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Prevention or treatment? The introduction of a new antimalarial drug in Angola

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Prevention or treatment? The introduction of a new antimalarial drug in Angola

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Abstract

In spite of massive efforts to generalize efficient prevention, such as insecticide- treated mosquito nets (ITN) or long-lasting insecticidal nets (LLINs), malaria remains prevalent in many countries and ITN/LLINs are still only used to a limited extent. We present a simple theoretical model of household preventive behavior in response to malaria prevalence. The novelty is to include a tradeoff between prevention and treatment which depends on the relative price of treatment with respect to prevention. We show that a relatively low price of treatment reduces prevention. However, this result depends on endemicity and income distribution. Next, we test the model and estimate the effect of the introduction of an effective treatment on prevention behaviors in the case of malaria. We rely on microeconomic data and build up a difference-in-differences analysis of individuals prevention behaviors following the introduction of Artemisinin Combination Therapies (ACTs) in Angola. We exploit differences in terms of treatment intensity across geographic areas and differences in individuals exposure to the introduction of ACTs. Our results suggest that the increase in access to treatment for malaria in Angola may have had a negative impact on the use of Insecticide Treated Nets even though the two were jointly promoted over the period. The effect disappears for the poorest category and the treatment effect is higher in higher endemicity levels.

Key words: Malaria, Treatment, Prevention

JEL Classification: O12, I15, I25

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Abstract

In spite of massive efforts to generalize efficient prevention, such as insecticidetreated mosquito nets (ITN) or long-lasting insecticidal nets (LLINs), malaria remains prevalent in many countries and ITN/LLINs are still only used to a limited extent. We present a simple theoretical model of household preventive behavior in response to malaria prevalence. The novelty is to include a trade-off between prevention and treatment which depends on the relative price of treatment with respect to prevention. We show that a relatively low price of treatment reduces prevention. However, this result depends on endemicity and income distribution. Next, we test the model and estimate the effect of the introduction of an effective treatment on prevention behaviors in the case of malaria. We rely on microeconomic data and build up a difference-indifferences analysis of individuals prevention behaviors following the introduction of Artemisinin Combination Therapies (ACTs) in Angola. We exploit differences in terms of treatment intensity across geographic areas and differences in individuals exposure to the introduction of ACTs. Our results suggest that the increase in access to treatment for malaria in Angola may have had a negative impact on the use of Insecticide Treated Nets even though the two were jointly promoted over the period. The effect disappears for the poorest category and the treatment effect is higher in higher endemicity levels.

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1 Introduction

A recent trend in policies aiming at controlling or eliminating malaria in countries where it is prevalent has been the attempt to provide greater and free access to new anti-malarial drugs. Notably under the impulsion of the Affordable Medicine Facility for malaria program (AMFm), most Sub-Saharan African countries began subsidizing Artemisinin based combination therapies (ACTs), becoming the main tool used in the fight against malaria. Over the past decade, African countries have therefore transitioned from chloroquine to artemisininbased combination therapies (ACTs) as a first-line policy for uncomplicated malaria (Flegg et al., 2013).

These policies have been motivated by the high cost-effectiveness of ACTs in curing clinical malaria. Moreover, promoting the use of combination therapies instead of mono-therapies could postpone the development of malaria parasites' resistance to artemisinin. However, the economic literature emphasized that subsidizing too much may lead to treatment misallocation (Dupas, 2014; Adhvaryu, 2014; Cohen, Dupas and Schaner, 2015).

Another important aspect that has been neglected in this literature is the synergy between treatments for malaria and the use of prevention tools, notably Insecticide Treated bed Nets (ITNs). Indeed ITNs are as well as ACTs a very cost effective tool for the control of malaria. There is therefore probably a need to jointly promote ACT and bednets (Arrow, Panosian and Gelband, 2004). But this mix between treatment and prevention may not be easy to reach. Indeed it is possible that the apparition of an effective cheap treatment lowers the incentives for prevention and therefore ACT promotion may be detrimental to the use of Insecticide Treated Nets. Such a negative impact has for instance already been observed in the case of the HIV epidemics (Lakdawalla, Sood and Goldman, 2006). However to the best of our knowledge, a similar relationship has not been documented for malaria so far.

