swiss Development Corporation (SDC) and Swiss Tropical Institute (STI)	• Funder of ITN cell
Ministry of Health National Malaria Control Programme (NMCP)	• Project management
Mennonite Economic Development Agency (MEDA)	• Logistics contractor • Voucher distribution and redemption
World Vision/CARE	• Conducting roll out training
Population Services International (PSI)	• Social marketing and technical support
District Health Management Team	• Costs of voucher distribution and reporting
Health Facilities	• Distribution of vouchers at ANC clinics
Retailers and wholesalers	• Handling vouchers
Households	• Top-up charges for ITNs • Time costs associated with collection of nets

Since 1999, a large network of stakeholders in Tanzania has promoted and supported a coordinated national ITN strategy (NATNETS). Household ownership of an ITN has increased substantially (from virtually nil to around 36% by 2007) and a strong commercial sector for the production, distribution and retailing of mosquito nets has emerged. The NATNETS strategy consists of four components: i) An ITN 'cell' based at the National Malaria Control Programme (NMCP), ii) SMARTNET a strategic social marketing program funded by the UK Department for International Development and the Royal Netherlands Embassy (this finished in June 2007), (iii) the provision of insecticide treatment and re-treatment kits to net manufacturers and retailers, and iv) the TNVS. A key decision in framing the analysis was determining the extent to which costs associated with the wider activities of the NATNETS

programme should be included. While it is clear that the TNVS could not have taken place without the existence of wider social marketing activities, the focus of the present analysis are activities that are directly related to the voucher scheme only. The ITN cell of NMCP comprises a team leader and two programme staff. Following discussions with staff they are estimated to spend between 75 and 80% of their time on TNVS activities and this allocation was used in the baseline analysis. The activities of the wider NATNETS programme are the subject of a separate evaluation (Yukich *et al*., 2007).

Recurrent and capital costs

Expenditure was disaggregated by recurrent and capital expenditure, showing the difference between investment costs that are one-off and recurrent costs that are ongoing and represent the running costs of any programme implementation (see Table 12). Capital costs included formative research, building space, equipment for office use (e.g. computers), vehicles and ITNs (includes voucher subsidy and user contribution). Formative research refers to the costs of running a pilot voucher scheme in two districts but excludes on-going monitoring and evaluation activities. All capital items were annualized over assumed life spans using a discount rate of 3%. This enables an annual equivalent cost to be estimated that is then added to the annual recurrent estimate. This process reflects the value in use of capital items, rather than reflecting when the item was purchased. The useful life of vehicles was estimated at eight years. Formative research, computers, furniture and equipment were all estimated to have a useful life of five years. Nets were assumed to last for three years, although the effect of initial treatment and any subsequent re-treatments were assumed to provide one year of protection. Recurrent costs included staff related costs, consumables and fees (such as banking charges, service fees, and communication charges).

Table 12: Costs included in the analysis

Capital	
	Formative research
	Planning costs
	Consensus building and meetings
	Initial training
	Buildings
	Vehicles
	Equipment and furniture
	ITNs (user contribution and subsidy)
Recurrent	
	Insecticide
	Personnel
	Fuel/Maintenance of vehicles
	Office/warehouse rental
	Advertising and promotion
	Supplies/overheads
	Management cost

All cost items were valued according to their market value in the year they were purchased in either Tanzanian shillings or US dollars, depending on where they were purchased. All costs were then translated into US dollars at the Tsh-US$ exchange rate for the year in which they were incurred (in July 2006 1340 Tsh = 1 US$). All costs are reported in 2006 US dollars.

An attempt was made to distinguish between start up costs and running costs of the programme. Start up costs are classified as one-time activities to get the programme up and running and includes formative research undertaken in two districts in 2004, planning activities by NMCP in the months leading up to the formal launch and the training of health workers by Care and World Vision. The start up costs of NMCP are defined as those relating to activities undertaken by the ITN cell staff from the appointment of the ITN cell leader to the official launch date in October 2004. In contrast to the formative research start up costs were not treated as a capital cost, as it is likely that some activities will need to be repeated at some point.

Estimating user and health facility staff costs

The voucher scheme works on the basis that part of the price of the net is paid for by users. An important part of this analysis is the inclusion of user costs as well as the cost incurred by the providers of the voucher scheme. The retail audit and household

survey provided information on the average top-up payment by users and typical travel costs involved in collecting nets (Hanson *et al*., 2006; Stephen *et al*., 2006). The household survey reported that it takes women on average 40 minutes to get to a shop to redeem the voucher (Hanson *et al*., 2006). The opportunity cost of the total time taken to redeem the vouchers was based on the minimum wage of an agricultural worker and estimated to be Tsh 520 ($0.39). The associated average travel costs were found to be 68 Tsh ($0.05). Data from the retail audit indicated that the mean top-up price charged by retailers was Tsh 1019 ($0.76) (Stephen *et al*., 2006). This figure was varied in the sensitivity analysis.

The distribution of the vouchers at the health facility involves a number of activities by clinic staff including communal health education talks, explaining how the scheme works to individual women during antenatal clinic sessions, filling in the ledger books, collecting new voucher books and delivering used voucher books to the District Medical Officer (DMO). Although difficult to quantify it is important that these opportunity time costs are reflected in the results. Based on informal discussions with clinic staff and those involved in the monitoring and evaluation of the scheme it was estimated that these costs would amount to around five minutes per voucher distributed.

Cost – effectiveness

As the effectiveness of ITNs in reducing infant and child mortality and improving maternal health has been amply demonstrated (Lengeler 2004), no health impact data were collected as part of this study. The focus instead is on programme outputs i.e. the number of nets delivered to users. Only outcomes for children under five years of age are considered here. Estimating the number of malaria deaths averted by the intervention depends on net coverage, usage and the relationship between treated net years and mortality. The review by Lengeler found that in areas with stable malaria, ITNs reduced the incidence of uncomplicated malarial episodes by 50% compared to no nets (Lengeler 2004). They estimated that 5.5 lives could be saved each year for every 1,000 children protected with ITNs. In order to translate output data into health outcomes, the baseline analysis assumes that all vouchers redeemed at shops are used to purchase a net. Survey data from the TNVS

household survey shows that on average each voucher net protects 0.88 children. This is reduced to 0.5 in the sensitivity analysis to take account of net wastage.

The outputs of the scheme are measured in terms of number of nets delivered to women and number of re-treatments performed. These outputs are combined into *treated net years (TNY)*. The combined indicator TNY is useful because it allows the inclusion of re-treatments of existing nets as part of the outcome measure. The WHO defines a conventionally treated net as any net that has been treated with a WHO recommended insecticide at least once a year (WHO 2007). The baseline analysis therefore assumes that either a re-treatment or a new ITN provides one year of protection for any individual using that net. The sensitivity analysis examines the impact of reducing insecticide effectiveness from 12 to 6 months. The following ratios are estimated: cost per voucher used (and, therefore, net delivered); cost per treated net year (TNY); cost per malaria case averted; cost per malaria death averted.

4.4 Results

Financial and economic costs

Over the first two years (2004–2006), the total provider financial costs of the TNVS programme were $10,680,516 (Table 13). Figure 8 provides a graphical breakdown of provider costs with staff costs making up the biggest component, followed by promotion activities and the costs of the ITNs themselves. Including the user contribution takes the total to $11,837,838. Economic costs include the user top up plus donated inputs in the form of ANC clinic time and user travel time. Capital costs are also annualized to reflect the annual equivalent value in use. The economic costs of the programme are $10,599,367 (see Table 14).

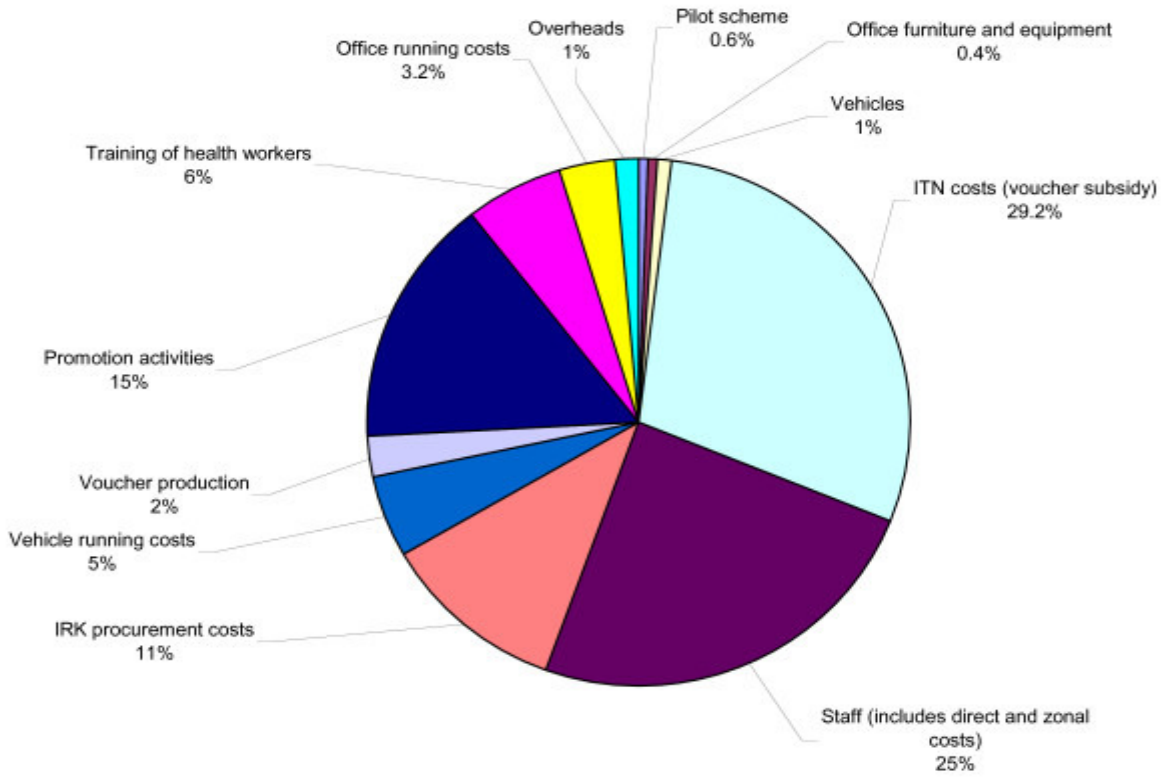
Table 13: Financial Costs, Provider plus User, 2004-2006

	US$	%	Financial cost per voucher used (US$)
Capital costs			
Formative research	68,736	1%	0.05
Office furniture and equipment	46,944	0%	0.03
Vehicles	83,110	1%	0.06
ITN costs (voucher subsidy)	3,123,294	29%	2.24
Total Capital	**3,322,084**	**31%**	
Recurrent costs			
Staff (includes direct and zonal costs)	2,609,508	24%	1.87
IRK procurement costs	1,200,355	11%	0.86
Vehicle running costs	522,204	5%	0.37
Voucher production	255,275	2%	0.18
Promotion activities	1,645,608	15%	1.18
Training of health workers	627,224	6%	0.45
Office running costs	347,077	3%	0.25
Overheads	151,182	1%	0.11
Total recurrent	**7,358,432**	**69%**	
Total provider costs	**10,680,516**		
User direct costs			
ITN user contribution	1,157,322	11%	0.83
TOTAL FINANCIAL COSTS	**11,837,838**		**8.49**

Table 14: Economic costs, 2004-2006

	$US	%
Capital		
Formative research	27,121	0.3%
Office furniture and equipment	18,652	0.2%
Vehicles	21,394	0.2%
ITN costs (voucher subsidy)	2,153,047	20.4%
Sub total	**2,220,213**	**21.0%**
Recurrent costs		
Staff	2,609,508	24.7%
IRK procurement costs	1,200,355	11.4%
Vehicle running costs	522,204	4.9%
Voucher production	255,275	2.4%
Promotion activities	1,645,608	15.6%
Training of health workers	627,224	5.9%
Office running costs	347,077	3.3%
Overheads	151,182	1.4%
Sub total	**7,358,432**	**69.7%**
User and ANC staff costs		
ITN user contribution	797,802	7.6%
Direct travel costs	118,134	1.1%
ANC clinic staff costs	64,786	0.6%
Sub total	**980,722**	**9.3%**
Total	**10,559,367**	**100%**

Figure 8: Breakdown of provider financial costs



Cost per voucher used and per treated net year

As at July 31st 2006 2,424,987 vouchers had been sent to District Medical Offices for distribution to pregnant women. Of these 1,157,885 vouchers had been utilized by pregnant women and the vouchers returned to MEDA. Based on data from the household survey and from MEDA's own calculations from vouchers returned compared with matching stubs (counterfoils), NMCP estimates that returned vouchers represent around 83% of all vouchers actually utilized by women at that point. Therefore the actual number of voucher nets delivered to pregnant women using the TNVS was at least 1,395,042 at the end of July 2006. This figure represents the baseline output figure for all the cost-effectiveness estimates. On this basis the financial cost (including user top up) per voucher used, and therefore ITN delivered, is $8.49 and the economic cost is $7.57. A total of 1,600,000 insecticide re-treatment kits were also distributed by the programme during the same time period. The household survey found that 69% of mothers who received a re-treatment kit actually used it to retreat their nets and the baseline analysis is adjusted

on this basis. If the impact of delivered voucher nets and re-treatment kits (adjusted for lower retreatment rates) are added together it is calculated this led to a total of 2,499,042 treated net years and a cost per treated net year of $4.23.

It is estimated that start up costs comprise around 8% of the total costs (see Table 15). If these costs are removed the economic cost per ITN delivered is estimated to be $6.93. The cost per treated net year is $3.87. The majority of start up costs represents training activities, some of which will need to be repeated at a future point in the scheme to ensure that skills and knowledge of health workers are maintained.

Table 15: Economic costs – 'start up' versus ongoing costs

	US$	**%**
'Start up' costs		
Formative research	27,121	0.3%
NMCP planning and pre launch activities	235,014	2%
Training of health workers	627,224	6%
Sub total	**889,359**	**8%**
Capital costs		
Office furniture and equipment	18,652	0%
Vehicles	21,394	0%
ITN costs (voucher subsidy)	2,153,047	20%
Sub total	**2,193,093**	**21%**
Recurrent costs		
Staff	2,374,494	22%
IRK procurement costs	1,200,355	11%
Vehicle running costs	522,204	5%
Voucher production	255,275	2%
Promotion activities	1,645,608	16%
Office running costs	347,077	3%
Overheads	151,182	1%
Sub total	**6,496,194**	**62%**
User and ANC staff costs		
ITN user contribution	797,802	8%
Direct travel costs	118,134	1%
ANC clinic staff costs	64,786	1%
Sub total	**980,722**	**9%**
GRAND TOTAL	**10,599,367**	**100%**
TOTAL COST MINUS START UP	**9,670,009**	

Cost per malaria case and death averted

The programme resulted in a total of 2,499,042 treated net years and the mean number of children protected per voucher net is 0.88. If it is assumed that 1,000 treated ITNs will avert 5.5 child deaths per year (Lengeler 2004), it is estimated that the programme averted 12,039 child deaths at an economic cost of $873 per child death averted. For averted malaria cases, the incidence of malaria outpatient attendances in children under 5 is reported as 723 per 1,000 per year (NMCP unpublished data). If it is assumed that ITNs lead to a 50% reduction in malaria incidence (Lengeler 2004), it is expected that 794,995 malaria cases could be averted each year at a cost of $13 per malaria case averted.

Sensitivity analysis

Sensitivity analysis was used to see if any of the results were sensitive to changes in uncertain parameters including: choice of discount rate; lifetime of vehicles; exchange rates; retail price of nets and proportion of nets retreated. On the effectiveness side the analysis varied the life time of ITNs, insecticide effectiveness, and utilization of ITNs amongst children. The main results from the sensitivity analysis are summarized in Table 16.

Table 16: Sensitivity analysis of selected parameters

Variable	**Baseline values**	**New value**	**Output indicators (baseline result)**			
			Cost per voucher used ($7.57)	**Cost per treated net year ($4.23)**	**Cost per malaria case averted ($13)**	**Cost per death averted ($873)**
User top up price	TZS 1019 ($0.83)	30% price reduction	$7.40	$4.13	$13	$857
		200% price increase	$8.14	$4.54	$14	$943
ITN Life expectancy	3 years	2 years	$8.59	$4.79	$15	$995
Mean number of children per net	0.88	0.5	$7.57	$4.23	$23	$1536
Insecticide re-treatment rates	69%	50%	$7.57	$4.81	$19.	$999
ITN definition	Treated within last 12 months	Treated within last 6 months	$7.57	$8.45	$27	$1754
Long lasting nets			$8.09	$2.70	$8.48	$560

On the cost side, changing the discount rate, useful life of vehicles, exchange rates and staff time administering the scheme had a negligible impact on overall economic costs and hence cost per ITN delivered. The average top up price charged was Tsh 1019 ($0.8). The sensitivity analysis examined the impact of increasing or lowering the top up amount by 30% and found that it had only limited impact on the cost per ITN delivered. However this assumes that the relationship between voucher redemption and price remains constant, which is unlikely. Examining the responsiveness (or price elasticity) of demand to changes in price is beyond the scope of this paper but will be the subject of future work using data from the household and retail surveys.

Varying parameters on operational and effectiveness variables had a bigger impact on results. The base case analysis assumes that 69% of re-treatment kits distributed are actually used to retreat nets. If this figure is reduced to 50%, the cost per treated net year increases from $4.23 to $4.81, the cost per case averted increases from $13 to $19 and the cost per death averted increases from $873 to $999. If the useful life of an ITN is assumed to be two rather than three years, the cost per ITN delivered increases to $8.59, the cost per treated net year is $4.79 and the cost per death averted is $995. If the mean number of children protected per voucher net falls from 0.88 to 0.5 the cost per malaria case averted increases from $13 to $23 and the cost per death averted increases from $873 to $1536.

Table 16 also shows the estimated economic cost per malaria case and death averted if all manufacturers switch to long lasting nets with three years life expectancy and a cost of $5. Aside from cost per ITN delivered, all cost per output ratios are substantially lower than with ordinary nets reflecting the greater effectiveness of long lasting nets versus the relatively high cost of procuring re-treatment kits and lower re-treatment rates associated with ordinary nets.

4.5 Discussion and Conclusion

A total provider financial cost of $10.6 million for the delivery of 1.3 million voucher nets represents around 5% of the Ministry of Health's total budget. The average economic cost of the voucher scheme, including the user top-up, was found to be $7.57 per ITN delivered and $873 per death averted. An analysis of a free distribution of long lasting nets with a measles immunisation campaign in Togo reported a cost of

$5.95 per net distributed, $4.40 per malaria case averted and $856 per death averted (Mueller *et al*., 2008). In Malawi, a study of social marketing programme which delivered heavily subsidized nets through health facilities reported a figure of approximately $3 per net delivered (Stevens *et al*., 2005). In line with other evaluations the costs presented here represent an economic cost (Goodman *et al*., 1999; Hanson & Goodman 2004). Importantly, we have attempted to capture as fully as possible all costs associated with running a national scale ITN distribution programme, including all training and logistical activities. This analysis differs from many others in that it captures the full costs incurred including time and travel costs of users to collect the nets as well as the top up prices charged by retailers. While the results presented here are somewhat higher than that reported in Togo and Malawi they are well within the benchmarks set by other malaria prevention studies. A review of all ITN cost effectiveness studies for the Disease Control Priorities Project found that the cost per death averted varied from $254 to $3,437 (Breman *et al*., 2006; Mulligan *et al*., 2005). The only other evaluation of a social marketing and voucher project, although on a smaller scale, reported a cost per death averted of $1,603 (Hanson *et al*., 2003).

Given the absence of pre- and post-incidence data on malaria, the calculations of effectiveness presented here are based on national averages and are indicative only. These estimates rely on the assumption that coverage and utilization remain at the same rate over the two years. The estimate of ITNs effectiveness is conservative since it only included effects for children under five and did not include any beneficial effects on the mother or other family members. As the TNVS is a targeted programme it is expected that a high proportion of nets will be used to protect infants and varying the usage rate of ITNs among children has a strong impact on its cost-effectiveness.

This analysis did not estimate the wider effects of using the retail sector as a mechanism for delivering nets. Evidence from the TNVS retail survey indicates that nets are now very widely available even in rural areas (Stephen *et al*., 2006). It is not possible to judge at this stage the extent to which this is a result of the voucher scheme alone. However, together with the social marketing activities of SMARTNET, the existence of a public subsidy for ITNs is thought likely to draw more retailers to the ITN market as well encourage existing retailers to remain. This has the potential

for wider economic benefits to wholesalers, retailers and ultimately consumers (in the form of lower prices) from an expanding market.

