Impact of Malaria Control on the Demand for ACTs

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Abstract: As planning for malaria shifts from control to elimination and eventual eradication, policymakers are faced with decisions about resource allocation, and best approaches for financing malaria control interventions. At the operational level, these decisions will determine the relative emphasis on different tools such as insecticide treated nets (ITNs), indoor residual spraying (IRS) and artemisinin-based combinations (ACTs) in various local settings. At a global level, these decisions will guide the appropriate role of global financing mechanisms such as the Affordable Medicines Facility for Malaria (AMFm) in the malaria elimination effort. Previous papers have separately examined the cost-effectiveness of individual tools like IRS and ITNs and financing mechanisms such as the AMFm. Here we look at the cost-effectiveness of AMFm at different transmission intensities and levels of malaria control. We find that deaths averted as a result of AMFm are maximized when other control measures such as ITNs are simultaneously applied. Although policymakers have to tradeoff between investments in AMFm and malaria prevention tools, our results indicate strong synergies that get stronger as malaria control is amplified.

Keywords: “Malaria Control”, “Artemisinin-based Combinations (ACTs)”, “Affordable Medicines Facility for Malaria (AMFm)”, “long-lasting insecticide treated nets (LLIN)”, “cost-effectiveness”

Disclaimer: The findings, interpretations and conclusions expressed in the paper are entirely those of the authors, and do not represent the views of the World Bank, its Executive Directors, or the countries they represent.

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PART I – INTRODUCTION

There has been a significant scaling up of malaria control in sub-Saharan Africa in recent years. Investments in insecticide treated nets (ITNs) and artemisinin-based combination treatments (ACTs) have been made possible by funding from a variety of bilateral and multilateral initiatives including the U.S. President’s Malaria Initiative, the Global Fund to Fight Tuberculosis, HIV and Malaria, the Nothing but Nets Campaign, Malaria No More, the World Bank Malaria Booster Program and the Bill & Melinda Gates Foundation. Overall it is estimated that donor spending on malaria has increased 12-fold between 1999 and 2004 and by a factor of 18 in sub-Sahara Africa during this period (Table 1). The consequences of this significant increase in malaria spending are striking. Countries like Eritrea, Kenya, Ghana, Zambia, Mozambique and Ethiopia (Nyarango, Gebremeskel et al. 2006; Fegan, Noor et al. 2007; Hommerich, von Oertzen et al. 2007; Mufunda, Nyarango et al. 2007) have reported dramatic reductions in malaria incidence, while Zanzibar and South Africa are within striking distance of elimination (Barnes, Durrheim et al. 2005; Bhattarai, Ali et al. 2007).

Recent thinking about malaria includes an explicit shift in emphasis from control alone. It now includes a progression from control to elimination and eventual eradication. While elimination may require new tools including a vaccine, resources in the short term are likely to focus on expanding coverage with existing tools. These include not just ITNs and indoor residual spraying (IRS) to reduce transmission, but also effective antimalarials that are essential to any sustained malaria control strategy. Efforts to discover and maintain a set of effective antimalarials include discovery efforts, such as by the Medicines for Malaria Venture (MMV) as well as financing efforts like the Affordable Medicines Facility for Malaria (AMFm). AMFm is a financing platform to expand access to ACTs through the public, NGO and commercial private sectors with the aim of saving lives and preventing emergence of resistance associated with the use of artemisinin monotherapies (Arrow, Panosian et al. 2004; Laxminarayan, Over et al. 2006; Dalberg Global Development Advisors 2007). It is critical to helping maintain the effectiveness of artemisinin as first-line treatment.

Although there is broader support for malaria control than ever before, and coverage of ITNs and ACTs through the public sector is increasing at a rapid pace (UNICEF 2007), much remains to be done to reach even the modest goals of rolling back malaria let alone elimination. Policymakers will have to decide how best to allocate resources between countries, time periods, tools and mechanisms for financing these tools\(^1\). These decisions will help develop robust projections of the medium- and long-term need for current technologies including ITNs and ACTs.