For the purpose of this analysis, we use data from two Malaria Indicator Surveys (MIS), malaria specific household surveys organized as part of the DHS program, that took place in Angola in 2006/2007 and 2011. Malaria Indicator Surveys focus on young children, the most at risk population when it comes to malaria, and have the advantage of providing accurate information on both ACT consumption and the use of Insecticide Treated Nets. The introduction of ACT in Angola began in 2006. There was therefore a significant increase in the use of this new treatment between the two surveys we are using. Indeed the 2006 MIS reported nearly no use of ACTs while the 2011 survey relates that children that experienced fever in this year were given ACT in more than 20% of cases. We can therefore estimate the effect of access to an effective treatment on the use of Insecticide Treated Nets through a difference-in-differences (DiD) where the treatment is the introduction of ACTs in Angola between 2006 and 2011.

In this DiD, the increase in access to ACT is given by the increase in the average level of use of ACTs in a given province and the use of bednets is estimated at the individual level using the information on the behavior of children contained in the Malaria Indicator Surveys. The impact of access to ACTs is differentiated both, across provinces, between which the increase in ACTs use has not been similar, and across children, using a variable of exposure that depends on the relative time a cohort spent exposed to the treatment, i.e. the policy change.

However several factors may lower the level of expected returns of an improved access to ACTs. The prevalence elasticity of preventive behaviors is probably the most important of these factors - when the prevalence of a disease decreases, due to prevention or another factor, the risk of getting infected is lowered and the expected returns of protecting oneself are therefore lowered as well. If the decrease in its expected returns, following a fall in prevalence, is too high, prevention may appear as non profitable, and some individuals may stop using ITNs (Seban, Thuilliez and Herbreteau, 2013). In such cases lowering the cost of using bednets, by for example subsidizing them or promoting long lasting insecticide treated nets, that require less maintenance, may help adoption. However this is already being done and may not be sufficient to allow for a level of use of ITNs that would lead to malaria elimination, particularly if other factors than reductions in malaria prevalence reduce the expected benefits of prevention. Access to an effective treatment may be one of these factors. We found that from 2006 to 2011 the spread of new treatments for malaria in Angola may indeed have had a negative impact on the use of bednets.

The paper is organized as follows. Section 2 provides suggestive evidence on the effectiveness of ACTs. Section 3 provides a simple model to analyse the trade-off between prevention and treatment. Section 4 describes our empirical strategy. Section 5 provides the results. We conclude in Section 6 and we discuss the implications of the results for policy makers.

2 Malaria in Angola and the National Malaria Control Strategy (2005-2010)

Malaria is a major health problem in Angola, accounting for an estimated 35% of the overall mortality in children under five, 25% of maternal mortality and 60% of hospital admissions for children under five. Provinces in the North of the country have higher prevalence rates, while southern provinces are epidemic-prone. About 85% of the population is at risk of malaria.

The National Malaria Control Strategy (NMCS) between 2005 and 2010 - covering our period of interest - has been developed with assistance from the WHO and UNICEF. Following this National Malaria Control Strategy, Artemether-lumefantrine (AL, Coartem®) was adopted as the new first-line drug for the treatment of uncomplicated *P. falciparum* malaria in September 2004. The efficacy of Coartem® has been confirmed in many different patient populations around the world (Makanga and Krudsood, 2009).

In January 2005, Angola received approval for a USD 27.5 million malaria grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria. The objectives were to increase coverage with ACTs, IPT (Intermittent Preventive Treatment), and ITNs and to build capacity within the National Malaria Control Program (NMCP). In addition, in July 2005, Angola has been selected as one of the first three countries in a new five-year President Malaria Initiative (PMI) to rapidly scale up malaria prevention and treatment interventions in high-burden countries in sub-Saharan Africa. The ambitious goal of PMI was to reduce malaria mortality by 50% by achieving 85% coverage of key prevention and treatment interventions in the country.

The new drug policy was implemented in 2006 (Flegg et al., 2013) and since then, Coartem® has been procured free of charge at public health facilities, with a rapid scale-up in distribution and use. Health care workers have also received intensive technical training on the use of artemisinin-based combination therapies (ACTs). The treatment of malaria in most MoH facilities in Angola is based on clinical diagnosis. Malaria microscopy is only available in hospitals and larger health centers in urban areas and the quality of diagnosis is unknown. Rapid diagnostic tests (RDTs) are used in some health facilities supported by non-governmental organizations/faith-based organizations (NGO/FBOs). Malaria cases may be significantly overstated, which has several implications, including an unreliable baseline for evaluating antimalarial activities, a waste of public resources for treating individuals who may not have malaria, and increased resistance (PMI, 2006).