Cost-effectiveness analysis cannot address directly issues of sustainability or equity, but both are important to any discussion of how to scale up coverage, especially to the most vulnerable groups. A voucher system in the context of wider social marketing activities can promote sustainability objectives by providing a long-term system for distributing nets. But charging top up prices threatens equity objectives if the poorest groups cannot afford to pay. Delivery systems for ITNs have been debated for several years, but the evidence base on cost-effectiveness of alternative delivery systems is still largely drawn from small scale projects and relatively short follow-up periods, and does not yet reflect what would happen in large scale national programmes over time. More information is also needed on how to use existing market channels to distribute nets, free or otherwise. Continued monitoring and evaluation has a role to play in establishing the extent to which these distribution channels are sustainable and how they can supplement campaigns. Webster and colleagues note that free distribution or delivery of ITNs through integration with other campaigns (eg immunization) provides a fast catch-up solution to scaling up coverage (Webster *et al*., 2007). But where no other system is in place to keep-up this coverage, ownership is transient. The TNVS is designed to keep-up coverage, but to properly compare the effectiveness and cost-effectiveness of these different systems, they should be monitored over a period of at least three to five years (Webster *et al*., 2007).

No-one can predict how the donor environment will change over the next five years, and there is no guarantee of long term commitment by donors for free net distribution. Even if that commitment is forthcoming, many believe exploring a mix of strategies of delivery which take account of the local context provides the best basis for scaling up (Muller & Jahn 2003; Stevens *et al*., 2005). In Tanzania it is recognized that neither the public sector nor the commercial sector alone can achieve and sustain the level of coverage required to meet the Abuja targets. Despite the success of free distribution systems for achieving rapid scale up of coverage, the WHO recognizes the importance of commercial channels in some settings (WHO 2007). Thus in Tanzania there has been a mixed approach to delivering ITNs: combining social marketing techniques with the targeting of vulnerable groups with subsidies

(Magesa *et al*., 2005). The results presented here suggest that the TNVS, a key part of that strategy, is a cost-effective method of delivering subsidized ITNs to targeted groups.

5. The costs and consequences of commercial sector ITN promotion in Senegal

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5.1 Abstract

Background

Insecticide-treated nets (ITNs) are known to be a cost-effective method for preventing malaria. Extensive debate has, however, surrounded the choice of distribution methods at the country level. Unfortunately, little information on the costs and cost-effectiveness of large scale ITN programmes is available to underpin this debate.

Methods

This study used a standardized methodology, as part of a larger comparative study, to collect cost data and project cost-effectiveness information from a large programme providing commercial sector promotion with an emphasis on sustainability for ITN delivery in Senegal.

Results

Base case analysis results indicated that the average annual cost of ITN delivery (2005 USD 8.05) was comparable with past ITN delivery studies at different scales. Costs to the provider (2005 USD 3.62) were much lower and compared favorably to costs examined in other countries, mainly because a large portion of financing for the intervention was provided by purchasers of nets. The intervention's cost-effectiveness is in an attractive range for sub-Saharan Africa: cost per DALY averted: USD 89-67. As a significant portion of all nets sold were long-lasting insecticidal nets (LLINs), the cost-effectiveness estimates presented here are conservative. Sensitivity analysis suggested that the cost per DALY averted could fall near USD 20 in a full LLIN scenario. Costs were largely driven by relatively high net purchase costs at the retail level and may fall with increasing scale.

Conclusions

Commercial sector subsidies appear to be a cost-effective method for the distribution of significant numbers of ITNs with the potential benefit of added financial sustainability, but do not appear to deliver enough ITNs to reach international targets. Commercial distribution of ITNs has the potential to serve as an important complementary role in larger ITN distribution systems, and could play an important role in providing a source of ITNs to those not targeted by subsidized or free distribution over the short term, and a source of resupply for all over the long term.

5.2 Introduction

Senegal is the western most country in Africa and lies at the upper edge of climactic suitability for malaria transmission. Nevertheless, essentially the entire population lives in areas regarded as endemic for malaria (www.mara.org.za). Transmission is generally seasonal and varies in timing and intensity, depending on the climactic region of the country. The *Programme National de Lutte contre le Paludisme* (PNLP) has developed a national strategic plan with the target of reducing the morbidity and mortality burden of malaria to below 50% of 2000 levels by the year 2010 (PNLP Senegal 2008).

Insecticide treated (bed) nets (ITNs) are a pillar of the international plan for malaria control (RBM 2005)) and are considered an important arm of the National Malaria Control strategy (PNLP Senegal 2008). Several approaches have and are being used for ITN delivery in Senegal, including subsidized sale by non-governmental organizations (NGOs) and community based organizations (CBOs). One strategy aimed at long term sustainability has been based on the continued development of the commercial market for ITNs as part of the USAID-supported NetMark project.

NetMark is a large multi-country project operated by the Academy for Educational Development (AED) (NetMark 2008). Its mandate is to increase demand for and expand the availability of ITNs with a market-based approach of shared risk and investment. NetMark is based on the premise that as demand for ITNs grows within a competitive market, consumers will benefit from improvements in the quality of nets, lower prices, and wider availability. The project also subscribes to the idea that though the commercial sector is more sustainable in the long run, coordination with other stakeholders and the use of public subsidies is important and appropriate. In recent years different subsidy mechanisms have been introduced and expanded in Senegal to complement the commercial market approach.

NetMark Senegal was launched in 2002, but formal commercial activities began in 2003. The programme has several partners in Senegal including, Bayer CropScience AG (local distributor: Senphyto), Siamdutch Mosquito Netting Co. Ltd. (local distributor: Palunet and now called Tana Netting) and Vestergaard Frandsen Group (local distributor: Negitra). Since the present study was completed, NetMark

Senegal has expanded to include BASF and Sumitomo as well. For demand creation activities the programme works with both international manufacturers and local distributors. Local as well as international advertisers develop, create and disseminate locally relevant promotional materials and activities, including provision of matching funds for local distributor advertising and promotion campaigns. Additionally, NetMark coordinates activities with the Ministry of Health and the PNLP. During the period under review, the Netmark programme included a small-scale targeted subsidy programme, which has since expanded to cover five regions.

In much of West Africa a commercial sector for bednets and a culture of use of nets for sleeping existed long before international ITN interventions. In the past many or most of these nets were locally tailored nets made from a variety of materials (Aikins *et al*., 1993; Aikins *et al*., 1994, D'Alessandro *et al*., 1994). In Senegal some imported nets were also sold, but these represented only a part of the total market. According to the NetMark baseline survey in the year 2000, a majority of nets in net-owning households were obtained from informal commercial sources, and approximately 19% of all nets in net-owning households were reported to be tailor-made (NetMark 2001). Only about 14% of all the nets were obtained from non-commercial sources such as projects or clinics (NetMark 2001). The high cost of nets was stated most commonly as the reason for not owning a net and was more commonly stated among the lower SES quintiles (NetMark 2001, NetMark 2001b). Few commercially available nets were treated with insecticide before the start of the NetMark Senegal project, and prices for untreated nets, based on market sampling and reports from net distributors, ranged from 8 to 16 USD (D. McGuire *personal communication*; NetMark 2000). Tax and tariff barriers to net and ITN market expansion were high with import duties on nets and individual finished insecticide re-treatment kits (IRKs) set over 40%, plus an additional 20% Value Added Tax (NetMark 2000). Later, NetMark was a major actor in the policy change to lift taxes and tariffs on imported ITNs in Senegal.

The 2000 UNICEF MICS round II survey showed very low levels (below 2%) of ITN usage among under-five children (Table 17). It also showed that nationwide only approximately 15% of under-five children slept under an untreated net (Government du Senegal & UNICEF 2000). The 2000 NetMark baseline survey showed similar

rates of coverage for any net in under-five children (17.7%) but a very low level of use for insecticide-treated nets. Household net possession was approximately 34% (NetMark 2001). In addition, the survey showed that the distribution of nets and ITNs was at least equitable, with indicators showing higher ownership and usage of both nets and ITNs in rural areas and lower socioeconomic groups, though these differences were not always significant. However, comparisons between NetMark surveys and nationally representative surveys such as UNICEF's MICS or ORC Macro's DHS surveys must be made with care. NetMark surveys are designed to focus on specific areas and target groups and to reveal market information and are therefore not necessarily nationally representative.

Table 17: Net ownership and usage in Senegal according to some recent surveys.

	2000 MICS		2000 NetMark		2004 NetMark		2005 DHS	
	Any net	ITN	Any net	ITN	Any net	ITN	Any Net	ITN
Children under nets last night All	15.2%	1.6%	17.7%	4.6%	35%	23.9%	13.9%	7.1%
Urban	13.3%	1.5%		3.9%		25.1%	13.7%	7.3%
Rural	16.3%	1.7%		5.0%		23.3%	14.0%	7.0%
Pregnant women under nets last night All				5%		31%	14.4%	8.5%
Urban							14.8%	9.9%
Rural							14.1%	7.8%
Household possession All			33.6%	8.2%	56.1%	38.7%	38.0%	20.2%
Urban			28.8%	7.3%	53.3%	40.3%	31.7%	18.0%
Rural			36.8%	8.8%	58.0%	37.3%	43.9%	22.2%

MICS= UNICEF multiple indicator cluster survey. DHS=Demographic and health Survey.
ITN=Insecticide-Treated Net.

Past experience indicates that subsidizing the commercial sector may be one possible avenue for delivery of ITNs in Africa (Schellenberg *et al*., 2001; Magesa *et al*., 2005; Webster *et al*., 2005). So far there has been no analysis of the cost of this

approach on a large scale in sub-Saharan Africa. Recently, the various approaches to ITN delivery have been the subject of a fierce debate, with some arguing that mass distribution of fully-subsidized ITNs provides the only way to rapidly achieve international health targets, while others arguing that commercial distribution systems offer an important and more reliable distribution mechanism (Lengeler *et al*., 2007). Only recently has information begun to be available for programmes operating on a large scale in other countries (Stevens *et al*., 2005; Mueller *et al*., 2008; Mulligan *et al*., 2008; Yukich *et al*., 2008). At present, there seem to be a strong consensus that multiple approaches are required in each country, with some strategies more suited to a rapid "catch-up" and other better suited to maintain sustainably high coverage (Lengeler & deSavigny 2007).

This work is carried out in the frame of a large multi-center assessment designed to produce estimates of cost and cost-effectiveness for the main ITN distribution strategies being considered in sub-Saharan Africa (Yukich *et al*., 2008). The information presented here aims to illuminate the debate about the best strategies for ITN distribution and further highlight the role commercial sector promotion can play in an integrated strategy.

5.3 Methods

Time frame and perspective

The present study captured costs from the beginning of US fiscal year 2000 through the end of US fiscal year 2005, thus covering both the start-up and running costs of the programme.

In general, we have used the provider perspective for cost analysis. We have, however, included the direct user costs of net purchase, because these are felt to be important to the usage and uptake of the intervention. Furthermore, in a programme using commercial sector delivery mechanisms, price changes may be important indicators of market development and expansion as well as returns to scale in the expansion of the delivery systems. Attempts have been made to follow existing guidelines for the cost evaluation of ITN programmes, as well as to use methodologies comparable to past studies in order to maximize comparability (Creese & Parker 1994; Stevens *et al*., 2005; Kolaczinski & Hanson 2006).

Additionally, this study was one part of a larger comparative study, so types of costs included, assumptions used in the base analysis as well as types of sensitivity analysis conducted were standardized across each study site (The full report of the multi-center study is available electronically (Yukich *et al*., 2007) and published in summary (Yukich *et al*., 2008)).

Types of costs included

NetMark programmes generally require few personnel and little capital in-country, therefore a significant amount of personnel and other costs are incurred in regional or national headquarters. An attempt was made to identify all of the central staff and overhead costs attributable to the country programme and include them in the analysis. However, since NetMark activities are distributed over no fewer than seven countries we expect to have missed some costs, although these likely to have been small.

Additionally, as the NetMark programme was focused almost entirely on the distribution of ITNs through the commercial sector in 2005, no costs related to the use of public resources were captured. At the time these costs were small and refer only to the targeted-subsidies scheme using vouchers, which operated in only a limited number of locations. Costs included are detailed in Table 18.

Table 18: Costs included in the Senegal analysis.

Capital	Formative research Brand creation/initial market research Setup meetings/conferences at all levels Initial training Buildings Vehicles Equipment and furniture ITNs
Recurrent	Insecticide Personnel Fuel/maintenance of vehicles Office/warehouse rental Advertising and promotion Supplies/overheads Management cost Basic evaluation and monitoring (excluding specific research cost)

Cost collection

Costs were collected by a review of the financial records of the NetMark Senegal project. Additional cost information was collected through review of other program records, including store check and survey data, activity reports, interviews with stakeholders, and reviews of commercial partner documentation. Interviews with stakeholders and site visits were also conducted to estimate levels of activity which were not reflected in the financial records.

Cost classification and adjustments

Costs have been divided into *capital* and *recurrent* costs based on the lifetime of the goods being purchased. Capital costs have been discounted in the economic analysis using lifetimes and discount rates determined through stakeholder interviews, expert information, and past literature. Varying discount rates and lifetimes were examined in the sensitivity analysis. Both financial and economic analyses were conducted, in order to show (1) what the actual expenses of running a programme would be, as well as (2) the level of all resources used. In the financial analysis, capital costs have not been discounted and are instead incurred in full at the time of purchase.

Costs were collected in CFA francs (XOF) or USD. XOF were converted to USD using the official yearly average exchange rate. All costs have been adjusted for inflation to 2005 USD prices using the US GDP deflator index produced by the US Bureau for Economic Analysis (US BEA).

Outputs

Two main output measures were used: (1) *number of nets sold* and (2) *number of re-treatments sold*. Both figures were aggregated from sales data reported by formal partners of NetMark. Additionally, sales to institutional purchasers, such as NGOs or the *Programme National de Lutte contre le Paludisme* (PNLP) who in turn sold subsidized nets, and retail purchasers were disaggregated.

The two output indicators above were used to calculate a third combined output measure: *treated net years (TNY)*, which blends the results of both outputs by assuming that either a re-treatment or a new ITN provides 1 year of full protection for

any individual using that net. This combined indicator is useful because it allows the inclusion of re-treatments of existing nets as part of the outcome measure, while the calculation of the cost per ITN delivered does not. Though some nets in each year were LLINs (approximately 40% of all partner sales), all nets have been treated as conventional nets for the calculation of outputs in the base scenario of this analysis. The number of TNYs delivered through an LLIN would be theoretically higher — approximately 3-5 years per net — and the inclusion of the extended benefits of using these nets would be expected to significantly lower the cost per TNY or the cost per health impact. Hence we also calculated the outputs using the assumption that all nets delivered were LLINs in the sensitivity analysis

Base scenario

In this analysis, the base case scenario relied on the following set of assumptions. A discount rate of 3% has been applied to both DALYs (see below) and to economic capital costs. Shared costs have been attributed to the interventions based on the actual value of the indicator chosen to allocate them. Nets have been assumed to last for 3 years and, as noted above, treated nets and re-treatments were assumed to provide 1 year of protection each. Fifty percent of the nets delivered were assumed to be used by under five children and only one child was assumed to sleep under each of these nets. This assumption was made for the purpose of comparison with four similar studies in Togo, Eritrea, Malawi and Tanzania (Yukich *et al*., 2008).

The cost of nets was calculated using two different methods. For net sales which were purely commercial, net costs have been calculated based on mean net prices drawn from NetMark survey data: XOF 4164 in 2000 and XOF 2756 in 2004 (NetMark 2001c; NetMark 2005). For sales which were made to institutions such as the PNLP, NGOs, or CBOs, net costs were determined based on the sum of the average distributor sale price of a net at the time of research plus the margin at the facility or NGO level, as determined by stakeholder interviews. In the base analysis all ITN and IRK sales from formal NetMark partners, whether purely retail or institutional, were treated as attributable to the programme. This assumption has been varied in the sensitivity analysis.

Net and Insecticide Prices

Retail ITN prices varied both with net size and brand. Distributor answers and NetMark store check data indicated that retail prices ranged from XOF 2,800 (USD 5.60) to XOF 6,350 (USD 12.70) in 2005, reflecting both a wide variety of net sizes, shapes and types including the LLIN Permanet™. NetMark's surveys also provided respondent-supplied information on the cost of nets. The median reported prices were XOF 4000 (USD 5.70) in 2000 and XOF 3000 (USD 6.00) in 2004. Average prices from the surveys may be affected by the shift in market shares from commercial nets only to an increased percentage of non-commercial nets in 2004. Though overall commercial sales of nets increased between 2000 and 2004, the market as a whole grew strongly as well, and non-commercial sources including clinics or NGOs - that may deliver highly subsidized nets for XOF 1000 (USD 2.00 approximately) - represented the majority of nets in households by the time of the 2004 survey (NetMark 2001c; NetMark 2005). For the present study we based our prices in the base scenario on the results of the two NetMark surveys and project the costs for intervening years linearly.

Impact estimates & Cost-effectiveness calculations

We applied the estimates of impact for ITNs based on data from the Cochrane review of ITNs (i.e. 5.5 child deaths averted per 1,000 child-years of use) (Lengeler 2004).

Disability-adjusted life years (DALYs) averted, discounted at 3%, were calculated based on years of life lost due to malaria-specific child mortality. Our calculations excluded: (1) DALYs due to disability, and (2) DALYs lost in persons over five years of age because no reliable data were available to quantify these effects. In highly endemic areas the burden of malaria is largely dominated by mortality in children under five years (DCPP 2006). In addition, quantitative data on the effects of ITNs are very limited for older children and adults (Breman *et al*., 2006; Lalloo *et al*., 2006). In areas of low malaria transmission or epidemic-prone areas, the burden of disease is more evenly spread over the different age groups and our assumptions do not hold. All child deaths were treated as infant deaths and assigned a value of 33 DALYs lost for each death (WHO-DALY 2006). Again, this is a conservative choice since estimating based on deaths among children between one and four years of age would have yielded a higher number of DALYs averted.

In a final analysis, the cost per TNY (for ITNs) were combined with the impact estimates to produce cost-effectiveness ratios.

Additional details on the methods are available in an unpublished report available on the Roll Back Malaria Partnership website: (Yukich *et al*., 2007).

5.4 Results and Discussion

By the end of fiscal year 2005, the NetMark Senegal programme had contributed to the delivery of approximately 750,000 ITNs and nearly 250,000 IRKs. In attaining this output, the programme incurred an estimated economic cost of USD 6 million or a total estimated financial cost of USD 7.7 million (including user charges). Table 19 shows the cost structure of the NetMark project through the end of fiscal year 2005. Figure 9 represents the percentages of key cost components. As in previous analyses, the cost of commodities represented the major portion of the economic costs. Nets and insecticide comprised approximately 64% of the economic costs. The next most important share was advertising and promotion which represented almost one-quarter of the total economic costs. This result is unsurprising, considering that one main focus of the NetMark approach is demand creation. Staff costs are also important, representing approximately 7% of the total costs. Vehicles and fuel maintenance costs were small here but this may not reflect limited use of these resources, but rather the fact that these costs have been captured in the commercial sector through the retail prices of the nets themselves.

Table 19: Cost composition of the Senegal ITN programme (2005 USD).

	Economic		Financial	
Line item	**Total cost**	**Contribution**	**Total cost**	**Contribution**
Recurrent				
Insecticide	462,458	8%	462,458	6%
Staff	482,970	8%	503,857	7%
Fuel maintenance/travel	183,096	3%	202,977	3%
Advertising and promotion	1,439,203	24%	1,544,742	20%
Overhead	59,190	1%	63,528	1%
Rent and other	376,752	6%	402,729	5%
Subtotal recurrent	**3,003,670**	**50%**	**3,180,292**	**41%**
Capital				
Start-up costs	145,023	2%	0	0%
Vehicles	6,678	0%	21,035	0%
Equipment	8,481	0%	36,669	0%
Nets	2,835,042	47%	4,471,147	58%
Subtotal capital	**2,995,225**	**50%**	**4,528,852**	**59%**
Grand total	**5,998,894**	**100%**	**7,709,143**	**100%**

In the financial analysis the majority of funding (61%) came from donor sources, while 39%, came from user charges. Though the programme is largely commercial sector driven, the reason that users' charges are not equal in magnitude to the total net costs is that a significant portion of net sales have gone to institutional subsidized outlets, including NGOs and the Government of Senegal.