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\(^1\) The choice of which financing methods to use is critical in determining the level of coverage, access and adoption of tools. For instance, ACTs can be funded to reach public sector clinics but this may limit access to those who are far away from these clinics. Similarly, free bednet distribution programs have been found to result in greater level of bednet use in the target population than social marketing programs that charge for bednets (Hoffman 2008). Here, the benefit of cost-recovery in the social marketing programs has to be weighed against the drawbacks of lower access.
ACTs. Many studies have tried to answer these questions by computing cost-effectiveness of individual tools (Binka, Mensah et al. 1997; Graves 1998; Goodman, Coleman et al. 1999), but more recent studies have also looked at various combinations of prevention and treatment resources (Morel, Lauer et al. 2005). For instance, Morel et al find that increasing ACT coverage is the most cost-effective strategy for reducing malaria control (see table 2 for their summary results). However, there is a limit to what ACTs alone can achieve; combining ACTs and ITNs or IRS can achieve much greater reductions in malaria prevalence. Similarly, wide deployment of insecticide treated bednets (ITNs) is capable of achieving as much as a 10 fold reduction in the entomological inoculation rate (Lengeler 2004; Le Menach, Takala et al. 2007) but the magnitude of reduction can be even greater with effective treatment.

Studies have also looked at the cost-effectiveness of specific financing models for delivery of these tools. Our focus here is on AMFm. Recent model-based studies have shown that a global subsidy for ACTs is likely to be effective in preventing emergence of resistance and cost-effective in averting malaria deaths (Laxminarayan, Over et al. 2006). However, the sensitivity of conclusions on the likely number of lives saved to changes in coverage of long-lasting insecticide treated nets (ITN) has not been established.

The impact and cost-effectiveness of AMFm at different levels of coverage of other interventions depends on synergies as well as tradeoffs between prevention and treatment. Malaria control, when done right, has relied on a diversity of tools based on the understanding that there are synergies between them. However, there are tradeoffs as well. More money spent on one tool could mean less of another. It is possible to have large budgets for both prevention and treatment but at the cost of malaria control activities in another country. Given these synergies and tradeoffs, the economic value of malaria treatment and of the AMFm under different levels of malaria control and transmission intensity remains to be shown.

In this technical note, we evaluate the sensitivity of the effect and cost-effectiveness of the AMFm. We explore whether the combination of ITNs and ACTs have a synergistic impact on ACTs, which over time would lower the demand for ACTs as the malaria burden falls. Our analysis depends on accurately characterizing the relationship between malaria transmission, disease burden and demand for antimalarials (section 2). We introduce a bioeconomic model in section 3. Section 4 describes the main results and section 5 concludes the note.

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2 In this paper, we assume that transmission intensity is a function of natural factors (such as temperature, rainfall, forest cover etc) but also of ITN coverage levels. Therefore, our goal is to estimate cost-effectiveness of AMFm at different levels of transmission intensity rather than at different levels of ITN coverage. The reason for doing so is that although transmission intensity is always lower with greater use of bednets, the extent of decrease varies significantly depending on the vector species and geography (Hay, Smith et al. 2008).

3 It is beyond the scope of this paper to optimize allocation of resources across the diverse set of tools but other groups are current working on this line of research (Guerra, Gikandi et al. 2008).
PART II – MALARIA TRANSMISSION, DISEASE BURDEN AND DEMAND FOR ACTS

The cost-effectiveness of ACTs (and AMFm) varies with the intensity of malaria transmission. In high transmission settings with high prevalence, there are relatively few symptomatic cases among adults who are generally immune. Children suffer from symptomatic infections and need treatment. In a large number of endemic countries, parents seek treatment in the private sector, but effective antimalarials are beyond the financial reach of many low income families. The availability of effective, affordable ACTs in the private sector as a result of AMFm is expected to increase access for all, but especially for children who have the most to gain from the availability of treatment close to the home. Provision of drugs through this financing mechanism is cost-effective because of the large number of child deaths averted. However, cost-effectiveness could be diminished to some extent because of the use of ACTs for fevers not caused by malaria.