With respect to ITNs, the National Malaria Control Strategy supports a market segmentation approach, consisting of free distribution of nets to pregnant women and children under five, with subsidized distribution to the general population and commercial sector distribution in urban areas. Because of very low re-treatment rates for conventional nets, the National Malaria Control Strategy encourages the distribution of long-lasting insecticidetreated nets (LLINs). However, the impact of large-scale and free access to Coartem® on the use of ITNs has not been estimated so far and may be an additional source of waste of resources. With respect to Indoor residual spraying (IRS), only limited IRS has been carried out by the NMCP. The National Malaria Control Strategy supported the use of IRS for malaria prevention in epidemic-prone areas of the southern provinces of Namibe, Cunene, Huila, and Cuando Cubango and in the capital, Luanda.

3 Model

A classical approach was used to model transmission of malaria between human populations and mosquito (Anopheles) populations. Following Berthélemy et al. (2013), Berthélemy, Gaudart and Thuilliez (2015), and Berthélemy and Thuilliez (2015), this transmission model can be synthesized by a dynamic equation in which malaria prevalence at time t + 1, i.e. the probability of being infected, X_{t+1} , is a concave function $Q(X_t, m)$ of malaria prevalence at time t and of mosquitoes density (m) for which the slope at origin is the basic reproduction rate, R_0 , and:

$$\begin{cases}
Q(0,m) = 0, \\
Q(1,m) < 1
\end{cases}$$
(1)

At the steady state solution of this model of dynamic interaction between humans and vectors the probability that a human be infected, determined by the function Q(X, m), converges towards the trivial disease free stable steady state, if and only if $R_0 \leq 1$. This case is not considered in what follows, as it does not coincide with the persistence of malaria in large regions of the developing world. Conversely, if the basic reproduction rate is above 1, it converges towards a stable steady state characterized by a strictly positive prevalence of malaria.

Policies can be introduced to reduce the basic reproduction rate, which could then be lowered below 1. This is the aim of LLIN-based policies: introduction of protection tools such as LLIN could reduce malaria transmission, leading possibly to a disease free stable steady state. But these policies only address the problem of LLIN distribution but rarely the LLIN use. Protection behavior has been added to the previous epidemiological transmission model, based on economic mechanisms fully described in Berthélemy et al. (2013). The protective behavior is defined at the individual level by a variable h, which is equal to 1 in case of LLIN use and to zero otherwise. It was assumed that the only mean to prevent from malaria exposure is to use a LLIN, and LLIN use was supposed to provide complete protection. These assumptions can be relaxed without affecting the main findings of the model (Berthélemy et al., 2013). At any time, depending on the use of LLIN before, the health status of the individual can be susceptible, $\sigma(h) = S$, or infected, $\sigma(h) = I$. The probability of being infected at any time, conditionally to the absence of protection before, can then be written as:

$$\pi_I = P(\sigma(h) = I | h = 0) = Q(X, m)$$
(2)

and then:

$$X = (1 - H)\pi_I \tag{3}$$

where H is the proportion of LLIN use among the population.

The mosquito density, m, is modified by LLIN use: the exposed human population decreases, being only the proportion 1 - H of non-protected population; the absolute number of mosquitoes decreases with H as LLINs kill mosquitoes (knock down effect). Hence m, which was a parameter in the pure epidemiological model, can be written as a function of H as follows:

$$m(H) = \frac{m(0)}{1 - H} (1 - \gamma(H))$$
(4)

where $\gamma(H)$ is the proportion of mosquitoes killed by LLINs, an increasing function of H, and m(0) is the value of mosquito density in case of no protection. It follows that, at the steady state, Q(X, m(H)), and then the probability of being infected in absence of protection depends on the aggregate proportion of protected individuals H.