Figure 9: Costs of the program by cost category

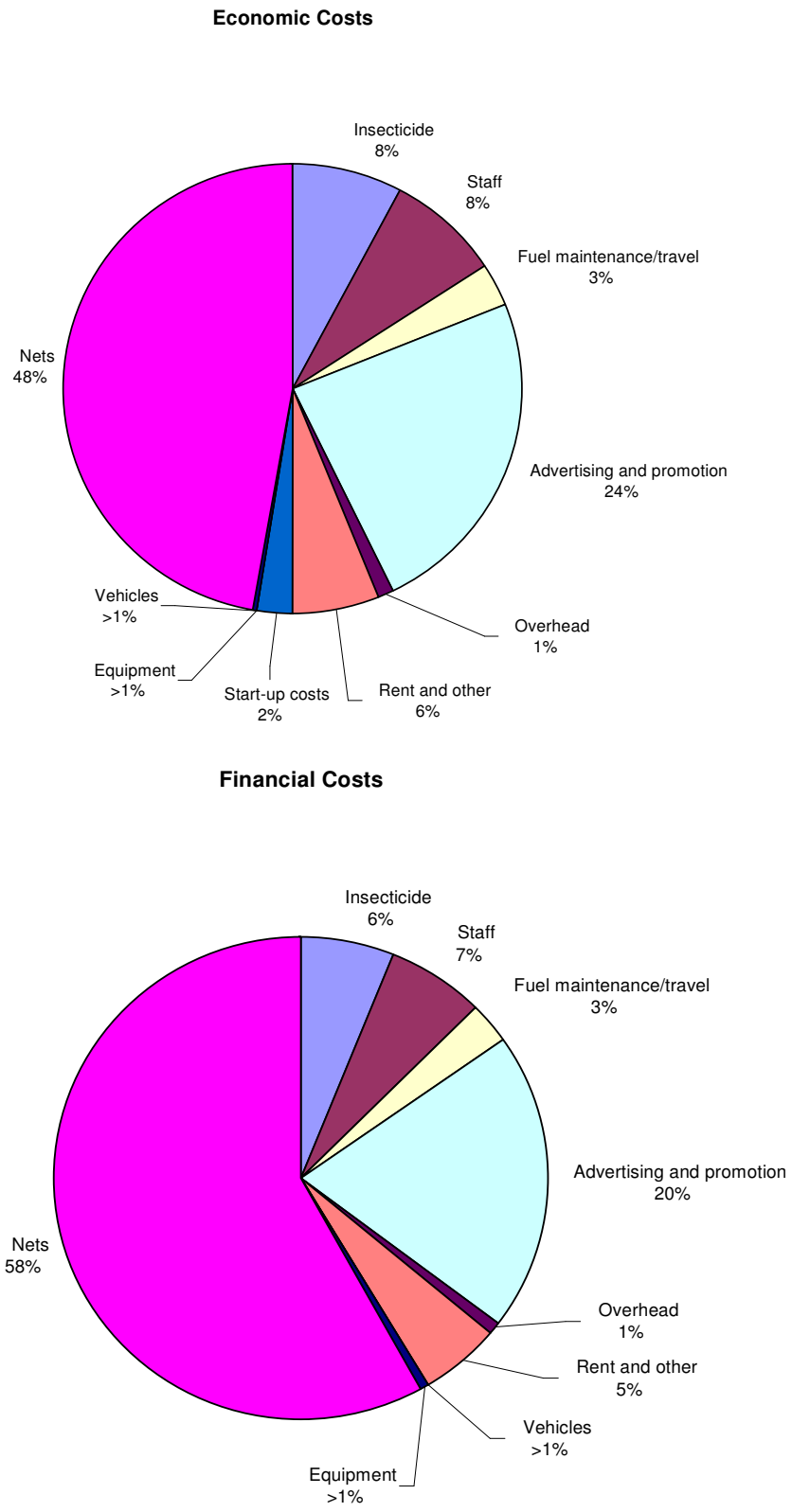

Table 20 shows the results of the analysis in the base scenario. The overall economic cost of the programme was USD 8.05 per ITN delivered. When the cost of nets sold through retail and institutional channels was excluded from the analysis, the economic cost was USD 3.62 per ITN, which is a proxy for the economic cost of the NetMark system. However, it is not a complete reflection of the total cost of delivery of an ITN, because some of the distribution costs of the commercial sector partners were captured in the retail prices of the nets. Costs per TNY are significantly lower than costs per ITN distributed because of the sales of a substantial number of insecticide re-treatment kits (IRK), which provide one full year of protection at a fraction of the commodity cost of a net.

Table 20: Average financial and economic costs of the Senegal Programme, per ITN and per TNY distributed (2005 USD).

	Including net and insecticide costs	**Excluding net and insecticide costs**
Per ITN distributed		
Financial	10.34	3.72
Economic	8.05	3.62
Per treated net-year		
Financial	7.00	2.52
Economic	6.05	2.45

Table 21 shows the costs of the NetMark Senegal project disaggregated into fiscal-year units. Some scale efficiency savings are apparently being realized: as ITN distribution numbers expanded through to 2005, costs per unit fell. Additionally, net costs have reportedly fallen by approximately 25% to 33% in local currency over the course of the programme (NetMark 2005). Changes in price may be due to the delayed results of tax and tariff policy change, exchange rate variation, increasing competition, reduced commodity costs due to an expanding international market for ITNs and economies of scale within Senegal or a combination of these factors.

Table 21: Annual costs of ITN and TNY distribution including net in Senegal (2005 USD).

	2002	2003	2004	2005	Total
Financial (ITN)	8.55	12.44	11.28	9.22	10.34
Economic (ITN)	5.08	10.58	10.55	6.93	8.05
Financial (TNY)	8.40	11.80	9.47	5.80	7.77
Economic (TNY)	4.99	10.03	8.86	4.36	6.05
ITNs	109,750	125,359	159,841	350,559	745,509
Re-treatments	2,000	6,840	30,511	206,983	246,344
TNYs	129,750	132,199	190,352	557,542	991,843

Financial and economic costs shown are total annual costs of program with annual numbers of ITNs or TNYs delivered as denominator.

There is no evidence for economies of scale in the TNY results, since the year with the highest annual delivery of TNYs also had the highest annual cost. Though some evidence for economies of scale is present the difficulty of disentangling distribution costs from procurement costs in the retail sector prevents us from examining the evidence in more detail. Costs were lower in the final year of data collection, when the number of ITNs delivered was also highest, this may be an indication of further improvements in cost-effectiveness in the future.

Cost-effectiveness calculations

Cost-effectiveness calculations begin with the base scenario cost analysis and are derived using either cost per ITN or cost per TNY, as noted in Table 21. While the TNY numbers are likely to be more representative of full program impact, previous evaluations of ITN programmes have often reported cost per ITN delivered. Thus calculating the effectiveness based only on protection from nets may aid with comparisons to other studies. Table 22 shows the predicted health impacts of the intervention in a base scenario analysis. Using the total TNY measure of protection, significantly more deaths and DALYs are averted by the intervention due to the inclusion of protection through re-treatment delivery. Consequently, when only ITNs are included in the calculation, health impacts are lower. The amount of protection provided varies over the period studied, due to a large fluctuation in the number of re-treatments delivered, which occurred despite the fact that actual numbers of ITNs delivered in each year increased through 2005. Our estimates indicated that over the

four year period of analysis the programme could have averted more than two thousand child deaths.

Table 22: Projected annual health impacts of the NetMark Senegal programme.

Year	2002	2003	2004	2005	Total
Deaths averted (ITN)	302	345	440	964	2,050
Deaths averted (TNY)	307	364	523	1,533	2,728
DALYs averted (ITN)	9,960	11,376	14,506	31,813	67,655
DALYs averted (TNY)	10,141	11,997	17,274	50,597	90,010

Table 23 illustrates the effect of the above protection on cost-effectiveness ratios. Overall, cost per death averted and per DALY averted were generally low in terms of WHO criteria for low income countries (Ad Hoc Committee 1996). TNYs yield significantly lower costs per death averted and DALY averted due to the large number of re-treatments provided by the programme.

Table 23: Estimated cost-effectiveness of the NetMark Senegal programme (2005 USD).

	Using cost per ITN	Using cost per TNY
Deaths averted	2,050	2,728
DALYs averted	67,655	90,010
Cost per death averted	2,926	2,199
Cost per DALY averted	89	67

There are reasons to regard the figures here as only rough estimates. One major reason is that the sensitivity analysis, discussed below, shows that net prices in the commercial sector had a major influence on the cost-to-output ratio. Unfortunately, the evidence base for the costs of ITNs in Senegal was limited. In this study, costs were estimated using information from store check records held by NetMark, the 2004 NetMark mid-term evaluation survey, and interviews with distributors (NetMark 2005). Store check records are not representative of the entire country and are likely to be biased towards urban areas, where prices may be lower. Interviews with distributors revealed only the suggested retail prices for nets but yielded no confirmed information as to what prices are actually charged in retail settings. Household survey results can also be distorted both by recall problems and

confounding due to project subsidized nets. The observed prices in the commercial sector were high compared to other African settings. These have already gone down since 2005 (D. McGuire, *personal communication*). Additionally, Senegal has a high GNI (Gross National Income) per capita compared to many sub-Saharan countries, and though it still qualifies as a low-income country by World Bank standards, the price level is expected to be higher than in other African settings.

Sensitivity analysis

The sensitivity analysis (Table 24 and Table 25) indicated high variability in the results. The variability appeared to be most heavily dependant on the costs of the nets used in the analysis as well as the attribution of sales to NetMark activities. Interestingly, a significantly lower price of nets due to competition could be a prime indicator of the success of the project, as well as potentially providing a positive feedback loop leading to increased sales. Evidence cited earlier indicated that retail prices have indeed fallen over the duration of the programme and after 2005. Additionally, attribution of sales dramatically affected the programme, as it effectively reduced the scale of the programme without a proportional reduction in provider costs. Results are similar in the TNY analysis, with the additional finding that the length of protection offered by an ITN or a re-treatment has a strong impact on the cost-output ratio increasing the cost per TNY to USD 24.19 if only 3 months of protection is assumed per ITN or re-treatment kit.

Table 24: Sensitivity analysis: cost per ITN and TNY distributed in Senegal (2005 USD).

Parameter	Values Assumed	Range (ITN)	Range (TNY)
Discount rate	1–10%	7.89–8.61	5.93–6.47
Cost of nets	2.00–12.00	5.58–12.26	4.19–9.21
Lifetime of nets	1 year–5 years	10.42–6.77	7.83–5.09
Cost of IRK	0.20–2.00	7.49–8.09	5.63–6.08
Net sales attributed	30–50–100%	17.95–12.29–8.05	8.54–7.40-6.05
LLIN use	Base – 3 years, USD 5 – 5 years, USD 7	8.05–7.58–7.36	6.05–2.64–1.67
Length of protection provided by ITN or re-treatment	3 months–6 months–1 year	N/A	24.19–12.10–6.05

The results of sensitivity analysis of the cost per death and per DALY averted are shown in Table 25. The same factors which are important to calculation of cost to output ratios also influenced the cost per death and DALY averted. Further, the assumptions regarding (1) the length of protection provided by an ITNs and re-treatments, or (2) assumptions about the usage of nets by children had a dramatic impact on the results. As it is difficult to make the link between a net delivered or sold and a net being used by a child, we have made assumptions which appear to be plausible. Usage rates have also been varied in the sensitivity analysis to include expected wastage rates.

Table 25: Sensitivity analysis: cost per death and disability adjusted life year (DALY) averted in Senegal (2005 USD).

Parameter	Values Assumed	Range (Death) (ITN)	Range (Death) (TNY)	Range (DALY) (ITN)	Range (DALY) (TNY)
Discount rate	1–10%	2,869–3,132	2,156 – 2,354	87–95	65–71
Cost of nets	2.00–12.00	2,029–4,457	1,525–3,350	61–135	46–102
Lifetime of nets	1 year – 5 years	3,790–2,461	2,848–1,850	115–75	86–56
Cost of IRK	0.20–2.00	2,725–2.942	2,048–2,221	83–89	62–67
Net sales attributed	30–50–100%	6,527–4,469-2,926	3,106–2,691-2,119	198–135-89	94–82-67
Length of protection provided	3 months–6 months–1 year	11,704–5,852–2,926	8,797–4,399–2,199	355–177–89	267–133–67
Usage of nets	25–50–100%	5,852–2,926–1,463	4,399–2,199–1,100	177–89–44	133–67–33
Children under net	1–2	2,926–1,463	2,199–1,100	89–44	67–33
LLIN use (TNY)	Base – 3 years, USD 5 – 5 years, USD 7	2,199–960–606		67–29–18	

One other important consideration is that NetMark was the most prominent provider of generic ITN promotion in Senegal, and thus may have had beneficial effects on the uptake of other ITN interventions. Such added benefits are impossible to quantify in this analysis, as estimation of the magnitude of this effect which might be attributable to the NetMark program is not possible with the available data.

Removal of taxes and tariffs

The NetMark project was a major driver for the policy decision to remove taxes and tariffs on nets and insecticide in Senegal. While it was not possible to determine

specific outcomes of the policy change and thus to include them in the in the cost-effectiveness calculations, it is clear that the removal of these tariffs likely had favorable effects on the prices of nets and insecticide. Following the methodology of Simon *et al.* (Simon *et al.*, 2002) we have attempted to estimate the potential effects of tax and tariff removal in Senegal on ITN and re-treatment sales.

Equation 1: Effects of removal of taxes and tariffs on ITN retail prices

$$P_r(T) = [p^w(1 + r^T) + M](1 + r^t)$$

Where $P_r(T)$ is the final retail price offered to consumers, and p^w is the c.i.f. price, r^T is the duty rate, M is the retail margin which is equal to (p^w)*30%, and r^t is the V.A.T. rate.

Using Equation 1 we can show what prices would have been assuming that current prices arose in a situation where the $P_r(T)$ is equal to those prices at the beginning of the study and both tax and tariff rates are zero. We can then back-calculate the *c.i.f* (cost, insurance and freight) price and re-calculate what the retail prices would have been with taxes and tariffs present. Assuming (1) the average prices of nets and insecticide used in this study, (2) that all nets were retail sales, and (3) a retail margin of 30% over *c.i.f.* prices, taxes and tariffs as they existed in the year 2000 (duty 47% on finished insecticide re-treatment kits and 42% on nets, plus VAT of 20% applicable to both) might have increased the cost of ITNs to USD 10.34 from USD 6.07 and for finished re-treatments from USD 1.88 to USD 3.32.

Price changes and demand (sales) of nets are related by the price elasticity of demand which is commonly defined according to the following equation (2).

Equation 2: Point price elasticity of demand

$$E_d = \frac{\Delta Q / Q}{\Delta P / P}$$

Where E_d is equal to the point price elasticity of demand, Q is equal to the quantity demanded at the starting price and P is equal to the starting price.

If purchase quantities had remained the same regardless of price (perfect price inelasticity of demand (E_d = 0)) the financial costs of the programme might have increased by approximately 3.5 million USD. However, the price elasticity of demand for ITNs and re-treatments is certainly non-zero, meaning that changes in price will result in some change in demand (or purchases) for ITNs and re-treatments. Few studies have estimated the price elasticity of ITNs and these have found divergent values (Onwujekwe *et al*., 2004; Cropper *et al*., 2000). One study which modeled the effects of tax and tariff removal from ITNs and re-treatments used values ranging from -0.5 to -1.5 (Simon *et al*., 2002). Using these same values and methodology here, the calculated changes in ITN price (41%) and re-treatment price (43%) could have increased the demand for ITNs or re-treatments by 21% to 62%, meaning approximately 160,000 to 460,000 excess ITN sales and 50,000 to 150,000 excess re-treatment sales. Thus under a highly elastic scenario the price effects of this policy change might have been responsible for more than half of all partner net sales. While this scenario is only illustrative, it is indicative of the importance and difficulty of considering impacts of programs that fall outside the rubric of traditional cost-effectiveness analysis.

LLIN Scenarios

When all nets delivered in the programme are assumed to be LLIN with a three year lifetime and a nominal cost of USD 5.00, the cost-effectiveness of the programme improves, with cost per DALY falling from USD 89 to 67 in the base analysis to USD 46 to 29 (the second number in each pair includes the benefits of re-treatments delivered). Further improvement in cost-effectiveness is seen if the nets are assumed to last five years and cost USD 7.00. The implications of these findings are that in the context of Senegal it appears that delivering LLIN at prices available on the world market could improve the cost-effectiveness of the programme, and in this scenario the cost-effectiveness of the programme might fall to levels deemed highly attractive for low income countries (Ad Hoc Committee 1996).

5.5 Conclusions

Based on the results of this study, it appears possible to deliver nets through an integrated commercial approach at acceptable cost levels. In relation to other models

for ITN delivery examined in the framework of the larger comparative study mentioned previously, total costs here were high. However, unlike most other programmes a large proportion of costs in the NetMark approach were borne by the users of the nets. When only the provider costs of each intervention were compared, NetMark's costs compared favorably with other programs (Yukich *et al*., 2008).

In addition, the main driver of high costs in the NetMark program was the high retail costs of the nets. Fortunately, these prices are subject to change and did show a downward trend over the period of the study. However, the changes in net or ITN usage nationwide have been slow and it is now clear that a commercial approach alone can not lead to the required 80% usage levels set by international targets. In several other settings, including Tanzania, Kenya, and Malawi commercial ITNs or socially marketed ITNs have contributed significantly to the overall net crop in the country, without playing a leading role (Noor *et al*., 2007; Khatib *et al*., 2008).

One additional advantage of the commercial approach that is not often discussed in the literature and cannot be valued accurately is that the stimulation of the commercial sector increased the stockpiles of ITNs available within the country and regionally. In events such as malaria epidemics ITNs could be purchased directly from distributors and moved into areas much more rapidly than would have been possible if an international tender had been required. Also, commercial nets provide a source of nets independent of any government sourcing, giving effectively another option for people living in endemic areas to protect themselves if they wish to do so (Lengeler *et al*., 2007).

Interestingly, while commercial sector approaches are commonly expected to produce inequitable results, all surveys in Senegal seem to indicate that net possession and usage is very similar across urban and rural settings and the most recent data indicate that households with lower socioeconomic status had higher ownership of recently treated nets (Schellenberg 2001; NetMark 2001c; NetMark 2005; CRDH & Measure DHS+ 2005). This high level of equity when compared to even some non-commercial approaches may, however, be due more to cultural patterns of net usage and possession than to factors inherent in the net delivery system. It is also possible that other campaigns and NGO activities which have

occurred in Senegal contributed to the relatively equitable ownership and usage levels.

Finally, commercial sector distribution carries additional benefits in the sense that profitable commercial sector activities are more likely to continue in the absence of donor funding and are thus more financially sustainable than other types of directly subsidized delivery. The level of funding provided here by the net users seems to indicate this as well, though donor input was still high. Unfortunately, the large volumes of ITNs needed to drive coverage levels to meet international targets were not reached in Senegal during the time frame of this study. It is also likely that the relatively small volumes of ITNs meant that retail prices were unlikely to fall as dramatically as was hoped. It is now clear from the Senegal, Kenyan and Tanzanian experiences that a purely commercial sector approach to net delivery seems will not lead to the fulfillment of international targets, but that such strategies can represent a valuable complement when combined appropriately with other approaches. In the case of Senegal, this approach provides an important policy option for the maintenance of net gains and it should be further supported.

6. Costs and consequences of large-scale vector control for malaria

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6.1 Abstract

Background

Five large insecticide-treated net (ITN) programmes and two indoor residual spraying (IRS) programmes were compared using a standardized costing methodology.

Methods

Costs were measured locally or derived from existing studies and focused on the provider perspective, but included the direct costs of net purchases by users, and are reported in 2005 USD. Effectiveness was estimated by combining programme outputs with standard impact indicators.

Findings

Conventional ITNs: The cost per treated net-year of protection ranged from USD 1.21 in Eritrea to USD 6.05 in Senegal. The cost per child death averted ranged from USD 438 to USD 2,199 when targeting to children was successful.

Long-lasting insecticidal nets (LLIN) of five years duration: The cost per treated-net year of protection ranged from USD 1.38 in Eritrea to USD 1.90 in Togo. The cost per child death averted ranged from USD 502 to USD 692.

IRS: The costs per person-year of protection for all ages were USD 3.27 in KwaZulu Natal and USD 3.90 in Mozambique. If only children under five years of age were included in the denominator the cost per person-year of protection was higher: USD 23.96 and USD 21.63. As a result, the cost per child death averted was higher than for ITNs: USD 3,933-4,357.

Conclusions

Both ITNs and IRS are highly cost-effective vector control strategies. Integrated ITN free distribution campaigns appeared to be the most efficient way to rapidly increase ITN coverage. Other approaches were as or more cost-effective, and appeared better suited to “keep-up” coverage levels. ITNs are more cost-effective than IRS for highly endemic settings, especially if high ITN coverage can be achieved with some demographic targeting.