As ITN coverage increases, malaria prevalence decreases and there are fewer infectious bites. Although there is some evidence that there may be more cases of clinical malaria necessitating greater levels of treatment (Snow, Omumbo et al. 1997), a Cochrane review concluded that ITNs unambiguously lead to lowering malaria intensity and cases (Lengeler 2004). This also suggests that ITNs would reduce the need for antimalarial drugs, and that the medical benefits of effective treatment would be lower as malaria transmission declines. However, it is plausible that increasing access to drugs and treating a higher fraction of clinical malaria episodes would enhance the reductions in malaria transmission achieved through ITNs.

However, weighing against this is the increased likelihood of resistance as transmission declines. A larger number of clinical malaria cases implies a greater demand for antimalarials and therefore greater selection pressure (Hastings 1997; White 1998). Moreover, recent work suggests that as transmission declines, the stock of semi-immune individuals who harbor sensitive parasites and do not seek treatment effectively declines (Klein, Smith et al. 2008). In high transmission settings, these immunes work as a buffer against the selection pressure imposed by antimalarials. Therefore, resistance is more likely to arise in low-transmission settings or unstable transmission, as is believed to be the case with resistance to both chloroquine (CQ) and sulfadoxine-pyrimethamine (SP)\(^4\) (White 1998; White and Pongtavornpinyo 2003). Since artemisinin combinations are likely to delay emergence of resistance relative to the use of monotherapies, their role is particularly important in low transmission settings.

Data on the volume of antimalarials sold and factors determining antimalarial demand in sub-Saharan Africa are notoriously poor. Previous studies have relied on mathematical model-based predictions (Laxminarayan, Over et al. 2006), key informant surveys (Kindermans, Vandenbergh

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\(^4\) Other hypotheses for greater likelihood of resistance in low transmission settings are described in Klein et. Al. (2008).
et al. 2007) and approximations based on the estimated number of clinical cases (Dalberg Global Development Advisors 2007). Moreover, reliable data have been lacking on the link between intensity of malaria transmission and malaria morbidity (Snow, Omumbo et al. 1997). Given these uncertainties, directly estimating the effect of changes in malaria transmission on demand for treatment may be challenging. Mathematical models of disease transmission, resistance and demand for treatment may be helpful in characterizing changes in volume of ACTs subsidized by AMFm and the cost-effectiveness of this mechanism at different levels of transmission intensity.
PART III – METHODS

To examine the results of a two-stage SIS immunity model for resistance evolution in malaria parasites with regard to the initiation of the subsidy for ACTs, we used the resistance structure described in our earlier work (Laxminarayan, Over et al. 2006). In the 2-stage immunity model, we assumed that individuals were infected either with a resistant parasite or a sensitive parasite (Klein, Smith et al. 2008). In this analysis, resistance was broken up into a number of compartments corresponding to resistance to CQ, SP, AMT or ACT and any combination of those drugs and the partner drug, which we assumed was not used as monotherapy.

We use a two-stage susceptible-infected-susceptible (SIS) model of malaria transmission and resistance in order to assess the cost-effectiveness of the AMFm subsidy at different levels of malaria transmission. (Klein, Smith et al. 2008). Infected individuals are assumed to build up clinical immunity over time. This immunity reduces the frequency and severity of clinical symptoms, and therefore the demand for ACTs, and also an individual's level of infectiousness (details are presented in the appendix). The basic model is calibrated using the parameters used in our earlier assessment of the cost-effectiveness of AMFm (Laxminarayan, Over et al. 2006). Baseline estimates of cost-effectiveness for different levels of the epidemiological inoculation rate (EIR) are assumed to be the same as in the earlier paper.

The reductions in transmission intensity that are achieved through a combination of malaria control activities can be understood by looking at the basic reproductive number, $R_0$, which describes the number of infectious mosquitoes that would arise from a single infectious mosquito after one generation of the parasite [1-3]. $R_0$ is derived from a quantitative description of the parasite life-cycle in the absence of malaria control. Parameters describe aspects of larval ecology ($\lambda$), adult Anopheles demography ($g$), Anopheles feeding behaviour ($f$ and $Q$), parasite development in the Anopheles ($n$), transmission efficiency ($b$ and $c$), the duration of the human infectious period ($1/r$), and heterogeneous biting ($\rho$). The effects of malaria control that targets different aspects of the parasite or Anopheles life-cycle are illustrated by writing $R_0$ in the following way:

\begin{equation}
R_0 = \lambda \frac{f^2Q^2e^{-gn}}{g^2} \frac{bc}{R}(1 + \alpha)
\end{equation}

\begin{align*}
\lambda & : \text{Larval Control} \\
\frac{f^2Q^2e^{-gn}}{g^2} & : \text{Adult Mosquito Control} \\
b & : \text{Sporozoite or Liver Stage Vaccine} \\
c & : \text{Transmission Blocking Vaccine} \\
1/r & : \text{Antimalarial Drugs or Blood Stage Vaccines}
\end{align*}

Transmission intensity in a population that has some measure of control is denoted $R_C$, a term that is directly analogous to $R_0$, except that it describes potential transmission under a specific level of control. Potential transmission intensity with ITNs is described by the expression $R_C(\lambda)$,
where is effective coverage with insecticide treated nets (Le Menach, Takala et al. 2007). The reductions in transmission intensity can be described intuitively as an effect size, defined by the ratio $R_0/R_C$: a 90% reduction in transmission intensity is equivalent to an effect size of 10 (from 100% to 10% for example).

Antimalarial drugs also reduce transmission intensity, but the expected effect size varies with transmission intensity because of clinical immunity. The duration of asexual parasitemia for an untreated, simple infection is approximately 200 days [5, 6]. The infectious period is related to the carriage of mature gametocytes, which are present 8-10 days after a patent asexual parasitemia, and that likely persist about 21 days after an infection is cleared by drugs, depending on the drug used. Fever usually occurs at the beginning of an infection, so prompt treatment with drugs that clears both asexual parasites and gametocytes can reduce the infectious period substantially. The critical parameters are the fraction of new infections that present with clinical symptoms, the fraction of clinical malaria episodes that are cured, and the fraction of fevers that occur in a person who is already infected. Intuitively, clinical malaria reduces the fraction of new infections that are cured.

This expression for $R_0$ is also conceptually useful because it clearly demonstrates that the combined effects of different modes of malaria control are multiplicative. For example, if ITNs achieve a factor of 10, and antimalarial drugs achieve a factor of 10, the total effect size would be 100, a 99% reduction. To put it another way, if drugs would give a 10-fold reduction in transmission intensity, this effect would be achieved in addition to any effect achieved with ITNs. This logic falters when malaria control effects are correlated (Koella 1991), for example, if people who are more likely to use a net are also more likely to properly cure an infection.

A more important consideration is that the use of ITNs reduces clinical immunity and increases the fraction of new clinical episodes that present with symptoms. These interactions among the effect sizes of drugs and ITNs are complicated; on the one hand, the loss of clinical immunity could increase the burden of malaria (Snow papers). On the other hand, the loss of immunity would lead to further reductions in transmission intensity in an area where a high fraction of clinical episodes are treated with effective antimalarial drugs. To examine these effects, we have evaluated a mathematical model.

To generate household drug demand functions, we adopt a nested, constant elasticity of substitution (CES) utility function defined over a period of duration $t$, where $\theta$ is the discount rate:
In (2a) the term in square parentheses is utility per unit of time from general consumption $x$ and a composite good of effective drug treatments $E$; $\sigma_i$ is the substitution elasticity between $x$ and $E$, which governs the responsiveness of aggregate drug use to the ACT subsidy. $\alpha_{cost}$ is the marginal disutility from incapacitation due to symptomatic infection and $\Sigma_k N_k^{INF} / \bar{N}$ is the probability that an individual will be infected with any strand of malaria at a given point in time.

In (2b), the drug composite is a CES function over consumption of the three drugs, weighted by their respective effectiveness. The elasticity $\sigma_a$ governs the degree of substitution between different drugs and therefore to what extent extra use of the combination drug will displace use of monotherapies; $\alpha_C$, $\alpha_M$ and $\alpha_P$ are distribution parameters chosen to imply an observed initial drug mix and overall drug coverage rate.