At the microeconomic level, the choice of protection is determined by maximizing the expected utility of each individual. The decision h of protection affects individuals' utility through two paths: (i) an expected positive impact on the health status in case of protection and (ii) a private cost, called κ . Protection decision is described through the following maximization program:

$$max_h E[u(\sigma(h))] - \kappa W(\omega)h \tag{5}$$

where $u(\sigma(h))$ is the utility levels attached to the health status (susceptible or infected thus depending on h, the use of a protection), with 0 < u(I) < u(S); ω is the individual income; $W(\omega)$ is the marginal utility of income, supposed as usual to decrease with income. The expected utility can be estimated using the following probabilities of being susceptible or infected, conditionally to the use of protection:

$$\begin{cases}
P(\sigma(h) = S | h = 1) = 1, \\
P(\sigma(h) = S | h = 0) = 1 - \pi_I, \\
P(\sigma(h) = I | h = 0) = \pi_I.
\end{cases}$$
(6)

As in standard economic epidemiological models, the individual will use protective tools when $W(\omega)$ is lower than the expected utility loss associated with the risk of infection that occurs in the absence of protection:

$$E[u(\sigma(1)) - u(\sigma(0))] \ge \kappa W(\omega)h \tag{7}$$

Thus protection occurs if and only if:

$$\pi_I \ge \frac{\kappa W(\omega)}{u(S) - u(I)} \tag{8}$$

The right-hand side of this inequality is termed $C(\omega)$, and the inequality (8) determines the income threshold beyond which protection is not used, depending on the probability of infection in absence of protection.

$$\begin{cases}
 h = 1 \text{ if } \omega \ge C^{-1}(\pi_I), \\
 h = 0 \text{ else}
\end{cases}$$
(9)

Knowing individual protection behaviors, the percentage of protected persons can be computed as follows:

$$H = \int_{C^{-1}(\pi_I)}^{+\infty} f(\omega) d\omega \tag{10}$$

where f is the probability density function of ω , describing the income distribution of the population. Hence H is increasing with π_I . The long term properties of the model are described in Berthélemy et al. (2013).

The equilibrium levels of protection H, of malaria prevalence X, of vector density m and or probability of infection in absence of protection π_I are then computed as a solution of the system of equations (2), (3), (4) and (10). The first three equations define implicitly π_I as a decreasing function of H (the more people use protection, the lower the prevalence of the parasite among vectors and then the lower the risk of infection of the non-protected people), which, interacted with equation (10), defines H at equilibrium. Under normal conditions a better protection, which could be obtained through distribution of LLINs at subsidized price will lead to a reduction of the steady state prevalence of malaria. Berthélemy et al. (2013); Berthélemy and Thuilliez (2015) discuss the conditions under which this policy can conduct to the disease free steady state, thus eliminating malaria.

Up until now, we have focused on the dynamics of prevention without the presence of a treatment choice. There are actually two scenarios of treatment:

- Firstly, malaria chemoprophylaxis is a preventive measure and can be assimilated to the use of LLINs in the model rather than to curative measures.
- Secondly, curative measures (or medical treatment in this case) will not play the same role as protection by LLINs in the model.

We consider here the introduction of a curative treatment. Treatment does not have an immediate effect on the infectious status of the individual but the decision tree changes. The

decision can be considered as sequential, given that the decision to buy medical treatment is only taken once infection has been observed. In second period, the infected individual will decide whether to buy medical treatment or not. In first period, this possibility of buying medical treatment if infected will affect the protection decision before infection.

It is assumed that an infected individual can buy medical treatment at a unit cost, λ , which reduces his/her illness. A decision variable, η , is introduced, which is equal to 1 if the individual buys medical treatment and 0 if he/she does not. The treatment decision is represented as:

$$\eta = 1$$
 if and only if $u(I|\eta = 1) - u(I|\eta = 0) \ge \lambda W(\omega)$ (11)

where $u(I|\eta = 0)$ is the value of the health status when infected and non-treated, $u(I|\eta = 1)$ is the value of the health status when infected and treated, with $u(I|\eta = 0) \le u(I|\eta = 1)$ and λ is the unit cost of treatment. An individual is susceptible after the treatment but the value of health is different from u(S) as the individual has been sick, so that $u(S) > u(I|\eta = 1)$.