6.2 Background

Prevention of malaria in highly endemic countries relies largely on vector control through one of two main methods: insecticide treated (mosquito) nets (ITNs) and indoor residual (house) spraying (IRS). Both methods are known to be highly effective and current evidence suggests they are very similar in their impact (Lengeler & Sharp 2003). Given the increasing availability of resources for malaria control, the Roll Back Malaria Partnership (RBM) has set the ambitious target for 2010 of 80% protection of high-risk groups by a "locally appropriate" vector control measure (RBM 2005). While few countries were near this objective in 2007, substantial progress has been made. Inevitably, this has been accompanied by vigorous debate as to the best way forward with regard to the different implementation models for ITNs, as well as the relative merits of ITNs versus IRS (Curtis & Mnzava 2001; Lengeler 2001; Curtis *et al*., 2003; Lines *et al*., 2003; Teklehaimanot *et al*., 2007; Lengeler & deSavigny 2007). While the implementation of IRS is typically through vertical programmes, available options for ITN implementation are more diverse.

Besides feasibility, sustainability and health impact, cost is obviously an important factor in the choice between different strategic options. Unfortunately, little is known on comparative costs and operational requirements for the delivery of ITNs and IRS. Direct comparisons in single settings in sub-Saharan Africa (SSA) have shown conflicting results on cost per person protected using either control method (Curtis *et al*., 1998; Goodman *et al*., 2001; Guyatt *et al*., 2002). A comprehensive modelling study has been conducted covering ITNs and IRS (Goodman *et al*., 1999) and the authors found overlapping cost-effectiveness ranges for the two interventions. For ITNs, four studies have examined large-scale programmes using field data in The Gambia, Malawi, Tanzania and Togo (Aikins *et al*., 1998; Stevens *et al*., 2005; Mulligan *et al*., 2008; Mueller *et al*., 2008). However, each of these studies focused on only one strategy and methodological differences make direct comparisons difficult (Kolaczinski & Hanson 2006). With the scale up of ITN activities in several SSA countries it has become possible to collect and analyse such information for a range of settings. This was undertaken for ITNs in five sub-Saharan countries, and for IRS in two countries. The present work allows, for the first time, a direct cost-

effectiveness comparison between different ITN strategies and IRS implementation on a large scale. Hence, this work provides a solid evidence base for a discussion of malaria vector control strategies in the most highly malarious areas of the world.

6.3 Methods

Programme selection

The ITN programmes were deliberately chosen to represent the major existing distribution strategies operating at large or fully national scale in sub-Saharan Africa. At the beginning of this research, few large-scale ITN programmes utilizing similar distribution systems existed, thus the choice of a representative country for each strategy was limited. The main exception was subsidized commercial distribution, which was implemented in several countries. Senegal was chosen for this category mainly to increase representation of West African countries. The strategies were defined using terminology derived from Webster *et al.*(Webster *et al.*, 2007): (1) free ITN delivery through public sector health services and at the community level – Eritrea (Macintrye *et al.*, 2006; Nyarango *et al.*, 2006); (2) free public sector ITN delivery through integrated vaccination campaigns – Togo (US CDC 2005); (3) highly subsidized mixed public-private sector ITN delivery through routine services – Malawi (Chavasse *et al.*, 2001); (4) partially subsidized private retail sector promotion – Senegal (AED 2005); (5) partially subsidized private retail sector promotion with a partially subsidized, mixed public-private, routine services voucher scheme – Tanzania (Magesa *et al.*, 2005). Table 26 presents programme details with regard to size, time frame, total economic costs and the latest available coverage figures.

Table 26: Main characteristics of the ITN and IRS programmes that were reviewed.

	Population covered (millions)	Period	Total num. of nets (mill)	Total num. of re-treat. (mill)	Total economic cost (Mio USD)	Net coverage in children under five years	
						Any net	ITN
ITN Programmes							
Eritrea	2.9	2001-05	0.9	2	3.7	Nav	59
Togo	5.3	2004	0.9	0	6.5	Nav	54
Malawi	12.2	1999-05	4.7	0.5	15.7	38	36
Senegal	10.0	2000-05	0.75	0.25	6.2	14	7
Tanzania	35.7	2002-05	6.4	7.8	30.5	41	28
IRS Programmes							
KwaZulu-Natal	0.6	1997-99	0.3 structures		2.2	High	High
Mozambique	0.8	1999-01	0.15 structures		1.0	>95% structures	>95% structures

Figure legend: Nav=not available. ITN=insecticide-treated net.

The ITN programmes also adopted different strategies for the provision of re-treatments for existing nets: Eritrea - free re-treatment through community level campaigns, Malawi - commercial sector cost recovery sales in urban areas, Senegal - partially subsidized private retail sector promotion, and Tanzania - cost recovery private retail sector sale and free delivery to pregnant women at antenatal care visits. Unfortunately, empirical cost evidence was only available for a single country where

long-lasting insecticidal nets (LLINs) were introduced, doing away with the need for re-treatment (Togo).

The two IRS programmes were chosen because they were large African programmes and cost data were available for both. They represented: (1) a programme funded locally (KwaZulu-Natal, South Africa) and (2) an international intervention funded by donors and a public-private partnership (Lubombo Spatial Development Initiative - LSDI, Southern Mozambique).

The full programme descriptions are available elsewhere (Yukich *et al.*, 2007).

Costs

The data on costs were either collected retrospectively for the purpose of the study from financial and operational records (Eritrea, Tanzania, Senegal, Malawi), or taken from raw data sets or published studies which could be adapted to this framework (KwaZulu-Natal, Mozambique, Malawi, Togo). The collection of cost data covered different periods between 1996-2005 (Table 26).

Where possible, the ingredients approach was used: inputs were identified, valued, and classified into activity categories. Where this approach was not possible, either because the information was deemed too sensitive (typically for salaries) or was not available in adequate detail, aggregated expenditures were used. All costs were converted to United States Dollars (USD) based on official yearly average exchange rates for the period during which the costs were incurred (excepting Togo where the exchange rate for the month when most expenditure occurred was used). All costs were adjusted for inflation to 2005 prices using the US gross domestic product deflator (US BEA). Some costs were estimated using the WHO Choosing Interventions which are Cost-Effective (WHO-CHOICE) unit cost and activity database, specifically those for public sector inputs in Tanzania (WHO-CHOICE). No adjustments for purchasing power have been made, and in some cases this may result in problems of comparability across countries due to differences in country specific price levels.

Where possible, both financial and economic costs were collected in order to both estimate the financing requirements for programmes and to examine their efficiency. Financial costs represent purely monetary flows, while economic costs represent the value (or opportunity cost) of all resources necessary to implement a given intervention. Only economic costs are presented here as they are considered the appropriate tool for comparisons of programme efficiency. Financial costs are available elsewhere (Yukich *et al.*, 2007).

A modified provider perspective was used; travel or time costs to users, or other household-level costs or cost savings have not been included. However, the direct costs of net purchases incurred by users have been included where the nets were partially subsidized or sold at full cost. Double counting was avoided by excluding the provider costs which were offset by these user fees. Details on included costs are presented in Table 27.

Table 27: Types of costs included in the analysis of the ITN and IRS programmes.

	ITN Programmes	IRS Programmes
Capital cost	Buildings	Buildings
	Vehicles	Vehicles
	ITNs (retail cost & subsidies) [1]	Sprayers
	Other equipment	Other equipment
	Start-up costs[2]	
Recurrent cost	Insecticide (when separable from nets)	Insecticide
	Personnel	Personnel
	Fuel/maintenance	Fuel/maintenance
	Management cost/training & meetings	Management cost/training & meetings
	Office/warehouse rental	Office/warehouse rental
	Supplies/overheads	Supplies/overheads
	Recurrent building costs	Recurrent building costs
	Advertising and promotion[3]	Basic evaluation and monitoring (excluding specific research costs)
	Basic evaluation and monitoring (excluding specific research costs)	

Figure legend: [1]Procurement costs in Eritrea and Togo, subsidies plus user payments in Senegal, Tanzania, and Malawi.
[2]Economic costs which arose before outputs of those programmes occurred; these costs apply in Tanzania, Senegal and Malawi; they accounted for fewer than 3% of total economic costs in all cases.
[3]Information, education and communication, health promotion, direct or indirect advertising and promotion subsidies or other similar activities.

Costing scenarios

The base case costing scenarios relied on the following set of assumptions: a discount rate of 3% was applied to capital costs; nets were assumed to last for three years (physical lifetime), but the effect of initial treatment as well as of subsequent re-treatments were assumed to provide only one year of protection (protective lifetime) (WHO 2007); fifty percent of the nets delivered were assumed to be used by children under five years of age and only one child was assumed to sleep under each of these nets on a given night. These are believed to be conservative assumptions (Macintyre *et al.*, 2006; Baume & Marin 2007). The cost of nets was based on the cost, insurance and freight (*c.i.f.*) price of the nets or on the full retail price paid by users plus any subsidies (direct or via vouchers) as estimated by survey

data (Senegal and Tanzania) or key informant interviews and project records (Senegal and Malawi). For IRS, it was assumed that the given number of annual spraying rounds (one or two) protected an entire household for one year, with perfect post-spraying compliance (no re-plastering of walls). Reported coverage by IRS was always very high, over 95% at the time of data collection in Mozambique, though high levels of re-plastering have been reported in some IRS interventions (Table 1) (Conteh *et al*., 2004; Mnzava *et al*., 1998).

Several alternative scenarios were also calculated. One involved the delivery of conventional ITNs in Togo, where only long-lasting insecticidal nets (LLINs) were actually distributed. The other programmes distributed a majority of conventional nets and therefore the costs and outputs in Togo were recalculated assuming a net cost of only USD 3.00 instead of the USD 4.33 paid per LLIN (Mueller *et al*., 2008; RBM 2004). Other alternative scenarios estimated the potential impact of LLIN use on the cost-effectiveness of the programmes. These scenarios were estimated in two ways. The first approach was simply to change the net parameters, including physical lifetime (three or five years), protective lifetime (three or five years) and cost (USD 5.00 to USD 7.00) to values believed to be representative of available LLINs, while not changing the properties, costs or benefits associated with re-treatments (Mnzava *et al*., 1998; RBM 2004; Tami *et al*., 2004; N'Guessan *et al*., 2001). The second approach used the same changes for the nets but removed the benefits and commodity costs associated with re-treatments. While it might be reasonable to expect that re-treatments will not be delivered in a LLIN programme, this dual approach was required due to difficulty in separating management and other costs associated with re-treatment. Thus, comparing the two approaches helped us to identify biases in the comparison between programmes due to different re-treatment approaches as well as to better quantify the potential benefits from a shift to LLINs, which would probably result in the discontinuation of most re-treatment activities. One way sensitivity analysis was conducted on all cost estimates.

Outputs

Two main output measures were used for ITN programmes: (1) number of nets delivered, and (2) number of re-treatments performed. These measures were used to calculate a third combined output measure: treated net years of protection (TNY),

assuming that either a re-treatment or a new conventional ITN provided one potential year of protection for anyone sleeping under the net. For IRS programmes two related outputs have been measured: (1) number of persons of any age protected, and (2) number of under-five children protected. Both calculations were made by applying the reported coverage rates to the total population of the sprayed areas - based on census information adjusted for population growth (WHO 2006; POP-Div UN 2004).

Outcomes

In order to combine cost data with public health impact, two outcomes were considered. First, the impact of ITNs and IRS on child mortality was estimated. Country-specific estimates were not available but robust impact estimates are available for ITNs from a Cochrane review (Lengeler 2004): ITN use in a high endemicity and high coverage situation averts 5.5 child deaths per 1,000 child-years. For IRS, however, unbiased impact estimates are scarce and have not been systematically reviewed. This is a recognized problem and a Cochrane review is currently investigating this issue (Pluess *et al.*, *in press*). In the absence of a better data set for IRS, and because the impact of ITNs and IRS was found to be similar in the five available randomized comparisons (Lengeler & Sharp 2003; Curtis & Mnzava 2000), the same estimate of impact for both ITNs and IRS (i.e. 5.5 child deaths averted per 1,000 child-years of use) was applied.

Secondly, disability-adjusted life years (DALYs) averted, discounted at 3%, were calculated based on years of life lost due to malaria-specific child mortality. These calculations exclude: (1) DALYs due to disability, and (2) DALYs lost in persons over five years of age. In highly endemic areas the burden of malaria is largely dominated by mortality in children under five years (Breman *et al.*, 2006). In addition, quantitative data on the effects of the two interventions are very limited for older children and adults (Breman *et al.*, 2006; Lalloo *et al.*, 2006). In areas of low malaria transmission or epidemic-prone areas, the burden of disease is more evenly spread over the different age groups and these assumptions do not hold. All child deaths were treated as infant deaths and assigned a value of 33 DALYs lost for each death (WHO-DALY). This is also a conservative choice as estimates based on deaths

distributed across children from one and four years of age would have yielded a higher number of DALYs averted.

Cost-effectiveness calculations

In a final analysis, the cost per TNY (for ITNs) and per child protected (for IRS) were combined with the impact estimates to produce comparable cost-effectiveness ratios for both interventions. For calculation of impact estimates for ITNs, the number of treated net years (TNYs) delivered was adjusted for net wastage and usage among children by assuming that only 50% of delivered nets (or re-treatments) would be used by under five children and that only one child would sleep under each of these nets. These assumptions are examined in the sensitivity analysis.

The full set of country-specific operational and costing results is available in an unpublished report (Yukich *et al*., 2007); selected results only are presented here.

6.4 Results

Tanzania and Malawi were the largest programmes and also the most expensive ones, with a total economic cost of 30.5 and 15.7 million dollars for the periods under review (Table 26). All the ITN programmes were larger in terms of population protected than the two IRS programmes. When the scale of the largest annual ITN delivery is compared to the size of the population at risk for the particular country (MARA/ARMA), Togo and Malawi had the highest ITN to population ratios (1:6) and (1:8), respectively, while Senegal had the lowest (1:30). According to the most recent data available for each country, Eritrea had the highest reported ITN usage rate among children under five years of age, while Senegal had the lowest. Both IRS programmes reported very high coverage rates in the targeted areas.

Economic costs for conventional ITNs

Annualized economic costs per conventional ITN distributed varied from USD 3.23 in Togo (or USD 2.75 if the net price is set to USD 3.00 instead of USD 4.33 - see methods) to USD 8.05 in Senegal (Table 28). Costs per treated net year (TNY) were lower in some cases due to the inclusion of re-treatment of existing nets, which offered additional years of full protection with low commodity costs (approximately

USD 0.30. Both measures (cost per ITN and per TNY) include the cost of re-treatments. Hence, the costs per TNY delivered by conventional ITN programmes ranged from USD 1.21 in Eritrea to USD 6.05 in Senegal. It is important to note that higher costs in Senegal were driven to a large extent by higher net costs in the retail sector.

Table 28: Average annual economic costs for ITN and IRS programmes.

ITN programmes	Average annual cost per ITN distributed	Average annual cost per TNY	Cost per death averted**	Cost per DALY averted**
Eritrea	3.98	1.21	438 / 1,449	13 / 44
Togo	3.23	3.23	1,174	36
Togo*	2.75	2.75	998	30
Malawi	3.36	3.04	1,105 /1,222	33 / 37
Senegal	8.05	6.05	2,199 / 2,926	67 / 89
Tanzania	4.80	2.17	788 / 1,745	24 / 53

IRS programmes	Cost per person protected (whole population)	Cost per under-five child protected	Cost per death averted	Cost per DALY averted
KwaZulu-Natal	3.27	23.96	4,357	132
Mozambique	3.90	21.63	3,933	119

*Assuming an average net cost of USD 3 instead of USD 4.33 (the actual cost incurred for LLINs by the campaign).
**In paired numbers the left value includes protection from re-treatment kits

There were important differences in the composition of costs for each programme. The percentage of the total cost born by the programme providers ranged widely: Togo 100%, Eritrea 83%, Malawi 69%, Tanzania and Senegal 45%. When a pure provider perspective is taken by removing all costs paid directly by users of nets, the annualized costs to the provider per net distributed were fairly similar between sites (range USD 2.75-3.63; for detailed results see (Yukich *et al*., 2007)).

Additional calculations for the year during which the programme delivered the largest number of nets were not substantially different from the cost data presented in Table 28 (Yukich *et al*., 2007). However, the programmes varied greatly in scale (200,000 to approximately three million ITNs per year) and this is likely to contribute to the observed differences in unit costs.

Economic costs for IRS

In both IRS programmes cost data were only available for one or two years of operations, after the start of the programmes. As a result, it was not possible to measure start-up costs. The annualized costs per person protected for IRS were USD 3.27 in KwaZulu Natal and USD 3.90 in Mozambique (Table 28). However, when only children under five years were included in the denominator for IRS (see methods section) the cost per under five child protected by IRS was substantially higher: USD 23.96 per child protected in KwaZulu Natal and USD 21.63 in Mozambique.

Sensitivity analysis: one way results

Sensitivity analysis was carried out on the main assumptions and parameters used to calculate cost to output and cost-effectiveness ratios. Discount rate, physical lifetime of nets and costs of insecticide or re-treatment kits all had relatively small effects on the results, however, other parameters were more important, and fit into two groups: (1) those relating to net properties (cost or protective lifetime) and (2) those related to net usage. For programmes involving retail net sales the attribution of commercial sales to programme activities also played an important role. All results were in the expected direction (Yukich *et al*., 2007).

For the IRS programmes the discount rate also had relatively little effect on the results of the analysis, as did a change in the population growth rate. Several parameters had larger effects on the results, especially the compliance of the population with spraying. Additionally, the cost of adding or removing one of the annual spray rounds or of switching types of insecticides had large effects on the cost-effectiveness of the programmes. Longer transmission seasons or shorter-lived insecticides would require additional spray rounds. The same applies if, for political

or resistance reasons, a shorter-acting insecticide were used; more spray rounds imply a higher cost (and potentially higher refusal rates).

Sensitivity analysis: LLIN cost scenarios

Table 29 shows the annualized economic cost per unit delivered for long-lasting insecticidal nets (LLINs) with three years duration and a cost of USD 5.00. In most settings, annualized costs per net distributed were higher than for conventional nets because of the higher initial purchase price. Senegal was the exception because the commodity costs observed in the programme were much higher than in other programmes. In Togo, the costs changed little because the programme only delivered such LLINs. The annualized delivery costs ranged from USD 3.47 in Togo to USD 7.75 in Eritrea. The cost per TNY was lower than for conventional nets in most cases, ranging from USD 1.46 in Eritrea to USD 2.64 in Senegal (when re-treatments were dropped: USD 2.04 in Malawi to USD 4.14 in Senegal).

Table 29: Average annual economic costs for ITN (3-year LLIN) programmes.

ITN programme	Average annual cost per LLIN distributed*	Average annual cost per TNY*	Cost per death averted*	Cost per DALY averted*
Eritrea	7.75 / 7.28	1.46 / 2.43	531 / 882	16 / 27
Togo	3.47	2.37	862	26
Malawi	5.18 / 4.50	2.19 / 2.04	798 / 743	24 / 23
Senegal	7.58	2.64 / 4.14	960 / 1,503	29 / 46
Tanzania	6.04 / 5.36	1.83 / 2.39	664 / 870	20 / 26

* In paired numbers the left value includes protection from re-treatment kits while the right value results from removing both protection and commodity costs related to re-treatment kits (see main text for details).
Assumes all nets are conventional ITNs. 2005 USD. TNY = treated net-year. DALY = disability-adjusted life year.

The annualized cost per delivered 5-year LLIN costing USD 7.00 generally fell compared to the three-year scenario, though the differences were not large (Table 30). They ranged from USD 3.23 in Togo to USD 10.08 in Eritrea (when re-treatments are dropped: USD 3.23 in Togo to USD 9.60 in Eritrea). The cost per

TNY was also lower than for conventional nets or for three-year LLINs, ranging from USD 1.38 in Eritrea to USD 1.90 in Togo (when re-treatments are dropped: USD 1.69 in Malawi to USD 3.25 in Senegal).

Table 30: Average annual economic costs for ITN (5-year LLIN) programmes.

ITN programme	Average annual cost per LLIN distributed*	Average annual cost per TNY*	Cost per death averted*	Cost per DALY averted*
Eritrea	10.08 / 9.60	1.38 / 1.92	502 / 698	15 / 21
Togo	3.23	1.90	692	21
Malawi	5.05 / 4.36	1.79 / 1.69	651 / 616	20 / 19
Senegal	7.36 / 6.96	1.67 / 3.25	606 / 1,181	18 / 36
Tanzania	5.74 / 5.06	1.62 / 2.28	588 / 828	18 / 25

* In paired numbers the left value includes protection from re-treatment kits while the right value results from removing both protection and commodity costs related to re-treatment kits (see main text for details).
Assumes all nets are long-lasting insecticidal nets (LLIN) with **5 years** duration and a cost of USD 7. 2005 USD. TNY = treated net-year. DALY = disability-adjusted life year.