Using duality theory, and an analogous budget constraint to that in (2.2), we obtain the drug demand functions:

$$a_i = \frac{(p_j^{-\sigma_a} / (\alpha_j e_j)^{-\sigma_a})^{-\sigma_a}}{\tilde{p}^{-\sigma_a}} \frac{\tilde{p}^{1-\sigma_a} \ln C}{1 + \tilde{p}} , \quad \tilde{p} = \sum_j p_j / (\alpha_j e_j)^{1-\sigma_a} , \ i, j = M, P, C$$

where drug prices $p$ are defined net of any subsidies, $\tilde{p}$ is an index of drug prices, accounting for drug effectiveness, and the price of $x$ is unity. The functions in (3) are independent of infections, that is, the proportion of infected people who use drug $i$ varies with (a) the price and effectiveness of that drug relative to the price and effectiveness of other drugs and (b) the price and effectiveness of drugs in general relative to the price of the general good. However, drug coverage rates do not vary with changes in overall malaria prevalence.

We ran this model with a base set of parameters across a range of demand elasticities (formulated using a CES demand function described earlier) and EIRs. The following figures show the number of deaths averted, the number of ACT treatments, the estimated cost of the subsidy and its cost-effectiveness, defined as dollars per death averted, as EIR increases, for different levels of subsidy in a well-mixing population of one million people. All four graphs are replicated for each elasticity level (low, med-low, med-high, and high). To see how demand
elasticity impacted the results, we compared each category at the full subsidy level (figure 5). All results assume 3% discounting.
PART IV – RESULTS

Figures 1 and 2 show deaths averted, number of treatments, cost of AMFm and cost-effectiveness of AMFm for two levels of demand elasticity. The greater the elasticity, the more that ACT demand will increase in response to a decline in retail prices because of AMFm. Increasing coverage with ACTs has the effect of extending effective treatment to those who might not have been able to afford these drugs, but also in terms of lowering parasitemia in those with asymptomatic malaria. The transmission reduction effect is likely small but meaningful in low transmission settings.5

The downside of greater demand elasticity is the greater likelihood that ACTs will be used for fevers not related to malaria, and a greater likelihood of resistance developing because of the selection pressure. Since demand is a function of price but also of malaria prevalence, the volume demanded is also a function of EIR.

Regardless of the level of demand elasticity, deaths averted are greatest for intermediate levels of vectorial capacity and are maximized for highest levels of subsidy ($8.60). But the cost of the subsidy is also greatest at the highest levels of AMFm subsidy. The cost-effectiveness of AMFm is highest (when cost/death averted is lowest in the fourth graph) as vectorial capacity declines. Although the precise cost-effectiveness numbers will depend on the part of the subsidy that is derived from manufacturer discounts and the part that is actually subsidized by donors (the current version lumps the two categories), greater use of ITNs and other measures to decrease vectorial capacity appears to have a positive effect on the cost-effectiveness of AMFm.

These results reflect the fact that in populations with a large number of immune individuals (which occurs as EIR increases), the fact that these individuals continue to transmit, negates the external transmission reduction benefit. In other words, the use of ACTs does not significantly alter the population dynamics, most individuals remain infected at all times. These results are pursuant to the percentage of the parasite population that is resistant to other drugs (CQ, SP). Increases in these percentages would increase the cost-effectiveness of using ACTs.

In figure 3, we compare the full subsidy ($8.60) across different levels of demand elasticity. Both deaths averted and cost-effectiveness appear to be largely invariant to demand elasticity, at least in our preliminary analysis.

5 There is evidence that ACTs can themselves help lower malaria transmission (Nosten, Vugt et al. 2000; Barnes, Durrheim et al. 2005; Sutherland, Ord et al. 2005). However, the transmission reduction effect has not been observed for mass drug administration with a combination of sulfadoxine-pyrimethamine and artesunate, for instance (von Seidlein, Walraven et al. 2003).
PART V – DISCUSSION

With expanded funding for malaria control, it is likely that the early successes of control in Ghana, Ethiopia, South Africa, Mozambique, Zambia and Zanzibar will be repeated elsewhere (UNICEF 2007). However, lowering malaria transmission does not take away the need for effective antimalarials – if anything, it increases it. With lower transmission, the number of symptomatic cases (both children and adults) first increases with lower population immunity to malaria. A larger proportion of untreated children over age five and adults will progress to infection (see table 1 in Lubell, Hopkins et al. 2008). Over time and with even lower transmission, cases and the need for treatment declines. Effective treatment plays a critical role in reducing transmission at already low transmission intensities (Le Menach, Takala et al. 2007).