The condition given in equation (11) can be written as:

$$\eta = 1$$
 if and only if $\omega \ge W^{-1}\left(\frac{u(I|\eta=1) - u(I|\eta=0)}{\lambda}\right)$ (12)

For simplicity reason, the right-hand side expression is denoted ω_1 . It depends only on parameters of the model (values attached to different health status) and on the price of treatment. The higher the price of treatment, the higher ω_1 , and the smaller the number of infected individuals who will decide to buy treatment.

Once this second period decision rule has been established, an individual will choose in the first period to use the protection device according to a rule comparable to that of the previous model without treatment. However there are now two thresholds on π_I , depending on the value of η , denoted $C_{\eta}(\omega)$, with $\eta = 0$ or $\eta = 1$.

$$h = 1$$
 if and only if $\omega \ge C_{\eta}^{-1}(\pi_I)$ for $\eta = 0$ or 1 (13)

where $C_0(\omega) = \frac{\lambda W(\omega)}{u(S) - u(I|\eta=0)}$ and $C_1(\omega) = \frac{\lambda W(\omega)}{u(S) - u(I|\eta=1)}$.

The complete solution then depends on how ω_1 , $C_0^{-1}(\pi_I)$ and $C_1^{-1}(\pi_I)$ compare. From $u(I|\eta=0) \leq u(I|\eta=1)$, it can be inferred that $C_0^{-1}(\pi_I) \leq C_1^{-1}(\pi_I)$, $\forall \pi_I$. Then, there are

only three cases to consider:

- Case 1: $\omega_1 \leq C_0^{-1}(\pi_I) \leq C_1^{-1}(\pi_I)$
- Case 2: $C_0^{-1}(\pi_I) \le \omega_1 \le C_1^{-1}(\pi_I)$
- Case 3: $C_0^{-1}(\pi_I) \le C_1^{-1}(\pi_I) \le \omega_1$

For case 1, h = 1 implies $\eta = 1$ and is obtained if and only if $C_1^{-1}(\pi_I) \leq \omega$, implying:

$$H = \int_{C_1^{-1}(\pi_I)}^{+\infty} f(\omega) d\omega, \text{ denoted } \phi_1(\pi_I).$$
(14)

For case 2, h = 1 either when $C_1^{-1}(\pi_I) \leq \omega$ (and $\eta = 1$) or when $C_0^{-1}(\pi_I) \leq \omega \leq \omega_1$ (and $\eta = 0$), then:

$$H = \phi_1(\pi_I) + \int_{C_0^{-1}(\pi_I)}^{\omega_1} f(\omega) d\omega$$
 (15)

For case 3, h = 1 when $C_0^{-1}(\pi_I) \leq \omega$ (and $\eta = 0$), then:

$$H = \int_{C_0^{-1}(\pi_I)}^{+\infty} f(\omega) d\omega, \text{ denoted } \phi_0(\pi_I).$$
(16)

Given the definitions of $\phi_0(\pi_I)$ and $\phi_1(\pi_I)$ it is clear that $\phi_1(\pi_I) \leq \phi_0(\pi_I)$. Overall, H can be represented as a function of π_I as illustrated in Figure 1. In the absence of treatment this function is simply $\phi_0(\pi_I)$, while in presence of a possible treatment it is below $\phi_0(\pi_I)$ for relatively low values of π_I , more precisely for

$$\pi_I \le C_1(\omega_1) = \frac{\kappa}{\lambda} \frac{u(I|\eta=1) - u(I|\eta=0)}{u(S) - u(I|\eta=1)} (17)$$

which depends on the relative price of protection to treatment. For relatively low treatment price, the equilibrium H will then be strictly lower in presence of treatment than in absence of treatment. Hence we conclude with the following general result: *introducing the possibility of treatment at low cost reduces the demand for protection, which in turn may increase malaria prevalence among the population.*

The empirical significance of this general result may however depend on the context. As already suggested above, the differential effect on protection of introduction of a possible treatment depends positively on the relative price of protection to treatment and then will increase with subsidization of the treatment. Conversely for high prices of treatment, $C_1(\omega_1)$ will tend to zero and then the differential effect will disappear, as long as the equilibrium level of π_I stays above $C_1(\omega_1)$. Therefore, we study two additional questions:

- Does this result hold independently of income distribution (and notably for the poorest segments of the population)?
- Does this result depends on endemicity (related notably to the density of vectors)?