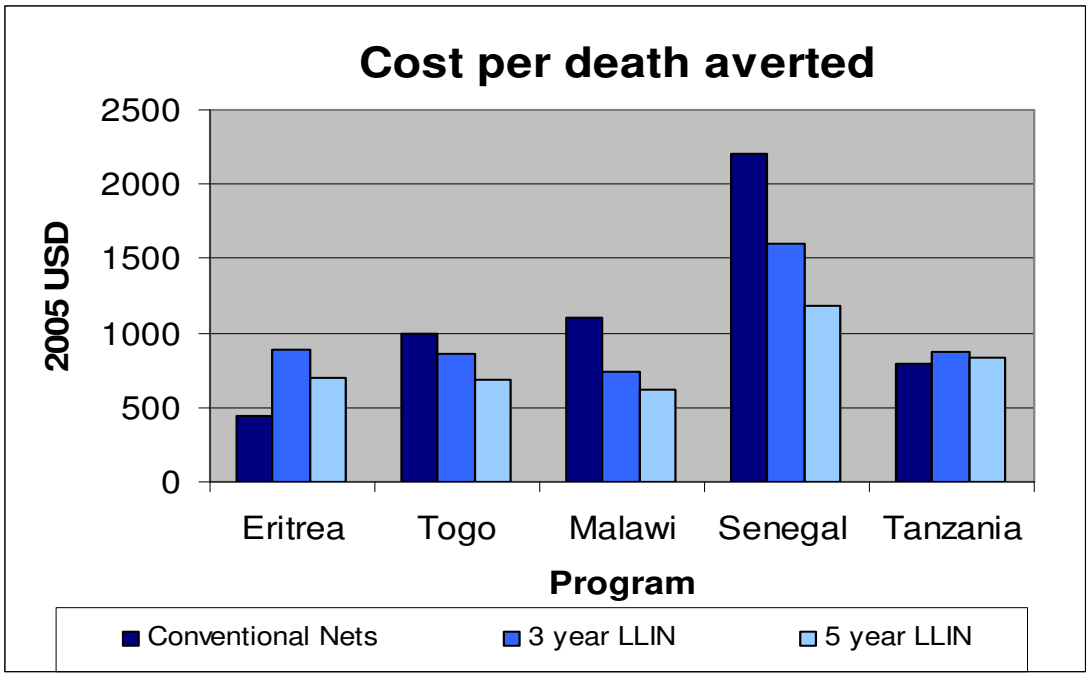
Cost-effectiveness of ITNs, LLINs and IRS for child mortality prevention

The results for targeted conventional nets are shown in Table 28, the cost per death averted ranged from USD 438 to USD 2,199. The cost per DALY averted was below USD 100 in all cases. Under scenarios with targeted LLINs with three-year physical and protective lifetimes (Table 29), the range of cost per death and DALY averted was lower than in conventional ITN scenarios, although when re-treatment benefits and commodity costs were excluded Tanzania and Eritrea did not show cost-effectiveness improvements. For targeted LLINs with five-year physical and protective lifetimes (Table 30), the cost per death averted in all cases showed cost-effectiveness improvements when compared to the three-year LLIN scenarios.

For IRS, the cost per death averted ranged from USD 3,933 in Mozambique to USD 4,357 in KwaZulu-Natal (Table 28). The cost per DALY averted ranged from USD 119 to USD 132.

LLINs, when targeted to high-risk groups in highly endemic areas appear more cost-effective than conventional nets and also more cost-effective than IRS delivered population-wide. Interestingly, the only circumstances in which LLINs did not clearly improve the cost-effectiveness of treated net programmes were in Eritrea and Tanzania (Figure 10). In Eritrea the initial commodity costs for nets were substantially lower than in other settings and in both countries the numbers of re-treatments delivered compared to nets delivered was high.

Figure 10: Cost-effectiveness results of shifting to long-lasting insecticidal nets



Cost-effectiveness results of shifting to three-year (USD 5) or five-year (USD 7) long-lasting insecticidal nets (LLINs) relative to conventional ITN estimates. LLIN CE estimates do not include protection from re-treatment kits but may include some costs associated with their distribution (see main text).

Sensitivity analysis: usage of nets by children

A major difference between ITNs and IRS is that the latter intervention cannot be targeted to high-risk demographic groups (pregnant women and small children), since IRS has to be applied to a large proportion of all houses in a geographic area to be effective. This has implications for total cost and also cost-effectiveness, which was explored in a sensitivity analysis. In the base analysis, only one child per net

was allowed and it was assumed that only 50% of nets were used to protect children. In sensitivity analysis this usage parameter had an important effect on the cost-effectiveness of every ITN programme because it altered the number of child years of protection provided without changing the costs. At lower usage levels (below 20-30%), the cost-effectiveness of net programmes (especially with conventional nets) resembled that of IRS programmes (Yukich *et al.*, 2007).

An important element that is not considered here for lack of reliable empirical evidence is how coverage of the intervention relates to its health impact. So far, few large-scale vector control programmes have been evaluated reliably with regard to health impact. However, it is well described that with ITN coverage above 50% there is a substantial community effect (Hawley *et al.*, 2003; Killeen *et al.*, 2007), while impact is reduced at lower coverage levels. Since all programmes aim at a high coverage rate (60-80%) and since all reliable impact data has been gathered under this level of coverage (Lengeler 2004), it seemed best to consider only one set of impact values.

6.5 Discussion

Main findings

These results confirm previous work showing that vector control for malaria in sub-Saharan Africa is extremely cost-effective, as even with conservative assumptions the cost per death averted was typically below USD 1,000 for LLINs. Clearly, the move from conventional ITNs to LLINs needs to be effected as soon as possible. In this review, all major types of programmes were covered, with the exception of programmes distributing free LLINs to the whole population (and not only special risk groups such as children) - as promoted recently by WHO (WHO 2007). No such programmes had taken place at the time of this work and, therefore, no data could be collected on this strategy. Although the implications of such a large change in the scale of ITN activities are difficult to quantify at present, it should be possible to estimate the cost of such an approach on the basis of this data.

In all programmes under review the cost per treated net-year was surprisingly close in the LLIN scenarios, indicating that programme managers do have real options. However, cost-effectiveness is only one criterion for comparing strategies and

decision makers must also consider other important aspects including: (1) the value of continuous promotion (such as found in social marketing programmes) versus a more intermittent approach; (2) the potential of a strategy to strengthen clinics / health facilities and improve uptake of antenatal care or immunization services; (3) the total cost of the strategy in relation to available resources; (4) the equity implications of each strategy; (5) which stakeholders and sectors bear the burden of a given strategy; (6) the opportunity cost in relation to other available health interventions.

It appears that the most cost-effective means of preventing child deaths from malaria is through successfully targeting LLINs to under-five children, while still achieving a relatively high coverage in the rest of the population. If nets were to only protect children little community effect would be realized as children represent less than 20% of the population in sub-Saharan Africa (Killeen *et al*., 2007). Under any scenario these findings suggest that LLINs are more cost-effective in high endemicity settings compared to IRS. In areas of year round transmission, especially those with limited physical and human infrastructure, LLINs are also likely to be more feasible than IRS. By contrast, IRS is competitive with ITNs and may be the better option in areas where few spray rounds are required due to either short transmission seasons, the use of inexpensive but long lasting insecticides (such as DDT), or in epidemic prone areas and other situations where good geographic and temporal targeting is possible (Worrall *et al*., 2007).

Economies of scale and scope need to be considered, as they may have significant effects on the unit cost per ITN by creating efficiencies within the supply chain or by improving demand through the integration of ITN delivery or promotion with a wider range of desirable products or services. In this study, the effects were found to be complex and not clearly present in all reviewed programmes. In Malawi this effect is well documented and the cost per unit in the 5th year of operation fell to approximately 30% of the first year (Stevens *et al*., 2005). To some extent, differences in scope and scale may also confound these comparisons given the large differences in the operational scale of each programme as well as relative to the context in which they operate.

Limitations in the comparability of vector control programmes

In making inter-country comparisons, uncontrollable differences in infrastructure, society, culture, and other variables can induce bias. This study presents selected case studies believed to be representative of different ITN and IRS programmes and delivery approaches in sub-Saharan Africa. However, there may be significant variations in the performance and costs of implementation of these strategies in other settings. Also, in comparing cost information other limitations inevitably arise because of the nature and timing of large scale implementation. For example, it was not possible to compare data sets corresponding to the exact same time period, either temporally or in the history of the programme, nor was it possible to completely control for differences in the scale of programmes. Similarly, it was not possible to control perfectly for variations in price level, although all five ITN countries fit the World Bank definition of a low-income country (GNI per capita below USD 905 in 2006). New country-specific impact data at varying levels of coverage and over the long-term could improve the impact predictions, although ultimately all malaria vector control programmes will aim towards a high coverage of LLINs and hence these differences might not ultimately be marked. Additionally, only the economic costs of programmes are presented here and though this can give guidance in and towards the selection of strategies, decisions must be made in each setting, in the light of both ecological and epidemiological factors as well as local health systems and resources.

Health system effects

Prevention of malaria can lead to a drastic reduction in the number of patients in health facilities, reducing pressure on over-stretched health facilities and thus benefit the whole health system. The provision of free or low-cost nets at health facilities (through vouchers or as a direct donation) may also be an enticement to pregnant women and mothers to use preventive services. In Malawi a portion of income received from the sale of highly subsidized nets is retained at the facility level and may act as an incentive for staff. On the other hand, comprehensive vector control programmes can burden weak health systems with new activities and lead to additional problems.

ITN programmes with their range of strategic options and possible interactions with non-health sectors appeared more flexible in their demands on the health system than the IRS programmes examined - though some recent IRS programmes, in Bioko Island, Uganda, and Zanzibar have shown that this burden may be shifted to NGOs or commercial organizations (PMI). In any case, vector control scale-up requires a capacity expansion in the preventive health care delivery sector. All of the ITN case studies examined here depended to some extent on public sector involvement (though levels of public input were highly variable). Table 31 attempts to summarize qualitatively the demands of the seven vector control programmes on three sectors (public, commercial, non-governmental) based on the results of interviews, document reviews and costing. In the case of the two programmes with a high commercial sector involvement (Tanzania and Senegal), reliance on this sector comes with profit incentives for the actors involved.

Table 31: Level of involvement of public, private and non-governmental (NGO) sectors in vector control programmes.

Programme	Public sector	Commercial sector	NGO sector
Eritrea	♦♦♦		♦
Togo	♦♦		♦♦♦
Malawi	♦♦	♦♦	♦♦
Senegal	♦	♦♦♦	♦♦
Tanzania	♦♦	♦♦♦	♦♦
KwaZulu-Natal	♦♦♦		
Mozambique	♦♦♦	♦	♦

Higher numbers of diamonds indicate more demands on that sector relative to other programmes; a larger total number of diamonds for each given programme does not necessarily indicate a more demanding intervention.

IRS programmes require a high level of expertise in entomology and management, which might put overwhelming demands to public systems in the face of the generally low availability of trained personnel in many endemic settings. However, a

programme can also help to develop local capacity in these areas. The South African example has demonstrated the many ways in which vector control programmes can contribute not only to the reduction of disease but also to the development of local capacity and the training of technicians and scientists.

Coverage and timing

Major differences were seen in both the levels of coverage achieved in the various ITN programmes, as well as in the duration of time that was required to achieve these coverage levels, or alternatively the time over which they were able to maintain coverage levels. The coverage levels achieved generally correlated with the price charged to users for ITNs: those programmes which delivered nets to users freely achieving the highest measured coverage levels and those with user charges reporting lower coverage and usage. The time to achieve increases in coverage was also generally much faster in programmes without user charges, but only one programme, Eritrea's, allowed for the examination of the long term implications of maintaining coverage with no user charges. While coverage in Eritrea has been successfully maintained for several years without user charges the overall cost per ITN was higher than in several other programmes. The free ITN programmes appeared to be highly effective at achieving higher coverage more quickly than those with user charges, while maintaining lower or competitive cost-effectiveness.

"Catch-up" versus "keep-up"

Currently, there is a consensus for ITNs that both "catch-up" (to rapidly increase ITN coverage) and "keep-up" (to maintain high ITN coverage) strategies are required in each country (RBM 2005; Lengeler *et al*., 2007). Integrated vaccination/ITN campaigns such as those carried out in Togo (studied here), Mozambique, Niger and other settings have achieved good coverage rates (50-60%) within a short period of time (US CDC 2005; Grabowsky *et al*., 2005). Such campaigns can therefore be seen as serving the initial need for "catch-up" in ITN usage levels. However, there is also a strong need for "keep-up" programmes to maintain high net usage levels, especially in newly pregnant women and newborns. Three of the ITN programmes reviewed tended to represent "keep-up" strategies (Malawi, Senegal, Tanzania) while one (Eritrea) mixed both. Recent work in Ghana (Grabowsky *et al*., 2005; Grabowsky *et al*., 2007) and on the Kenyan ITN programme (Noor *et al*., 2007) have

highlighted the complementarity of both “catch up” and “keep-up” approaches in achieving high ITN coverage and impressive health impact. Further information and effort will be required to determine which methods can be the most effective and cost-effective to “keep-up” coverage over time.

Financing

None of the ITN programmes appear to be independently financially sustainable. Even the largely commercial systems, such as the SMARTNET programme in Tanzania or the NetMark programme in Senegal, had substantial donor input and would be unlikely to continue operating at the same scale without continuing donor funding. However, all the programmes under review appeared to be operationally feasible and sustainable in the presence of continued funding. Additionally, in terms of financing, particular attention should be paid to pure provider costs which are more reflective of the inputs of programmes, donors or health ministries because they exclude costs which are borne specifically by users. These costs were similar across the ITN programmes examined here (Yukich *et al*., 2007).

6.6 Conclusions

These findings confirm that large-scale delivery of ITNs and IRS in sub-Saharan Africa is feasible and highly cost-effective using a range of strategies. Delivery of LLINs through campaigns provides a highly cost-effective and achievable method for rapidly improving ITN coverage. However, many other options exist for ITN programming, some well suited to maintain coverage levels after campaigns. IRS, or a combination of ITNs and IRS, remain attractive and viable options in some settings. Given that sustainable high-level funding appears to be available in the long-term through new global financing mechanisms, every malaria endemic country should aim to upscale their vector control programmes as rapidly and sustainably as possible.

7. Lack of cost-savings from Rapid Diagnostic Tests for malaria in Dar es Salaam, Tanzania

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Working paper

7.1 Abstract

Background

The switch to expensive artemisinin combination therapy (ACT) in a time of decreasing malaria transmission rates calls for more rational use of anti-malarial drugs in African health facilities. Rapid Diagnostic Tests (RDTs) provide one way to rationalize anti-malarial use by introduction of reliable and simple laboratory diagnosis. The economic effects and desirability of these tests appear to be highly situation dependant.

Methods

We recruited 257 patients in 6 primary health care facilities (4 with RDTs and 2 controls) and conducted in-charge interviews and records reviews during a trial of routine RDT roll out in Dar Es Salaam, Tanzania. Using these tools we collected data on patient-specific expenditure and patient-specific provider costs.

Results

RDTs significantly lowered patient expenditure on drugs (savings: USD 0.37; p=0.001) as well as provider drug costs (savings: USD 0.44; p=0.014). However, RDT introduction did not significantly reduce patients' overall expenditures (USD 1.08 (0.82 – 1.41) vs. USD 1.36 (1.01 – 1.79)) and may have increased total provider costs (USD 3.62 (3.39 – 3.87) vs. USD 2.31 (1.97 – 2.68)). Clinician's compliance with test results was higher in clinics with RDTs than in clinics with routine microscopy (95% in RDT clinics vs. 83% in control facilities; p=0.001).

Conclusions

RDTs reduce drug costs in this low-transmission setting but may not reduce them by a large enough amount to offset the cost of the tests themselves. Nevertheless, the test also brought additional benefits including shortened clinic visits, improved provider compliance with lab results and ultimately better case management.

7.2 Background

Malaria is largely diagnosed in African public health facilities on clinical grounds alone, and fever cases are routinely treated without laboratory confirmation (World Malaria Report 2008). Malaria microscopy, when available, is often of poor quality (Mundy *et al.*, 2000). However, with the high costs of the new generation artemisinin combination therapy (ACT), as well as concerns about the development of drug resistance due to drug overuse, many donors and health system managers are searching for ways to improve the rational use of drugs for malaria treatment. Additionally, intense malaria control activities and rapid urbanization in many endemic areas have led to falling incidences rates of clinical malaria. As a consequence, the malaria-attributable rates in fever episodes have been falling (D'Acremont *et al.*, 2009), further increasing the need for improved diagnostic strategies.

The modern generation of HRP2 antigen based rapid diagnostic tests (RDTs) have been shown in trials to have high sensitivity and specificity for the diagnosis of *P. falciparum* infection among clinical patients in Africa in some settings (Bell *et al.*, 2006, Reyburn *et al.*, 2007; Abeku *et al.*, 2008). Given the poor standard of microscopy in endemic areas, RDTs are likely to produce more accurate diagnostic results, even though expert microscopy should still be regarded as the gold standard for research purposes (Mundy *et al.*, 2000; Reyburn *et al.*, 2007; Abeku *et al.*, 2008).

There are potential drawbacks to their use for routine malaria daigosis including the persistence of the target antigen in the blood stream for up to several weeks after an infection has been treated, hence they cannot be used to estimate treatment success (Mayxay *et al.*, 2001; Iqbal *et al.*, 2004; Swarthout *et al.*, 2007). Additionally, such tests cannot determine parasite load and the specificity of such tests may vary according to the setting (Bell *et al.*, 2006; Abeku *et al.*, 2008).

While more accurate laboratory diagnosis may help to rationalize anti-malarial drug use at health facilities in Africa (Reyburn *et al.*, 2007; Hume *et al.*, 2008), there is also a clear possibility that any cost-savings made from the reduction of anti-malarial prescriptions may be outweighed by increases in prescription of antibiotics or other

drugs to treat test-negative patients. Additionally, RDTs add cost to case management which is not proportional to throughput, and which could outweigh cost-savings from reduced anti-malarial consumption (Lubell *et al.*, 2007). The effects of diagnostic changes will also depend on the adherence of clinicians to the diagnostic result, the frequency with which they request a test, as well as on the prevalence of parasitaemia among the clinical population (Zurovac *et al.*, 2006; Lubell *et al.*, 2008b).

There is a sizable body of literature which has examined the implications of improving malaria diagnostic methods, including both empirical and modeling studies. The results of the empirical studies have shown that there is a possibility to reduce average cost per patient and household costs through improved malaria diagnosis, and that such interventions could be highly cost-effective (Jonkman *et al.*, 1995; Hume *et al.*, 2008; Lubell *et al.*, 2008b; Zikusooka *et al.*, 2008).

Modeling studies have helped to confirm and highlight the myriad factors which could influence both the cost-effectiveness and the overall cost-saving potential of improved diagnosis. The main factors which influence the desirability of one testing strategy over another relate to the proportion of febrile cases which are parasite positive, the sensitivity and specificity of the new method and its alternatives, the costs of the tests, as well as the cost of the drug regimens prescribed to parasite positive and parasite negative patients (Shillcutt *et al.*, 2008; Jonkman *et al.*, 1995; Lubell *et al.*, 2007a; Lubell *et al.*, 2007b; Lubell *et al.*, 2008a; Lubell *et al.*, 2008b; Hume *et al.*, 2008; Zikusooka *et al.*, 2008).

Since the potential for improvements in outcomes and cost savings appear to be highly situation dependant it is necessary to evaluate the decision to shift to rapid diagnostic test locally and at specific levels of the health care system. While models can be used to explore decision making (Lubell *et al.*, 2008a) there is still a strong rationale to assess alternatives empirically in representative settings. This paper describes a study of the economic implications of the implementation of RDT diagnosis with RDTs in a low-endemicity urban African setting in Dar es Salaam, in the United Republic of Tanzania.

7.3 Methods

Study area

Dar es Salaam is the economic capital of the United Republic of Tanzania. It is a large urban area (population approximately 3 million) with highly heterogeneous land use, including commercial districts, industrial districts, residential districts, urban slums, and areas with high levels of urban agriculture (Dongus *et al*., 2009). As a result there is a high variability in the number of *Anopheline* breeding sites and hence adult mosquito densities. As of 2009 it is considered a low but stable malaria transmission area: EIR ≈ 1.3 with low parasitaemia prevalence (less than 10% in the general population) (Geissbuhler *et al*., 2009). All of the health facilities included in the costing exercise are located in densely populated low-income areas, though one facility's catchment area (Kawe dispensary) also includes some peri-urban and higher income areas.

Twelve public health facilities were selected for inclusion in a trial of RDT rollout (d'Acremont *et al*., in preparation). Of these, six primary health care facilities were included in the costing exercise. Four primary care facilities (three dispensaries and one health center) were experimental facilities in which RDTs replaced routine microscopy for the diagnosis of malaria. Two primary care health facilities, both dispensaries, remained as controls with only routine microscopy.