In this paper, we use an economic-epidemiological model of malaria control and prevention to estimate the cost, deaths averted and cost-effectiveness of the AMFm under different transmission scenarios. We find that the need for the subsidy goes up as malaria control lowers intensity of transmission. However, the cost-effectiveness of the subsidy also increases as the number of averted deaths is also greater. Once a threshold has been crossed, the level of the subsidy needed also goes down but so does the cost-effectiveness of the subsidy because of the smaller number of averted deaths.

We can draw two conclusions. First, transmission reductions because of investments in ITNs and IRS do not preclude the need for effective treatment. In fact, demand for antimalarials could rise initially with malaria control because of the greater number of symptomatic infections. In this range of EIRs, the cost-effectiveness of AMFm is higher than at high EIRs. As a corollary, the demand for effective antimalarials will increase use of artemisinin monotherapies unless the price of ACTs in the private sector is lowered to a level comparable to that of other antimalarials. Second, the cost-effectiveness of AMFm and deaths averted are robust to assumptions about demand elasticity.

There are a number of important caveats. First, our knowledge of antimalarial demand has not changed much in the last decade. We have used plausible parameters in our CES function but these are not based on field data. Second, the model is theoretically accurate at describing the impact of malaria control on demand for treatment over a wide range of transmission intensities. However, as malaria prevalence reaches levels at which elimination can be achieved, the dynamics change substantially. New research is looking at the possibility of a bistable equilibrium where malaria is stable either at elimination or at a positive prevalence. Our model likely does poorly at characterizing the relationship between malaria control and treatment at very low levels at prevalence. Third, the estimates of AMFm cost-effectiveness presented in this version are based on the total cost reduction in the private sector. Since some of these reductions will be achieved through pooled procurement, they do not necessarily represent costs to the AMFm mechanism. In other words, we urge the reader to pay attention to the qualitative changes in cost-effectiveness rather than quantitative levels.
Finally, we have largely ignored the issue of public versus private sector provision of ACTs. We have assumed that ACT availability at an affordable price will increase in public sector clinics as well as through the commercial private sector. A further refinement of this research would include separating demand functions by public and private sector. However, this would require far better data on volume of antimalarials consumption through these different channels than is currently available.
APPENDIX: SIS TWO-STAGE MODEL

The full model is provided in (Klein, Smith et al. 2008). Susceptible individuals \((S)\) become infected \((I)\) with wild-type infections at the rate \(h_w(1-\xi_1)\) and resistant infections at the rate \(h_x\), where \(h_i\) is the happenings rate (see text) and \(\xi_i\) is the rate at which new infections result in clinically manifested symptoms that are treated and resolved prior to the formation of gametocytes. Infected individuals naturally clear resistant infections at rate \(r_{x1}\) and they clear wild-type infections at the rate \(\rho_i+r_{w1}\), where \(\rho_i\) is the rate of drug treatment. Infected individuals acquire semi-immunity at rate \(\theta\) and lose immunity at rate \(\gamma\) if they are no longer infected.

Individuals die from all states at a background rate of \(\mu\) and are born at rate \(B\) as nonimmune susceptibles (process not shown).

![Diagram of SIS Two-Stage Model](image)