As for the first question, the answer is that there is no differential effect for extremely poor people. Berthélemy et al. (2013) developed an analysis in which extreme poverty is defined by an infinite marginal utility of income, in which case individuals are insensitive to policies of subsidization of protection. Then they are insensitive to policies of subsidization of treatment too. More precisely the differential effect on H of the introduction of a possible treatment is equal to:

$$\Delta(H) = \int_{C_0^{-1}(\pi_I)}^{C_1^{-1}(\pi_I) + \Delta(\pi_I)} f(\omega) d\omega$$
(18)

Where $\Delta(\pi_I)$ is the positive variation of π_I induced by the reduction of protection $\Delta(H)$. Hence, if we consider the sub-population of individuals who are below the threshold income that would justify protection, the differential effect of introduction of a possible treatment disappears.

As for the second question, we can characterize a low-endemicity situation as a case where given an intrinsically low level of vector density the equilibrium level of π_I is low. From the above equation it is clear that $\Delta(H)$ tends to zero when π_I tends to zero, hence the differential effect of introduction of a potential treatment would be lower in lower endemicity regions.

4 Empirical framework

4.1 Data

We use data from two distinct *Malaria Indicator Surveys* (MIS) that were conducted in Angola respectively in 2006-2007 and 2011 (repeated cross-section). The MIS was developed

by the Monitoring and Evaluation Working Group (MERG) of Roll Back Malaria, an international partnership developed to coordinate global efforts to fight malaria. A stand-alone household survey, the MIS collects national and regional or provincial data from a representative sample of respondents. The data are of excellent quality and provide information on households behaviors, including both treatment and prevention, in response to malaria. However, the information regarding treatment (Coartem® use) is only available for children aged five and under for all years. Coartem® use is not given for pregnant women in 2006-2007. Consequently, we focus on children under-5 as the observational units, which constitute the most vulnerable group. It is important to notice that, though the data is not a panel of observations, we are able to exploit a time dimension by focusing on larger geographical areas than households or clusters, namely the provinces.

4.2 Empirical equation

Our empirical strategy can be interpreted as a difference-in-differences estimator, with the treatment being the introduction of ACTs in 2006. For an individual i in region j, who is a member of cohort c and surveyed by MIS in year t, we estimate the following equation:

$$h_{icjt} = \alpha + \beta [Exposure_{ict} \times ACT_{jt}] + \Gamma X_{ijt} + \delta_c + \delta_j + \delta_t + \delta_{ct} + \delta_{cj} + \delta_{jt} + \epsilon_{icjt}, \quad (19)$$

where h_{icjt} is the use of ITN, following the notation used in Section 3. $Exposure_{ict}$ is a variable that aims at capturing exposure to the policy change, namely the introduction of ACTs in 2006. It is defined as the time a child spent living since the introduction of ACTs, assuming ACT was introduced on January 2006 (Flegg et al., 2013), divided by the time that passed since his birth (in months). It captures the percentage of life a child passed exposed to the new policy regarding free access to treatment. A child's lifetime is defined as the difference between the MIS date of interview and the child's date of birth. Therefore, exposure to the new policy varies along two dimensions: across age cohorts for a single DHS survey round and across DHS survey rounds for a single age cohort. ACT_{jt} is the the average use of ACTs, among children that experience fever, at the province level which varies across survey years. X_{it} is a vector of control variables, including mother education,

an interaction term between the average use of ACT and the age of the child to avoid an omitted variable bias. Indeed, by definition, an individual's exposure to the new policy depends on his or her age. X_{it} also includes wealth, gender, urban location, and provincial malaria prevalence (the proportion of children aged from 6 to 59 months that were tested positive to malaria in the province the observed child live in). All regressions also include the transmission season when the child was interviewed. Angola is divided in 18 provinces and 4 levels of malaria endemic areas. δ_j , δ_t , δ_c are province, MIS survey-year, and cohort fixed effects. δ_{ct} are cohort-year fixed effects, δ_{jt} are not included in the regression, we add ACT_{jt} and $Exposure_{ct}$ separately in Eq.(19). The main conclusions were unchanged (results available upon request).. We estimate this equation on the sample of households that own a functional ITN and the general population. In the later case, ITN ownership is included as an additional control in X_{ijt} .