Collection of patient and facility costs and resource use

Costing was conducted both from the patient and provider perspectives. A larger survey examining the effects of RDT introduction on health worker practices and patient response was used as a platform for collecting patient-specific and facility costs (D'Acremont *et al*. in preparation). Within the six selected facilities the inclusion criteria were the following: (1) first consultation for the present complaint (not a follow-up visit), (2) absence of severe disease, and (3) main complain not trauma related. Eligible patients or caretakers of young patients were included if they gave oral informed consent. Their consultation was then passively observed by a survey worker with clinical training. These patients or caretakers were then questioned during an exit interview, which included questions relating to their perceptions of the clinical and laboratory consultation, as well as episode-related expenditures and any

previous treatment seeking and related expenditures. The questionnaire also probed travel time and costs, time spent accessing the facility and missed work or lost income due both to the attendance at the facility and/or any time taken to care for the patient at home.

All patients or caretakers who participated in the exit interview (and therefore had costing questions) were requested to return to the same health facility one week later for a follow-up interview. They were also provided with a small incentive to cover transportation costs. At this follow up, all patients or caretakers were administered a second questionnaire which solicited information on their current health status and any treatment seeking activity or expenditure during the intervening week, as well as lost income and time taken to care for the patient at home. They were also asked about the previous consultation and any associated expenditures, mainly as a check on consistency, as well as to potentially garner information about informal payments. If in-person follow-up was not possible we attempted a shortened follow-up interview via mobile telephone. All follow-up patients who reported at a health facility were tested with an HRP2 based RDT in order to check for missed infections, as well as to identify false negatives or positives in the control facilities given the persistence of the HRP2 antigen in treated patients. In patients who tested positive by RDT during follow-up it was ascertained whether they had received appropriate first line treatment, and whether their condition had improved. If this was not the case we ensured that they were subsequently treated at the health facility.

In order to assess treatment costs to the provider a health facility survey was conducted in the six facilities participating in the cost study to identify per patient resource use at the facility level. In-charge interviews and a health facility level data survey instrument were used to collect information on the number of outpatients and malaria cases seen at the facility over the past three years, as well as numbers of blood slides and RDT tests performed. Additionally, they collected information on numbers and grades of staff and estimated effort dedicated to outpatients. We also collected additional information used to calculate overhead and patient visit costs, including the facilitiy's spending on electricity, water, other overhead costs, and the numbers of capital items in the facility – including microscopes and other clinical equipment. We also utilized facility records to collect information on the use of

consumables including laboratory books, giemsa stain, blood slides, lancets, syringes and other items.

Valuation of Resource use

Costs of resource inputs were determined for the provider costs on the basis of (1) the Tanzania pharmaceutical and supply price list for 2008, and (2) interviews with the appropriate financial managers of the Dar Es Salaam City Medical Office of Health. Information on drug prices was obtained from the International Drug Price Indicator Guide database published by Management Sciences for Health (MSH) or from a WHO-AFRO database of indicator drug prices (MSH, 2009; WHO-AFRO, 2008). Patient costs were valued according to patients reported expenditures and lost income.

Costs for the initial implementation of RDTs, including training and quarterly supervisory visits were calculated based on reported expenditure and activities, excluding specific research costs. Costs were reported in the local currency (TSH), U.S. Dollars (USD), or Swiss Francs (CHF). All costs were converted to USD using official exchange rates for the year in which the cost occurred and adjusted into a common year (2008) using the U.S. GDP deflator (US BEA, 2009). Capital costs were discounted and annualized using a 3% discount rate and assumed lifetimes for equipment based on expert opinion and past literature. All costs attributable to RDT implementation were then divided by the estimated total number of RDT tests performed in the nine experimental health facilities (328,000 – 435,000) over the entire duration of the project (approximately two years) to calculate an average implementation cost per test. The number of tests was estimated in two ways: the first and lower number was the number of RDTs performed according to facility records, and the second and larger number referred to the number of RDTs delivered to the facilities according to project records. This range had little effect on the cost of implementation per test (excluding the cost of the test itself).

Statistical analysis

We tested the differences in patient expenditure and provider costs using two different statistical tests. We first applied the Kruskal-Wallis test for equality of

populations. We used this test because, as is typical of expenditure data, the distribution of both patient specific provider costs and patients expenditures was highly non-normal, due both to a significant right skew and a large zero-mass. Thus performing significance testing with a non-parametric method was necessary.

Additionally, we used non-parametric bootstrapping to estimate confidence intervals for each expenditure value. This approach was adopted due to the fact that alternative non-parametric methods do not compare arithmetic mean costs and transformation of the data to a log scale would result in comparison of geometric means, and further transformation did not result in a normal expenditure distribution. Methodological studies and reviews have suggested this methodology to appropriately deal with the need to compare arithmetic means and generate confidence intervals on such data (Barber & Thompson 1998; Nixon *et al.*, 2009)

Total time for patient visits to the health facility was normally distributed and thus amenable to standard parametric tests. Data was entered in EpiInfo 3.4.1 (US CDC), and analyzed in STATA 9.2 (Stata Corporation, College Station, TX).

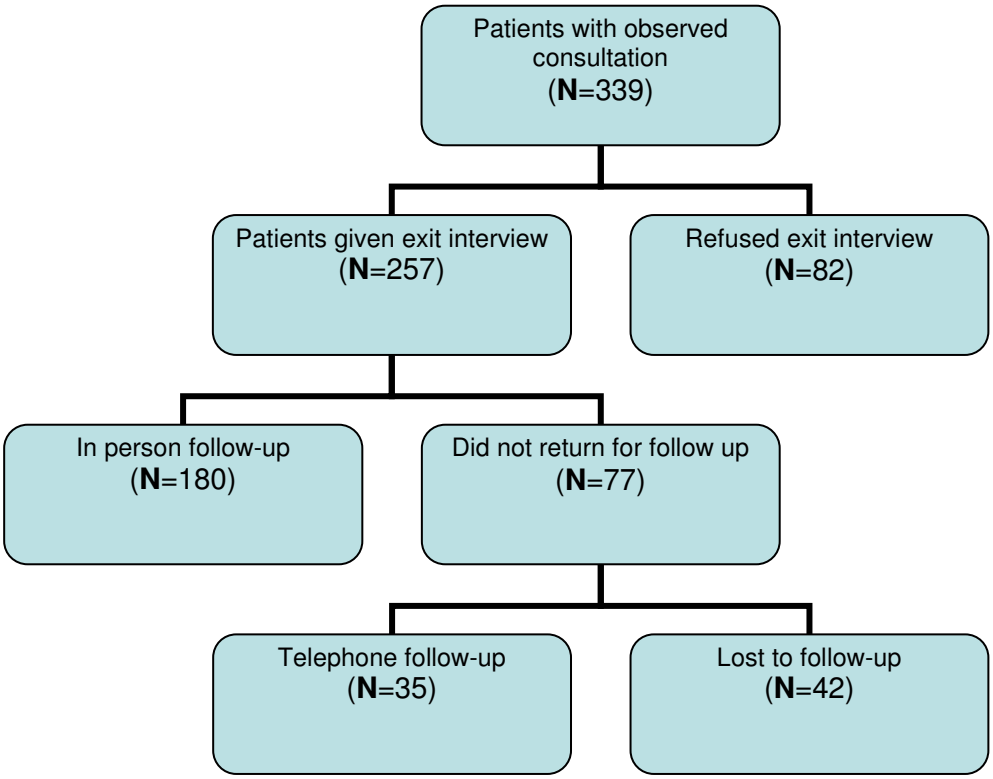
7.4 Results

General results

339 patients were recruited at each of the six selected facilities for exit interviews. 257 patients were successfully administered an exit interview. The final rate of follow-up (for patients participating in the full costing study) was 84%, and is illustrated in

.

Figure 11: Losses to follow-up during the study



Patients who were lost to follow-up were not significantly different on several measures of demographic information from those who were successfully re-interviewed (Tables 32a and 32b). No significant differences were found for age distributions, sex, methods of travel to and from the health facilities or the occupation of the patients' head of household. Additionally, we found no significant differences on the same set of measures between facilities which offered RDTs and those facilities which did not offer RDTs (Tables 32a and 32b).

Table 32a: Comparability of control and experimental populations, and those lost to follow-up

	N	Estimate	95% confidence interval	*p*-value
Proportion of patients age five years and older				
Control facility	80	52.5	41.6 – 63.4	0.45*
RDT facility	177	47.5	40.1 – 54.8	
Lost to follow up	42	59.5	44.7 – 74.4	0.14*
Not lost to follow up	215	47.0	40.3 – 53.6	
Proportion of patients who were female				
Control facility	80	55.0	44.1 – 65.9	0.98*
RDT facility	177	54.8	47.4 – 62.1	
Lost to follow up	42	54.8	39.7 – 69.8	0.99*
Not lost to follow up	215	54.9	48.2 -61.5	

**p*-values are based on Pearson's χ^2 test with d.f.(1)

Table 32b: Comparability of control and experimental populations, and those lost to follow-up

Patients method of travel to health facility (proportion)				
	Lost to follow up (N=42)	**Not lost to follow up** (N=212)	**RDT facility** (N=176)	**Control facility** (N=80)
Walking	66.7	60.4	61.5	61.3
Mini-bus	33.3	35.9	35.1	36.3
Other	0.0	3.8	2.5	3.5
p-value	0.501**		0.967**	

***p*-values based on Fischer's Exact Test

Of the 257 patients who were administered exit interviews 177 were interviewed at experimental facilities (with RDTs) and 80 were patients at control facilities (no RDTs). Within the RDT facilities, patients were significantly less likely than in control facilities to receive results for a laboratory test for malaria (84% vs. 95%; p=0.014 Fischer's exact), a difference that was also significant in patients five years and older (86% in RDT facilities vs. 98% in control facilities; p=0.04) but not for children under five years (82% in RDT facilities vs. 92% in control facilities; p=0.13). Patients in RDT facilities were also significantly less likely to test positive for malaria parasites (14% vs. 42%; p<0.001). While in both control and RDT facilities large fractions of all patients received laboratory diagnosis, clinicians in the RDT facilities appeared to be more parsimonious in their use of tests, at least among adults.

Unexpectedly, adults were significantly more likely than children under five years to test positive for malaria in control facilities, but not in RDT facilities (55% vs. 26% in control facilities; p=0.01 and 15% vs. 12% in RDT facilities; p=0.54). These results clearly suggest a problem with microscopic examination, and indeed the low quality of routine microscopy was confirmed in more detailed studies in the same facilities (Kahama *et al*., in preparation).

Patients within RDT facilities were significantly less likely to receive the first line anti-malarial drug ALU (Artemether-Lumefantrine) compared to patients in control facilities. This was seen when the analysis was restricted to patients who left the facility with any drug prescription as well as among all patients observed: 11% vs. 51% p<0.001 (with any prescription); 10% vs. 48% p<0.001 (all patients). This difference remained highly significant regardless of the age of the patient.

Patients in RDT facilities were also more likely to receive ALU in correct correspondence with the results of their diagnosis. When only patients with a laboratory diagnosis were examined, those in RDT clinics received ALU in correspondence with the laboratory diagnosis 95% of the time vs. 82% in control facilities (p=0.002). A related study has shown that most positive blood slide results in these facilities are false positives (Kahama *et al*., *in preparation*). Thus high clinician compliance with microscopy results in control facilites leads to overuse of anti-malarial drugs. When patients with only clinical diagnosis were included the results were similar: 95% in RDT facilities vs. 83% in control facilities (p=0.001). This difference remained significant when examined only for children under five years (97% in RDT facilities vs. 83% in control facilities; p<0.01), and nearly significant for patients age five and older (92% in RDT facilities vs. 80% in control facilities; p=0.07). Patients under the age of five years appeared no more likely to be correctly prescribed ALU than those over five years of age (93% under five vs. 88% five and older; p=0.19). Differences remained statistically insignificant when restricted within either RDT facilities or within control facilities (details not shown).

The diagnostic results on the full study sample are described in more detail by D'Acremont *et al.* (in preparation) and Kahama *et al*. (in preparation).

Implementation costs of RDT programme (provider)

Cost data on implementation was collected over a 14 month period. During this 14 month period approximately 435,400 RDTs were issued to implementing facilities and usage data indicated that approximately 330,000 RDTs for malaria had been performed. Due to the high volume of tests (approximately 400,000), the cost of implementation training and support for RDT roll-out was relatively low when considered per test. The total cost of the RDT intervention over this period (not including the test kits themselves) was estimated to be $16,946 in 2008 USD, or $1,883 USD per implementing facility. Thus we estimated that the cost of implementation per RDT test (excluding the test kits themselves) was between 0.04 USD and 0.05 USD. The test kits themselves were estimated to cost USD 0.66 each. When calculating the cost per patient in RDT clinics we include the cost of RDT implementation.

The bulk of the expenses went to staff salaries for the implementation of the RDT rollout (72%) and for training and quality control at the implementing facilities (22%). The only other substantial line item cost was transport, which accounted for 3% of the total cost of implementation.

Patient perspective – direct costs (expenditure)

Patient costs consist of two main parts: direct costs due to expenditure on medicines, transport, diagnostics and other health services, and indirect costs, such as lost productivity or the opportunity cost due to time spent seeking care. We attempted to measure both.

Patient expenditures were directly reported by patients. Table 33 shows arithmetic mean expenditure per patient in RDT or control facilities arising before and during the first consultation, as well as after the first consultation for the subset of patients with follow-up. Expenditures have been subdivided into several categories, and are reported here in Tanzanian Shillings and USD.

Table 33: Patient expenditures. HF=Health Facility, Totals are different than sum of means because of varying sample sizes for each group

Type of Expenditure		N	Mean cost per patient		Standard Deviation	Significance[+]
			TSH	USD	(TSH)	
Care pre-HF	RDT	177	89	0.07	639	0.554
	Control	80	46	0.04	304	
Drugs at HF	RDT	177	466	0.38	1064	0.001
	Control	80	914	0.75	1413	
Out-patient charges	RDT	124	80	0.07	122	0.319
	Control	55	105	0.09	126	
Lab fee at HF	RDT	121	245	0.20	418	0.938
	Control	55	256	0.21	430	
Post visit	RDT	125	286	0.23	1017	0.633
	Control	55	71	0.07	452	
Travel	RDT	177	365	0.30	905	0.801
	Control	80	274	0.22	811	
Total	RDT	121	1320	1.08	2057	0.044
	Control	55	1660	1.36	1832	

[+]significance results are based on Kruskal-Wallis tests

Table 33 shows that significant differences in reported expenditure were found between patients at RDT clinics and those at control clinics. Patients' mean total expenditures were lower in RDT clinics (USD 1.08) compared to control clinics (USD 1.36), and were significantly different using the Kruskal-Wallis test for equality of populations. Patients mean expenditure on drugs was 0.47 USD lower in RDT clinics than in control clinics.

Table 34 shows bootstrapped means and bias corrected confidence intervals for each of the parameters shown in Table 33 above. Each estimate is based on 10,000 re-samples of the observed data.

Arithmetic mean patient expenditures, when reduced into smaller component parts, failed to show significant differences in all but the line item expenditure for drugs at the first health facility visit, which was highly significantly different in RDT clinics (using the Kruskal-Walis test: TSH 466 (USD 0.38) vs 914 (USD 0.75); p=0.001). Bootstrapped confidence intervals showed, however, that the difference was only close to significance.

Table 34: Results of non-parametric bootstrap for confidence interval estimation of patient expenditures. Totals are different than sum of means because of varying sample sizes for each group

Type of Expenditure		Mean cost per patient	95% Bias Corrected C.I.
		2008 USD	TSH
Expenditure for care pre-HF	RDT	0.07	0.02 – 0.18
	Control	0.04	0.01 – 0.12
Drug expenditure at HF	RDT	0.38	0.27 – 0.53
	Control	0.75	0.53 – 1.03
Out-patient charges	RDT	0.07	0.05 – 0.08
	Control	0.09	0.06 – 0.12
Lab fee at HF	RDT	0.20	0.15 – 0.27
	Control	0.21	0.13 – 0.32
Post visit expenditure	RDT	0.23	0.10 – 0.42
	Control	0.07	0.00 – 0.22
Travel expenditure	RDT	0.30	0.19 – 0.41
	Control	0.22	0.15 – 0.31
Total expenditure	RDT	1.08	0.82 – 1.41
	Control	1.36	1.01 – 1.79

The similarity of expenditure across the two types of facilities helped to support our assumption that the populations of patients in control and RDT facilities were similar since the cost of transportation and actions taken before attending the health facility would not be expected to be significantly different between the two groups. Further, it supports the argument that effects on patient expenditures were largely limited to those on drug purchases.

Expenditures on drugs at the health facility accounted for the largest single component of patient expenditure, followed by laboratory fees and travel costs.

Patient Perspective – indirect costs

Additionally, patients incured indirect costs through lost income, reduced productivity, and the opportunity cost of lost time due to attending the facility either as patients or as caretakers of patients. One hundred-six (41%) patients or caretakers reported missing work to attend the health facility; of that group, 85% reported lost income as a result. Neither result was significantly different at the 10% level between RDT and control facilities: p=0.17; d.f.(1) and p=0.78; d.f.(1). Among those reporting lost income, mean lost income was reported as 7234 TSH (5.92 USD) a figure which was

not significantly different between control and RDT groups (Kruskal-Wallis p=0.135). This figure is significantly larger than patients' expenditures on all other categories. For patients who lose income to attend the facility, the opportunity cost of facility attendance is far larger than the direct costs of health care and such large opportunity costs might prevent significant numbers of people from accessing care.

Total time per visit, including transportation time was measured by adding estimates of time at which the patients or caretakers left their home or work place to attend the facility to the time they spent at the health facility (determined by the time of the start of their exit interview), with an additional time factor added for their estimated time to return home. In control clinics mean time per visit was estimated to be 4.7 hours while in RDT clinics it was estimated at only 4.0 hours (t=2.8703; p=0.005). Being a patient in an RDT clinic in our sample was associated with approximately 42 minutes shorter total visit time. Though a certain amount of this variation can be attributed to slightly shorter travel times to RDT facilities (mean travel time 44 minutes) compared to control facilities (35 minutes; p=0.049) resulting in a mean difference of approximately 9 minutes of travel in each direction, or 18 minutes total. Reduced waiting times and total visit times might help to reduce the opportunity costs of facility attendance and thus could improve access to care, though the reductions seen here are small (~10%) in relation to total visit time.

Provider perspective

In this analysis we focus on gross provider economic costs and not net costs, which would account for the collection of user fees by health facilities. We measured resource use at each of the six facilities through a questionnaire administered to the in-charge of health facility, as well as the collection of routine data on facility use, numbers of outpatients treated, numbers of malaria test performed, and records of consumable used. Additionally, we conducted data collection at the central offices of the City Medical Office of Health to estimate the costs of construction of health facilities and other costs which we could not obtain directly from the health facilities themselves, including salary ranges for various grades of health workers. The following table (Table 35) lists the costs which were included in the analysis.

Table 35: Costs included in provider perspective analysis

Recurrent Costs
Clinical staff salaries
Lab technician salaries
Support staff salaries
Consumables
Drug costs
Diagnostics
Electricity
Water
Communication

Capital Costs
Building and furnishings
Microscopes
Other equipment

All costs were related to their allocation to outpatient services (as opposed to maternal and child health services) and then related to the number of out-patients seen at the facility during the period under which their consumption could be measured (between 2005 and 2008). Because some resource usage could not be measured at each facility due to missing records (26% of requested records were missing) these costs have been estimated using the mean values per patient from the facilities where information could be collected. Prices of drugs have been adjusted to account for transport costs and wastage according to the following assumptions. Drugs costs were inflated 20% over actual costs to adjust for wastage, then an additional 10% for local transport, and finally an additional 10% for international transport where CIF (Commodity insurance and freight) prices were not available.

Table 36 shows the results of the provider perspective analysis for the RDT and control facilities and illustrative results when the analysis was limited only to patients who had laboratory diagnosis (either by blood slide or RDT). The table shows the results of non-parametric tests for each of three sub-divisions of total provider costs. They are analyzed either within control or experimental facilities or for patients with laboratory diagnosis, by type of laboratory diagnosis. “Drug costs” represent the cost to the provider of all drugs and prescription provided to a given patient. “Marginal costs” include drug costs and RDT costs and thus represent the cost of treating a patient excluding the facility costs for staff, overhead consumables and capital

equipment. "Facility cost" is the cost of the commodities whose usage is measured at the facility level but not linked to specific patients (overhead, staff costs, equipment and general consumables, excluding drug costs), thus there are only six observations corresponding to the number of facilities in our study. Significant differences were found for all costs except facility cost, though the latter result is compromised by the extremely small sample size.

Table 36: Provider costs per patient. Totals are approximately marginal cost (which includes the drug cost) plus facility cost, but vary due to differences between facilities.