Table A1: Baseline Parameter Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquisition of clinical immunity</td>
<td>(\theta) 10 years</td>
</tr>
<tr>
<td>Loss of clinical immunity</td>
<td>(\gamma) 2 years</td>
</tr>
<tr>
<td>Fraction of new infections that are treated and cleared</td>
<td>(\xi_1) 0.3  (\xi_2) 0.01</td>
</tr>
<tr>
<td>Rate clinical symptoms arise ((\sigma_i)) times Fraction treated ((f_i)) equals rate existing infections are cleared by drugs ((\rho_i))</td>
<td>(\sigma_1 = f_1 = \rho_1 = 0.025(0.2) = 1/200)  (\sigma_2 = f_2 = \rho_2 = 0.01(0.2) = 1/500)</td>
</tr>
<tr>
<td>Disease induced death rate</td>
<td>(M) 180/100000/year</td>
</tr>
<tr>
<td>Human feeding rate</td>
<td>(A) 0.3</td>
</tr>
<tr>
<td>Infectivity rate</td>
<td>(B) 0.8</td>
</tr>
<tr>
<td>Mosquito death rate</td>
<td>(G) 1/10</td>
</tr>
<tr>
<td>Number of days required for sporogony</td>
<td>(N) 10</td>
</tr>
<tr>
<td>Recovery rate</td>
<td>(r_w = 1/(165/b))</td>
</tr>
<tr>
<td></td>
<td>(r_x = r_w) (fitness cost)</td>
</tr>
</tbody>
</table>
REFERENCES


Table 1: Estimated donor funding for malaria by region (USD)

<table>
<thead>
<tr>
<th>Recipient Region</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas</td>
<td>382500</td>
<td>1660200</td>
<td>3580900</td>
<td>4533200</td>
<td>4209601</td>
<td>9443892</td>
</tr>
<tr>
<td>Eastern Europe/Central Asia</td>
<td>0</td>
<td>195000</td>
<td>0</td>
<td>961000</td>
<td>6674195</td>
<td>2376417</td>
</tr>
<tr>
<td>South Asia</td>
<td>159800</td>
<td>716000</td>
<td>2937039</td>
<td>2254041</td>
<td>2764337</td>
<td>9120588</td>
</tr>
<tr>
<td>South East Asia</td>
<td>7188640</td>
<td>7858399</td>
<td>5003220</td>
<td>5210568</td>
<td>14449272</td>
<td>19367190</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>9365076</td>
<td>21749251</td>
<td>47555385</td>
<td>53068120</td>
<td>95335266</td>
<td>1.65E+08</td>
</tr>
<tr>
<td>Total</td>
<td>17096016</td>
<td>32178850</td>
<td>59076544</td>
<td>66026929</td>
<td>1.23E+08</td>
<td>2.06E+08</td>
</tr>
</tbody>
</table>

Source: Authors’ calculations.
Table 2: Costs, effectiveness, and cost effectiveness of interventions in Afr-D

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Average yearly costs ($int)</th>
<th>Average yearly effectiveness (DALYs averted)</th>
<th>Average cost effectiveness ($int/DALY averted)</th>
<th>Incremental cost effectiveness ($int/DALY averted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case management with artemisinin based combination therapy (80% coverage)</td>
<td>72 386</td>
<td>626</td>
<td>7 771 018</td>
<td>9</td>
</tr>
<tr>
<td>Case management with artemisinin based combination therapy (95% coverage)</td>
<td>95 609</td>
<td>717</td>
<td>9 254 473</td>
<td>10</td>
</tr>
<tr>
<td>Insecticide treated bed nets plus case management with artemisinin based combination therapy plus intermittent presumptive treatment in pregnancy (95% coverage)</td>
<td>315 546</td>
<td>119</td>
<td>12 972 791</td>
<td>24</td>
</tr>
<tr>
<td>Indoor residual spraying plus insecticide treated bed nets plus case management with artemisinin based combination therapy plus intermittent presumptive treatment in pregnancy (95% coverage)</td>
<td>467 673</td>
<td>321</td>
<td>14 561 792</td>
<td>32</td>
</tr>
</tbody>
</table>

DALY=disability adjusted life year; $int=international dollar.
AFR-D covers Western Africa.
Source: (Morel, Lauer et al. 2005)
Figure 1: Medium-Low Elasticity

Deaths Averted

ACT Treatments
Figure 2: Medium-High Elasticity

Deaths Averted

ACT Treatments
Figure 3: Elasticity Comparison at Full Subsidy

Deaths Averted

ACT Treatments

Elasticity
- low
- medium-low
- medium-high
- high
Subsidy Cost

Cost Effectiveness
La gestión de los hospitales en América Latina

Resultados de una encuesta realizada en cuatro países

Richard J. Bogue, Claude H. Hall, Jr. y Gerard M. La Forgia

Junio de 2007