5 Results

5.1 Descriptive results

Table 1 provides summary statistics for the main variables of interest. For each child, MIS provide information on whether or not he/she slept under an insecticide treated net the night prior to the interview. From table 1 we can see that the proportion of children sleeping under an ITN increased slightly between the two surveys. In 2006/2007, 20% of the surveyed children had slept under a net the night prior the interview while in period two, 2011, 27% of the surveyed children had slept under a net.

Regarding the main explanatory variable (ACT use), we do not directly observe access to ACT in the data. The only information we have is regarding the treatment sick children are given. Indeed during their MIS interview, for each of their child, mothers were asked if he/she was feverish or got malaria during the last two weeks. If so, the mother was asked if the child took an ACT. Table 1 shows that the proportion of sick children that were given ACT increased dramatically, as expected, between period one and period two (from 3% to 22%). This increase was large not just in percentage terms but also in levels and thus could have a substantial effect on the use of other preventive measures. It was also concentrated in this five year period (2006-2011), allowing us to separate the effects caused by the policy from longer term changes in malaria prevalence. As mentioned in Section 2, Insecticide Treated Nets were simultaneously promoted over the period and should have increased. Lastly, it exhibited significant geographic variation across Angola's provinces.

Table I about here.

5.2 Difference-in-Differences

Table 2 provides OLS estimates of Eq.(19). The β of interest is the coefficient associated to $Exposure_{ict} \times ACT_{jt}$, the interaction between treatment intensity and individual exposure. The dependent variable is the use of ITN at the child level. We provide in separate columns similar regressions for both the full sample of households, and a sub-sample of households that own an ITN.

 β is significantly negative in all regressions and relatively stable when more control variables are introduced. Put differently, for children that have been exposed a significant part of their life to the treatment (ACT access), an increase in the overall consumption of ACTs in their province leads to a decrease in ITN use. The coefficient of interest is for instance estimated to be -5.187 in regression (4) that controls for the full set of fixed-effects. This means that an increase of 1 percentage point of ACT use in a given province is estimated to reduce the propensity to sleep under an ITN of a fully exposed children by 5.187 percentage points. This is an important impact.

The coefficient associated with the non interacted average level of ACT use should only capture the correlation between the consumption of ACT and the use of ITNs that stems from the co-linearity of distribution polices that was evoked in the data description part. The strong positive coefficient may be one more evidence of this col-linearity between ACT and ITNs distribution policies.

Of the two variables of the interaction term $Exposure_{ict} \times ACT_{jt}$, only the ratio of exposure can be assumed as completely exogenous. Indeed it depends on two exogenous terms, the date of introduction of ACT in Angola that does not vary across regions nor depends on current individual behaviors, and the age of the child that is randomly distributed and whose individual impact on the use of ITNs is already accounted for with the introduction of the age of children alone, its interaction with the access to ACT, and cohort-survey fixed effects.

On the other hand, the second term of the interaction giving the treatment effect, the access to ACTs cannot be assumed as completely exogenous. Indeed it is most likely that the level of ACT consumption in a given province does not only capture the effect of access to ACT. It probably correlates with other province characteristics like the prevalence of malaria. However with the inclusion of province and time fixed effects, what we are considering in the model is the effect of the increase in the use of ACT in a province between 2006 and 2011. The variation in the use of ACT might have been affected by changes in the characteristics of specific provinces but most of the change must have been caused by the change in policy over the period.

Regarding the exogeneity of the policy change across provinces two thing must be also kept in mind. First regarding the timing of introduction of ACT, it has been strongly influenced by (i) the discovery of ACTs (Klayman, 1985)¹, (ii) the formation of the Global Fund to Fight AIDS, Tuberculosis and Malaria in 2002 that became the largest source of external funding for malaria control, the President's Malaria Initiative, launched in 2005 by President George W. Bush, and the World Bank Booster Program for Malaria Control in Africa and (iii) the Affordable Medicine Facility for Malaria program (Arrow, Panosian and Gelband, 2004). These changes led to treatment adoption throughout Africa in less than a decade, there is therefore no reason to believe that it has been caused by a change in overall individual preferences. It also seems unlikely that ACT introduction was anticipated. Second regarding geographical differences in access, subsidization policies aim at global access, it is thus impossible to assume that the level of treatment access in provinces could be impacted by non observed considerations and that one province could be implicitly favored. As a consequence, the provinces where the increase of treatment access has been the highest cannot be assumed as being inhabited by individuals with particular preferences in terms of prevention.