Type of cost (per patient)	Group	N	Arithmetic mean		Standard Deviation	Significance
			TSH	USD	TSH	
Drug cost	RDT facility	177	1554	1.27	1796	0.014[+]
	Control facility	80	2083	1.71	1950	
Facility cost	RDT facility	4	1926	1.58	904	0.161[*]
	Control facility	2	720	0.59	424	
Marginal cost	RDT facility	177	2504	2.05	1783	0.017[+]
	Control facility	80	2083	1.71	1950	
Total cost (facility cost +marginal cost)	RDT facility	177	4421	3.62	2009	<0.001[+]
	Control facility	80	2818	2.31	1986	

[+]Kruskal-Wallis based *p*-values
[*]t-test based *p*-values

When patients who received RDT results were compared to patients whoreceived blood slide results, drug costs were significantly lower for patients with RDT results (USD 1.13 vs. USD 1.73; p=0.002). However, provider costs were higher for patients who received RDT results, both for marginal cost (including the RDT cost) and total cost: USD 2.14 vs. USD 1.73; p=0.003 for marginal cost and USD 3.71 vs. USD 2.33; p<0.001 for total cost.

Again we were confronted with results which were highly non-normally distributed, including in some cases a large zero mass and in all cases a significantly right-skewed distribution. Hence we estimated confidence intervals using non-parametric re-sampling (bootstrapping) with 10,000 re-samples for each outcome, excepting facility cost (Table 37).

Table 37: Results of non-parametric bootstrap for confidence interval estimation of provider economic costs. Cost values in 2008 USD.

		All Ages		Under Five		Over Five	
Type of cost (per patient)	**Group**	**Mean cost**	**95% bias corrected C.I.**	**Mean cost**	**95% bias corrected C.I.**	**Mean cost**	**95% bias corrected C.I.**
Drug cost	RDT facility	1.27	1.06 – 1.50	1.17	0.88 – 1.51	1.38	1.12 – 1.69
	Control facility	1.71	1.36 – 2.06	1.05	0.71 – 1.55	2.29	1.82 – 2.79
Marginal cost	RDT facility	2.05	1.85 – 2.27	1.94	1.64 – 2.27	2.18	1.91 – 2.48
	Control facility	1.71	1.37 – 2.08	1.05	0.71 – 1.53	2.29	1.82 – 2.81
Total cost	RDT facility	3.62	3.39 – 3.87	3.56	3.23 – 3.92	3.69	3.37 – 4.05
	Control facility	2818	1.97 – 2.68	1.68	1.33 – 2.22	2.87	2.38 – 3.39

Bootstrapped confidence intervals generally confirm the results of the Kruskal-Wallis tests. However important differences do exist between the two results. The confidence intervals for drug costs between RDT and control facilities show a large overlap when analyzed for all age groups. However, when the sample is stratified by over and under five years of age a significant difference exists for patients five years of age and older. This may be the result of a combination of high rates of ALU prescription in control facilities and the higher cost of this drug for adults in relation to other adult drugs. Marginal costs (including RDTs) were significantly different in RDT facilities compared to the control facilities using the non-parametric Kruskal-Wallis test. Bootstrapped confidence intervals, however, show overlap for mean marginal cost to the facility, though this overlap is small. When this result disaggregated by age group we see that costs for under five children are significantly higher and there is no significant overlap in the bias corrected confidence interval. The addition of the costs of the RDT diagnostic push the cost for under five patients significantly higher in RDT facilities and bring the marginal costs of older patients into a similar range as those in control facilities. Once facility costs are included, the total cost of treating a patient including all provider costs is significantly higher in RDT facilities than in control facilities.

Summary of all results

In all the results indicate that in the presence of RDTs drug cost savings are likely to accrue to patients, and may also accrue to the providers, especially for adults. However, whether these savings translate into overall cost savings is more in doubt.

For patients, it appears likely that there is some reduced overall spending when RDTs are availiable. However, the savings is small (USD 0.37) and it represents only a small component of the total economic costs to patients.

For providers the drug cost savings is of a similar order (USD 0.44) as a result of RDT introduction. Unfortunately, these savings appear to be too small to offset the entire cost of RDT introduction and use. In fact, it appears that RDTs may increase the cost of treatment per patient in public facilities, despite reducing anti-malarial drug usage and creating drug cost savings for the health system. Additionally, the cost savings arise largely from reduced anti-malarial usage among adults who are most likely to be charged a user fee for drugs. Hence, the resulting reduction in user fee revenue due to reduced patient drug expenditure will reduce the financial incentives for RDT implementation.

7.5 Discussion

This study was conducted under routine conditions in health facilities and sampled patients were taken from six different health facilities. While randomization was not possible for logistical and political reasons, care was taken to select the facilities that were as comparable as possible. As there is likely to be a tendency towards similar prescribing practices within facilities, the results should be adjusted for clustering within health facilities (Rowe *et al*., 2002). Unfortunately, because of the small sample size and small number of health facilities included in the study, we were unable to formally account for this in most of the statistical analysis. Nevertheless we believe that these results are likely to be robust, although the extent to which they are generalizable depends on how representative these facilities are of typical Tanzanian facilities or more widely of other sub-Saharan African health systems.

These results are of course sensitive to the relative prices of malaria drugs and antibiotics (ALU: USD 0.41 to USD 1.60 depending on dosage; Antibiotics USD 0.20

to USD 3.50 depending on drug, dosage and formulation) as well as any other drugs used to treat test positive and test negative patients. It is possible that given changes in drug prices our results could change. One of the most expensive drugs commonly in use among this type of patients is artemisinin combination therapy for malaria. Much of the drug cost savings seen in this study, both to the patients and to providers is due to reduced anti-malarial usage in RDT facilities. Hence, a reduction in the price of anti-malarial drugs may erase the drug cost savings seen here. Currently a global subsidy scheme for antimalarials is at an advanced stage (Gelband & Seiter, 2007) and a virtually free drug at country level might prove to be a disincentive to testing for malaria.

It has been postulated in several studies that RDTs could produce cost savings to health facilities in low transmission settings (Shillcut *et al.*, 2008; Zikusooka *et al.*, 2008). Here we show based on empirical data from six health facilities in Dar Es Salaam that indeed significant drug cost savings and reductions in anti-malarial drug usage appear to be achievable in such settings. In addition, clinicians' compliance with test results was significantly better when RDTs were in use, and this is likely to have contributed to the drug cost savings seen here (Lubell *et al.*, 2008b). Increased compliance by providers may be a result of intense training or their perception of the increased accuracy of RDTs compared to their routine laboratory diagnostic methods (D'acremont *et al.*, in preparation).

However, despite demonstrable drug cost savings we did not see overall cost savings due to the use of RDTs and in fact provider costs appeared to significantly increase in the presence of RDTs. Though some of this increase is likely due to higher fixed costs within the set of facilities selected for this study, the drug cost savings that we observed (USD 0.44) were not likely to be large enough to offset the cost of the RDTs themselves when a high percentage (84%) of the patients at the facility have the test administered. Further, reduced patient expenditure on drugs leads to falling revenue from user fees, which might make the intervention appear less attractive at the facility level.

Unfortunately, in the context of this study it was not possible to measure differences in health outcomes between the groups of patients, nor to asses whether patients

were truly malaria infected using expert microscopy or polymerase chain reaction (PCR) methods. Thus, it was not possible to asses the cost-effectiveness of the intervention, either per health outcome or per additional correct diagnosis. An in-depth analysis of case management practices will determine if RDTs improved compliance with standard treatment guidelines and improved case management (d'Acremont *et al.*, *in preparation*). That information could also be used to calculate a cost per additional correct treatment, as has been done in previous diagnostic costing studies (Reyburn *et al.*, 2007; Lubell *et al.*, 2007b).

An additional benefit is that with a more reliable laboratory test it becomes more realistic to monitor malaria trends on the basis of routine data. Though it is unclear what monetary value such a benefit would have for the health system, improved knowledge of malaria incidence rates could lead to efficiencies in other health care domains. Distribution of malaria prevention and treatment resources could potentially be more efficiently allocated to high incidence areas. Alternatively, more accurate measures of malaria incidence could enhance the responsiveness of health systems to malaria epidemics (Abeku *et al.*, 2004).

Finally, reduction of irrational anti-malarial use is important to limit the development of resistance to ACTs (Wongsrichanalai *et al.*, 2007).

7.6 Conclusions

Our results show significant savings on drug expenditure to patients and on drug costs to providers in the presence of RDTs. However, the savings are outweighed by other fees and charges and lost income for patients, or the cost for RDTs and higher facility costs for providers.

Clinicians' compliance with test results was higher when RDTs were in use, showing that they trusted this new technology. It is also likely that the use of such tests accrues significant other benefits, including improved case management, more rational anti-malarial use, and reductions in development of resistance to ACTs. While valuation of such benefits is outside of the scope of this work they are highly important from a public health perspective.

8. Discussion

8.1 General Discussion on the costing of vector control programmes

The main purpose of this thesis was to collect high quality cost data on large scale vector control operations in sub-Saharan Africa and to apply a standard methodology both to the collection and analysis of these data. Because so much of the previously available information on this topic suffered from lack of comparability (Kolaczinksy and Hanson 2006), standardization we introduced has improved the quality of information available to decision makers in Africa and globally. For the first time, consistent costing information on large-scale vector control programmes has become available.

Generally our findings show that ITN programs appear to be more cost effective for highly endemic areas of sub-Saharan Africa. In some situations, however, the results are less conclusive. These include areas of low-endemicity and areas prone to epidemic malaria transmission. The shift from conventional nets to LLINs should be rapidly made in all programs which have yet to do so, as our results clearly show that this would substantially improve the cost-effectiveness of ITN programs. Nevertheless, re-treatments to existing nets can be delivered at lower costs than entirely new nets and re-treatment of already existing nets is an efficient way to provide protection during the transition to LLINs. As mass-distribution campaigns are increasingly the distribution method of choice, LLIN distribution can be effectively mandated by international donors and ministries of health. Our results also highlight the need for more research on the economic implications of switching from a model of ITN distribution targeted towards children, to a full population coverage model.

As scale is important in the functioning of any economic production system (including the delivery of ITNs or IRS) we chose to examine only programs which were operating on national or very large scales, the types of programs that decision makers are likely to consider. While all the programs we examined were large relative to previous costing attempts, their scale still incorporated substantial variance - as much as three fold in the number of persons protected per year. The programs we examined also varied significantly in their operational goals and targets, and

correspondingly in their operational strategies. All these factors, which are inherent in a case study approach, can contribute to difficulties in interpreting results. The following sections discuss methodological and interpretive problems with data of this type, potential steps for remedying some of these problems, as well as extending the LLIN estimates to better reflect the current global policymaking environment.

8.2 Methodological problems with uniform methods of cost collection

A uniform method of cost collection was aimed for so as to minimize variability in the results of the study. Despite our best attempts, however, there were several specific issues which varied from setting to setting. Because this study incorporated the collection of retrospective data the quality of data sources was inevitably variable. Differences arose either because the information was not collected in the first place, was poorly (or not) preserved, or was simply recorded in incompatible manners.
By way of example, vehicle costs were largely recorded as cost of temporary rental in Eritrea and available as aggregate data, while in Malawi almost all of the vehicle time used was derived from vehicles in a shared pool for which purchase prices or replacement costs could be accurately measured, but vehicle use data had to be estimated based on proxy indicators.

Another frequent difficulty was the estimation of personnel costs, as salary information is generally considered sensitive and some institutions were reluctant to release files with specific costs of employment. In some cases it was possible to get salary ranges for employees of specific grades and use these to estimate the costs of personnel, in others only the number of persons employed related to a program and their general level of responsibility was available. In such situation their level of effort was estimated based on a proxy indicator or an interview and their cost of employment based on WHO-CHOICE data (World Health Organization, 2006).

In all cases solutions were available which fit existing guidelines for the economic analysis of programs (Phillips *et al.*, 1993; Creese & Parker, 1994; Drummond *et al.*, 2005; Kolaczinski & Hanson, 2006), but in many cases completely uniform standards for retrospective data collection were difficult to maintain. Fortunately, in both types of vector control intervention studied here the major cost centers were those related to

either ITNs/LLINs or to insecticide and these costs were also the most amenable to uniform methods of data collection.

With ITNs the greatest variability arose from the issue of when and where program outputs and costs were measured. In order to measure the denominator it was necessary to address questions such as: are ITNs considered delivered when they reach a user, or when they reach a district health facility or a primary health care facility? Alternatively, how are commercial sector sales measured and how are they attributed to social marketing or public-private partnership effort? For IRS the primary question was: how does operational coverage relate to actual coverage? One must consider the possibility of inadequate insecticide dosing or reporting by spraymen, and leakage of insecticide outside of the spraying program. Any of these issues can confound cross-country measurement. For cost of commodities in both interventions the question of which accounting method is most appropriate, either LIFO (Last In First Out) or FIFO (First in First Out) or an average cost method (used here) and how to account for delivery of slightly different types of commodity become important.

Further, one very important issue is price level since it is well established that purchasing power varies greatly across different country settings (World Bank Group, 2009). While the magnitude of such variations appears to be greatest when low-income countries are compared with high-income countries, there is still considerable variation within the low-income countries of sub-Saharan Africa, and even across various components of the same economy (World Bank Group, 2009).

Unfortunately, the methodological prescriptions for dealing with such variation are a source of considerable debate (Rogoff, 1996). The use of Purchasing Power Parity (PPP) adjustments across countries to establish uniform opportunity costs for non-traded goods is a standard method of adjusting for price level differences between countries. This, however, presents the problem of defining what is and is not a traded good; while the issue of misclassification bias in such circumstances is probably relatively small it still must be considered (Rogoff, 1996; Hutton & Baltussen, 2005). More problematic is that the basis for such adjustments are baskets of goods designed to represent the full scope of the economy of a country and are unlikely to be reflective of the basket of goods actually used by a vector

control program (Hutton *et al.*, 2005). The construction and maintenance over time of a properly sampled basket of goods for estimating price level variations is not trivial and indeed is generally beyond the scope of the economic analysis of a health care intervention. Even the international institutions which maintain global baskets of goods do not update these annually and price levels, although they tend to fluctuate less than nominal exchange rates, are not constant. Furthermore, even when updated these measures present a moving base line which may be shifted by changes entirely unrelated to costs in the sector of interest (Rogoff, 2006; World Bank Group, 2009).

8.3 Methodological issues related to program outputs

Generally, each program was evaluated economically with regard to either the number of ITNs/LLINs delivered or the number of total persons who slept in a sprayed dwelling. Both of these measures incorporated uncertainty on several levels. For ITNs this uncertainty largely revolves around two issues: (1) the accuracy of the reported numbers of ITNs/LLINs delivered, and (2) by whom are those nets used? For IRS there are two main problems which arise: (1) how does the operational definition of coverage relate to actual coverage, and (2) how are population estimates derived?

A “delivered” ITN can be measured at many separate stages in the process of actual ITN delivery. The measurement point has a potential to bias the results of a study in one direction or another. In systems which use commercial sector delivery without direct user subsidies another methodological issue arises, the attribution of net sales to program activities since it is certain that not all market sales are likely to be attributable to a program’s promotional.

Further, it is quite clear from extensive anecdotal evidence that some fraction of ITNs are used for alternative purposes, such as the commonly touted fishing nets and bridal veils - this type of alternative use is commonly called wastage (Minakawa *et al.*, 2008). Unfortunately, empirical estimates of the size and scale of this phenomenon are very limited. While there is currently an ample amount of evidence available relating to net possession and usage, relatively little attention has been paid to either understanding the “demographics” of the net and ITN “populations” in large scale

operational settings or to estimating the main factors which determine the size of the gap between net possession and usage (Macintyre *et al.*, 2006).

For IRS the factors relating operational coverage to actual coverage are also many and complicated. Spraying of houses requires a high level of training of spraymen to produce a uniform and appropriately dosed coating of insecticide on walls of varying sizes and materials. When operational definitions are used to define spray coverage it is clear that some houses or structures defined as sprayed will be in fact inadequately dosed with insecticide either because of low application rates or the failure to spray all of the appropriate rooms or surfaces. Furthermore, without high quality supervision, structures may be reported sprayed which are in fact missed all together. Neither is IRS exempt from behavioral and demand-side factors which can influence effective spray coverage. Householders may refuse entry to spray teams or be absent and lock buildings or homes preventing access, and they may re-paint or re-plaster walls even after allowing their homes to be sprayed (Mnzava *et al.*, 1998). Little quantitative information is available on these phenomena but what is available indicates that large fractions of the population may engage in refusal or re-plastering in some situations (Mnzava *et al.*, 1998).

8.4 Methodological concerns with the estimation of health outcomes

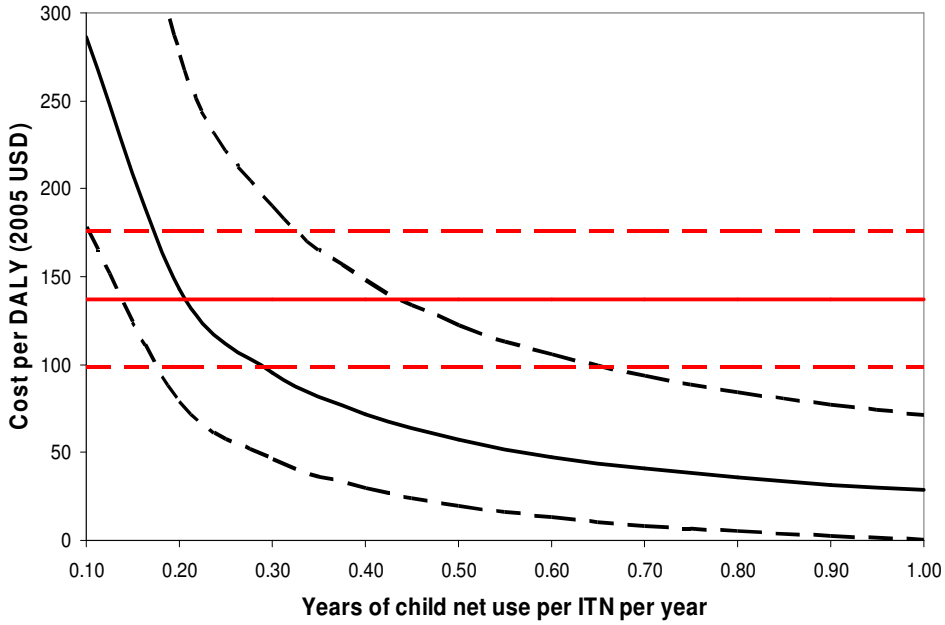
The estimation of health outcomes or impact presents further problems for inter-country comparisons. These methodological issues come on several fronts. One main issue is the lack of current and reliable efficacy estimates for IRS. A recent Cochrane review on this topic showed that despite the identification of over one hundred thirty studies on the health impact of IRS only six fit the inclusion criteria for a rigorous systematic review, and none of these studies estimated the impact of the intervention on mortality in children (Pluess *et al. in press*). As a surrogate, comparative evidence between ITNs and IRS shows that when both strategies are employed at high coverage there seem to be little difference in the entomological and health impact (Curtis & Mnzava, 2001; Lengeler & Sharp, 2003; Pluess *et al.*, *in press*).

The main problem for health impact estimation in specific settings relates to (1) the difficulty to get representative coverage measures, and (2) a lack of empirical

evidence on how impact of the interventions vary with coverage levels. Both interventions can provide some level of personal protection from malaria transmission (under some circumstances for IRS) as well as community protection based on a mass killing of vectors. The community effects, however, vary with effective coverage and quantification of the relative importance of these effects at varying levels of coverage with each intervention is difficult, despite some recent advances through modeling (Killeen *et al*., 2007). The estimates of impact used here are based on high levels of coverage, and thus may not accurately reflect health impact if high coverage is not achieved, as was the case for example in Senegal.

What follows is one example of how uncertainty in making the link between known efficacy and field effectiveness can be complicated by factors relating to the uptake and use of the intervention (Figure 12). The following figure shows a threshold analysis between the cost-effectiveness for ITNs and IRS, where the number of years of child protection derived from each net is varied. Hypothetical confidence intervals are shown based on an assumption that the true cost effectiveness at each point is somewhere between the highest measured CE + 20 USD per DALY and the lowest measured CE for that intervention – 20 USD per DALY (approximately the cost difference which would arise from choosing either the highest or lowest end of the 95% confidence interval from the Cochrane review of ITNs). Under these conditions it is clear that though the point estimates of average CE show that ITNs are favored at around one child year of protection for every five nets delivered, if uncertainty is incorporated this might increase to one child year of protection for every 1.5 to 2 nets.

Figure 12: Threshold analysis of child usage of nets with theoretical confidence bounds. See text for explanation.



8.5 Average cost-effectiveness and the one number effect

Much evidence on the cost-effectiveness of interventions has typically been based on trial data and focused on the use of average cost-effectiveness, as is largely this case in this study. This simplification, though it adds to the appearance of clarity, may also mask important areas of variation in the cost-effectiveness of health interventions and implications for decision making (Hanson, 2004; Johns & Baltussen, 2004). From the studies of ITN programs undertaken here it is clear that the scale and scope of interventions, as well as the timing of measurement can have clear impacts on the measures of cost reported, and thus on the cost-effectiveness estimates.

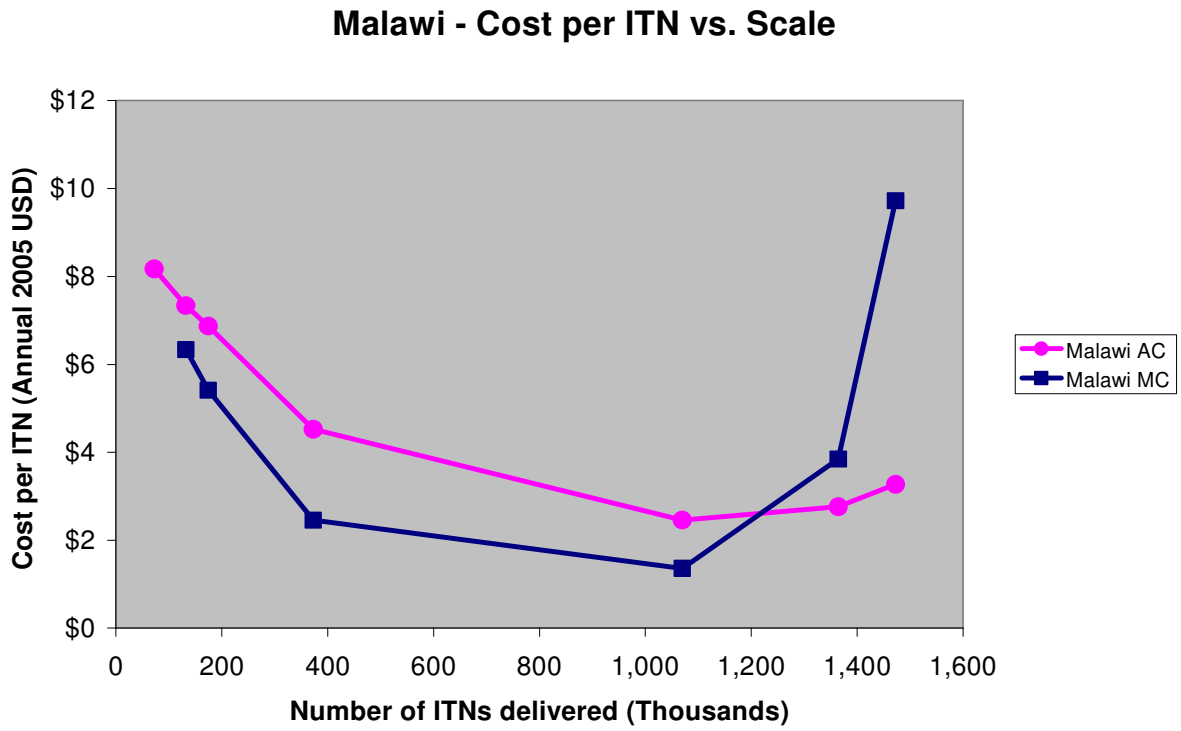
For instance, in Malawi, the average annual cost per ITN distributed fell by more than 50% over the course of the program's evolution. Which part of this cost curve is the most relevant for decision makers contemplating a similar strategy in another setting? The average cost, which is the easiest number to consider and reference, incorporates higher costs at lower scales which might not be replicated in another

setting, where a program began immediately on a large scale. Thus, it might be more appropriate to consider only the cost of delivery at a scale close to that which could be achieved in a similar program. However, it is not entirely clear from the limited evidence available whether similar effects would be replicated by all programs or whether specific operational or context specific factors may have contributed to this phenomenon.

Additionally, even the average cost of delivery at full scale may be different than the marginal cost of delivering an additional net through a given system, thus giving decision-makers incorrect information on how to make further decisions once a given strategy is already in place. Figure 13 graphically illustrates the relationship between average and marginal costs as the scale of a production system changes, using data from Malawi. The figure shows the relationship between the annual average and marginal costs ITN distribution in Malawi. Point estimates of cost and cost effectiveness may be misleading due to these types of relationships.

Health intervention effectiveness in terms of absolute burden may also vary with scale, with an additional net or house sprayed in an already high coverage area likely to avert fewer deaths and infections than a net or house sprayed in a low coverage situation. Further, a population which is covered first by any intervention is usually the easiest and least costly to cover. For these reasons it is likely to be more costly to go from 70% coverage to 80% coverage with an intervention than to go from 20% coverage to 30% coverage, though the absolute increase in population protected is the same (Johns *et al.*, 2004).

Figure 13: Average and marginal costs of delivering ITNs in Malawi. MC=marginal cost curve (shows the average annual cost of delivering the additional ITNs in each year as the program expanded). AC=average annual cost of delivering all ITNs in a given year.



8.6 Estimating the cost per person protected under a full coverage scenario

On the basis of this work we are interested in describing the economic cost of a full population coverage LLIN program, which is now the model recommended by WHO (WHO 2007). Given known distribution or delivery costs, the cost per person year of protection (PYP) with LLINs depends on three factors: (1) how many nets are wasted, (2) how many nets are used, and (3) by whom. We do assume here that the population under nets will be representative of the entire population.

For IRS, full protection is taken to mean 95% of the population of a sprayed area is protected. The IRS programs in our work represent one round of pyrethroid spraying in KwaZulu-Natal and two rounds of carbamate spraying in Mozambique, and both are assumed to provide one full year of protection.

Under this scenario we understand that the cost per PYP is indicative of cost per child year of protection (CYP). Based on our results we can then generate costs per PYP according to the following relationship (Equation 3):

Equation 3: Cost per person year of protection under full coverage

$$CostPYP = \frac{CostTNY}{(1 - wastage) * numpernet * usage}$$

Where *CostPYP* is the cost per person year of protection, *CostTNY* is the cost per treated net year of protection, *wastage* is the wastage rate, *numpernet* is the average number of persons sleeping under each used net, and *usage* is the rate at which all nets which remain in households are used.

Assume that 10% of nets will simply vanish – *e.g.* become fishing nets or bridal veils Also assume that each TNY protects one person for one year (a very conservative estimate), or alternatively that a net protects two people but that only half of the nets are used or they are all used but only half of the time. Table 38 illustrates the results derived from our data.

Table 38: Scenario analysis, full population coverage with no scale effects

	3 year LLIN @ 5 USD	5 year LLIN @ 7 USD
LLIN	**Cost per PYP**	**Cost per PYP**
Eritrea	2.70	2.13
Togo	2.63	2.11
Malawi	2.27	1.88
Senegal	4.60	3.61
Tanzania	2.66	2.58
IRS		
KwaZulu-Natal	3.27	3.27
Mozambique	3.90	3.90

The cost per PYP using LLINs appears to be lower in all cases except Senegal when compared to IRS. Of course, the margin is much lower with regard to CYP compared to when successful LLIN demographic targeting scenarios are considered. This scenario analysis assumes that the average cost of delivery per LLIN would not decrease when programs shift to full population coverage, which is unlikely but there are no data on this at present.

8.7 Parasitological diagnosis with RDTs and costing methodology

Results from our Rapid Diagnostic Test (RDT) costing study showed that significant drug costs could be saved by shifting from routine microscopy and clinical diagnosis of malaria to parasitological diagnosis using RDTs. However, overall case management cost were not reduced and the implications of our findings are therefore important in practice. This result is in contrast to some studies which have estimated the potential for cost savings from RDT use in low transmission areas (Shillcut *et al*., 2008; Lubell *et al*., 2008) However, neither of these studies projected certainty of cost savings and both suggested that savings would be dependant on clinicians' compliance with the test result. Though in our study compliance with test results was high we still did not observe cost savings. A recent study in Zanzibar also showed that cost savings may not accrue with RDTs despite improved case management in that setting (Msellem *et al*., 2009). RDTs have been shown to improve case management, rationalize drug use and could theoretically help to slow the spread of drug resistance (Bell *et al*., 2006). All these factors could contribute to them being a good investment despite higher costs and studies have estimated that they would be cost effective in large areas of sub-Saharan Africa (Shillcut *et al*., 2008; Lubell *et al*., 2008).

Our study was small, both in terms of numbers of patients recruited and, more importantly, in the number of facilities surveyed. Further, our study was conducted at the primary health care level in a relatively low transmission area. Generalizability may be compromised both due to heterogeneity within the limited number of facilities as well as by the issue of whether these facilities are representative outside Dar Es Salaam. In order to deal with both sources of variability it would be appropriate to extend the study to a larger number of facilities, as well as to account for heterogeneity with multi-level statistical methods which adjust for clustering within facilities. At least our results apply to the primary care level, which is by far seeing most patients in malaria-endemic areas.

Low transmission areas are characterized by lower malaria attributable fractions of fever cases, and thus more potential for reductions in anti-malarial drug use through improved diagnostic accuracy. Hence, it is important to note that despite this

favorable situation, the overall case management cost tends to be higher following RDT use. On this basis it is reasonable to assume that case management costs would further increase in higher endemicity areas, where the proportion of fever cases requiring antimalarial treatment is higher.

The results of the present study are also dependant on the assumed drug prices. In the context of a global ACT subsidy which would significantly reduce the cost of antimalarials, the actual drug cost savings to health systems may no longer be present. Under such a scenario (which is increasingly developing at the global level), a shift to parasitological diagnosis with RDTs would inevitably increase the overall costs to the health system.

8.8 Possible extensions to this research

One possible avenue for an additional analysis of the vector control data we collected is to develop Monte Carlo (MC) simulation based estimates of the uncertainty associated with input and output measures. This would allow for better quantification compared to one-way sensitivity analysis of the areas where the decision space may be more or less certain. While this approach would make some inferences more robust, it also faces the problem that where information on the variance or probability distributions of variables does not exist, or is itself poorly understood or un-quantified, the simulations may add little value (Drummond *et al.*, 2005).

More information could be garnered on costs by continuing to sample ITN and IRS programs in a variety of settings and operational conditions over time, and thus build a larger evidence base on the cost of delivery of these interventions. Additional data are available for at least two additional IRS programs in Bioko Island, Equatorial Guinea (Schwabe *et al.*, 2007) and some PMI countries (Brantly and Worrall *et al.*, 2007) An urgent addition in terms of implementation model will be the costing of a universal LLIN coverage campaign, since this is now implemented or planned in a number of countries. With more data from country studies it might be possible to use econometric methods to examine the drivers of delivery costs and outcomes achieved in a more accurate and reproducible way. However, based on the time and effort required to collect the primary data in this thesis this requires a substantial investment of time and effort. Efforts are currently underway via the Global Malaria

Program at the World Health Organization to collect this type of data in an increasing number of countries.

Finally, mathematical models are becoming available which can robustly examine the health effects of vector control in varied eco-epidemiological settings, with varied levels of effort or success in terms of coverage, usage and insecticide properties (Smith, 2007; Smith *et al.*, 2008). Our data will be used in this modeling effort and it is our hope that applying our cost data to models which better quantify the health impact in the study settings might yield improved estimates of the cost-effectiveness of vector control programs. Such efforts may provide improved aid to decision making in the context of uncertainty and with the long time horizons needed to properly advise malaria control programs throughout varied settings in sub-Saharan Africa.

9 Conclusions

9.1 Implications of results

Vector control with ITNs and IRS

This thesis represents an extensive and unique collection of large scale cost data on malaria vector control operations in Africa. It has the additional advantage that the data have been collected in a methodologically similar way and analyzed by one person according to a standard set of principles and with transparent assumptions. Thus, it provides a substantial amount of evidence which can be used to guide decision making in areas where interventions have yet to reach real scale. The study yielded several interesting and important results:

- In many situations LLINs appear more cost-effective than IRS; characteristics of such situations are:
    - The uptake of the intervention is good and averting mortality in children is the primary outcome of interest
    - The transmission season is long, and/or the presence of insecticide resistance precludes the use of the inexpensive and longer lasting classes of insecticide for IRS
    - Preferential usage of bednets by children
- Large expansion of vector control and improved treatment with ACT may decrease the applicability of the base results
- Our results have less relevance when elimination of all malaria transmission is the goal since maximization of control efforts might imply the need for using multiple approaches.
- Operational requirements of the different strategies varied greatly, and this needs to be considered when choosing interventions.
- The financial sustainability of any of the examined programs appears weak in the absence of international funding.

Introduction of RDTs for malaria diagnosis

- Drug cost savings were apparent after RDT implementation, but despite this overall provider costs increased.
- Clinicians were more compliant with the results of an RDT test than with routine microscopy, given adequate training.

There may be substantial additional benefits of introducing RDTs, and these should be considered and measured.

9.2 Recommendations to control programs

- LLINs are generally the most cost-effective way forward for malaria vector control in sub-Saharan Africa
- Conditions which favor ITNs/LLINs over IRS are:
    - The area is highly endemic with a long transmission season
    - Burden of disease is concentrated in under five children
    - Bednets will be used by the population, preferentially by children, and wastage is low

- Decision makers should also consider the use of IRS, especially when
    - The transmission season is short
    - Longer lasting and inexpensive insecticides (such as DDT) are available and can be used
    - Pyrethroid resistance becomes an impediment to the use of LLINs
    - Operational capability for IRS is present or easily mobilized

- ITN distributions should primarily consider the use of integrated campaigns for the “catch-up” phase and highly subsidized distribution approaches for “keep-up” strategies
- Maintenance of high and stable levels of donor funding for vector control of any type is critically important

9.3 Steps forward

The previous chapters have described the results of and methodological issues related to the studies contained in this thesis. They raise certain questions as to

what could be done to either to improve the quality of the information available, or to use what exists to better quantify the level of uncertainty associated with imperfect information. Several options for continuing this work are available:

- Development of Monte Carlo (MC) simulation based estimates of the uncertainty associated with the measures within this thesis.
- Continued sampling of ITN and IRS programs in a variety of settings and operational conditions over time (especially universal coverage with LLINs), combined with the use of econometric methods, to examine the drivers of delivery costs and outcomes achieved
- Mathematical modeling of vector control and associated costs and effects
- Diagnostic studies expanded both to a larger number of facilities and into different transmission and health system contexts.

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PhD in Public Health & Epidemiology

(Supervisor: Christian Lengeler PhD)

Thesis: Costs and consequences of malaria control in sub-Saharan Africa:
The economics of vector control and parasitological diagnosis

- Conducted field work in Malawi, Eritrea, Senegal, Tanzania, and South Africa
- Performed cost and cost-effectiveness analysis of several large (national scale) vector control operations
- Conducted field study on economics of implementation of rapid diagnostic tests For malaria in Dar Es Salaam, Tanzania

2003-2005 Tulane University SPHTM New Orleans, LA

M.P.H. in International Health & Development (August 2005)

- Focus in Health Policy, Monitoring & Evaluation and Infectious Disease
- Off campus master's class Kenya 2004

1997-2001 Tulane University New Orleans, LA

B.S. Biochemistry / B.A. Latin American Studies

- Magna Cum Laude with Honors in Biochemistry
- Senior Scholar in Biochemistry, R.C. Read Scholar's Award
- George Lurcy Grant in the Sciences
- Higgins Science Scholarship, Tulane Distinguished Scholar Award

Experience

2004-2005 Tulane University New Orleans, LA

Research Assistant (Supervisors: Kate Macintyre PhD, Paul Hutchinson PhD, Thom Eisele PhD)

- Wrote literature review on cost effectiveness of malaria control and prevention methods
- Performed data analysis on DHS and other survey data from Eritrea
- Performed district level cost analysis of Eritrean malaria control activities (May-June 2005)
- Used Stata and SPSS to conduct data analysis

2004 Tulane University New Orleans, LA

Teaching Assistant (Supervisor: Kate Macintyre PhD)

- Assisted in management of International Health Policy Course
- Graded written assignments and exams
- Conducted review sessions and otherwise advised students on course content

2002-2004 Tulane University New Orleans, LA

Medical Research Technician (Supervisor: James Robinson, MD)

- Responsible for data collection and analysis in HIV Immunology Laboratory
- Assisted in vivarium experiments with Guinea Pigs and Rabbits
- Performed ELISA, Western Blot and PAGE Assays
- Conducted Protein Modification and Chromatography
- Prepared Charts and Graphs of Data for Grants and Publications

1999-2001 Tulane University Dept. of Chemistry New Orleans, LA

Research Assistant (Supervisor: Russell Schmehl, PhD)

- Conducted Research on light to energy conversion, laser triggered protein folding, and electrochemical activity of Cytochrome p450
- Maintained notebooks, wrote an undergraduate thesis and gave several formal talks on the research material

Publications

Peer Reviewed

Yukich J, Zerom M, Ghebremeskel T, Tediosi F, Lengeler C. (2009) Costs and cost-effectiveness of vector control in Eritrea using insecticide-treated bed nets. *Malaria Journal* **8**:51

Yukich J, Lengeler C, Tediosi F, Brown N, Mulligan JA, Chavasse D, Stevens W, Justino J, Conteh L, Maharaj R, Erskine M, Mueller D, Wiseman V, Ghebremeskel T, Zerom M, Goodman C, McGuire D, Urrutia JM, Sakho F, Hanson K, Sharp B. (2008) Costs and consequences of large-scale vector control for malaria. *Malaria Journal* **7**:258

Mulligan J, **Yukich J**, Hanson K. (2008) Costs and effects of the Tanzanian National Voucher Scheme for insecticide treated nets. *Malaria Journal* **7**:32

Hutchinson PL, Mahlalela X, **Yukich J**. (2007) Mass media, stigma, and disclosure of HIV test results: multilevel analysis in the Eastern Cape, South Africa. *AIDS Educ Prev. 2007 Dec;**19**(6):489-510.*

Eisele TP, Macintyre K, **Yukich J**, Ghebremeskel T (2006) Interpreting household survey data intended to measure insecticide-treated bednet coverage: results from two surveys in Eritrea. *Malaria Journal* **5**:36

Non-Peer Reviewed / Reports

Yukich J, Tediosi F, Lengeler C (2009) (*in press*) ITNs and IRS, vector control for malaria in Africa costs and consequences. Bayer Health Sciences Journal

Yukich J, Tediosi F, Lengeler C (2007) Operations, Costs and Cost – Effectiveness of Five Insecticide-Treated Net Programs (Eritrea, Malawi, Tanzania, Togo, Senegal) and Two Indoor residual Spraying Programs (KwaZulu-Natal, Mozambique) (USAID/RTI)

Yukich J, Tediosi F, Lengeler C (2007) Compartive Cost-effectiveness of ITNs or IRS in sub-Saharan Africa. In *Malaria Matters* #18 July 2007 (Health Bridge Canada)

Yukich J, Hutchinson P, Macintyre K (2005) Zobal level costs of malaria control activities in Eritrea. (Integrated Vector Management Project/RTI)

Presentations

Yukich J (2009) Costs and consequences of ITNs and IRS in seven sub-Saharan African settings. Costing of Malaria Prevention

Programmes meeting, WHO Headquarters, Geneva. February 2nd 2009

Yukich J, Tediosi F, Lengeler C (2007) Costs and effects of large scale vector control in sub-Saharan Africa: ITNs vs. IRS. *Oral presentation.* American Society of Tropical Medicine and Hygiene annual meeting. November 6th, 2007

Yukich J, Mulligan J, Hanson K, Brown N, Chavasse D,Stevens W, Justino J, Mtema J, Mueller D, Zerom M, Ghebremeskel T, Khouma M, McGuire D, Tediosi F, deSavigny D, Lengeler C (2006) Effectiveness versus cost of five national scale ITN distribution systems in sub-Saharan Africa. *Poster.* American Society of Tropical Medicine and Hygiene annual meeting. November 14th, 2006

Yukich J, deSavigny D, Tediosi F, Lengeler C (2006) The cost and cost-effectiveness of ITN distribution systems in sub-Saharan Africa. *Lecture.* Joint meeting of the Swiss Society of Tropical Medicine and Parasitology and the Royal Society of Tropical Medicine and Hygiene. September 23rd, 2006

Other Professional Activities

Temporary Advisor, Regional Scientific and Technical Advisory Committee WHO-EMRO/GEF Project: Demonstration of viable DDT alternatives for vector control. 2008-Present

Professional Memberships

American Society of Tropical Medicine and Hygiene
Swiss Society of Tropical Medicine and Parasitology

Skills

Languages: English, Spanish
Data management and analysis: STATA, advanced SPSS, Epi-Info, Stata. Experienced user of Microsoft Office Package.
Laboratory–based skills: ELISA, Western Blotting, PAG Electrophoresis, Tissue culture, Viral Culture, and guinea pig and rabbit immunologic experimentation. ^{13}C and ^{1}H NMR, FTIR, Organic and Inorganic Synthesis, Column Chromatography, UV-Vis Spectroscopy, Protein Modification and purification, Fluorescence Spectroscopy, electro-analytical techniques (cyclic voltammetry, differential pulse polarography) time resolved laser spectroscopy.