Table II about here.

¹The first ACTs were provided at reduced prices to the WHO only in 2001

5.3 Heterogenous effect and Robustness check

The treatment effects conditional on poverty levels and pre-exposure regional malaria prevalence are provided in Table 3 and Table 4 and confirm the predictions of the model. There is no effect for the poorest category and the treatment effect is lower for lower endemicity levels. As a last robustness check, Table 5 provides the effects of fake interventions, using 2001 and 2010 for the introduction of ACTs in Angola (instead of 2006). Unsurprisingly, the treatment effect is not significant when we use 2001 as a the introduction date. When 2010 replaces 2006, regressions (2) and (4) show a significant effect that is however positive.

Table III about here.

Table IV about here.

6 Conclusions

We have examined the impact of the introduction of an effective treatment on prevention incentives in the case of malaria. To do so we used the large increase in the use of Artemisinin Combination Therapies that occurred in Angola between 2006 and 2011. During this period new anti-malarial treatments became the most promoted tool in the fight against malaria in Sub-Saharan African countries. This large increase in treatment use allowed us to build up an empirical assessment of the effect of the introduction of an effective treatment on the use of Insecticide Treated Nets, the main preventive tool against malaria.

We find that the increase in access to ACTs between 2006 an 2011 had a negative effect on the use of prevention, even though the raw correlations between the two show a positive association that is most probably caused by the fact that they have been jointly promoted over the period. These findings are in line with our theoretical model, where free access to an effective treatment reduces the costs associated with the disease and therefore may reduce prevention adoption through a fall in prevention incentives.

This negative relationship has, to the best of our knowledge, not already been empirically assessed by economists in the case of malaria and the policy implications for malaria control are obvious. The negative effect of ACT access on the use of ITNs is statistically significant and may also have a significant economic impact. Indeed if the negative impact of access to treatment on prevention is too high it could limit and even offset the reduction of on malaria prevalence caused by ACTs policies. The relationship between malaria treatment and prevention should therefore continue to be empirically investigated in other contexts, in order to test the external validity of our results and provide policy recommendations.

References

- Adhvaryu, Achyuta. 2014. "Learning, Misallocation, and Technology Adoption: Evidence from New Malaria Therapy in Tanzania." *The Review of Economic Studies*, rdu020.
- Arrow, Kenneth J., Claire Panosian, and Hellen Gelband. 2004. Saving lives, buying time: economics of malaria drugs in an age of resistance. National Academies Press.
- Berthélemy, Jean-Claude, and Josselin Thuilliez. 2015. "The Economics of Malaria in Africa." In *The Oxford Handbook of Africa and Economics*., ed. Célestin Monga and Justin Yifu Lin. Oxford University Press.
- Berthélemy, Jean-Claude, Josselin Thuilliez, Ogobara Doumbo, and Jean Gaudart. 2013. "Malaria and protective behaviours: is there a malaria trap?" *Malaria journal*, 12(1): 200.
- Berthélemy, Jean-Claude, Jean Gaudart, and Josselin Thuilliez. 2015. "Prevention or treatment? The case of malaria." *Economics Letters*, 131: 16–19.
- Cohen, Jessica, Pascaline Dupas, and Simone Schaner. 2015. "Price Subsidies, Diagnostic Tests, and Targeting of Malaria Treatment: Evidence from a Randomized Controlled Trial." *American Economic Review*, 105(2): 609–45.
- Dupas, Pascaline. 2014. "Getting essential health products to their end users: Subsidize, but how much?" Science, 345(6202): 1279–1281.
- Flegg, Jennifer A., Charlotte J. E. Metcalf, Myriam Gharbi, Meera Venkatesan, Tanya Shewchuk, Carol Hopkins Sibley, and Philippe J. Guerin. 2013. "Trends in Antimalarial Drug Use in Africa." *The American Journal of Tropical Medicine and Hygiene*, 89(5): 857–865.
- Klayman, Daniel L. 1985. "Qinghaosu (artemisinin): an antimalarial drug from China." Science, 228(4703): 1049–1055.
- Lakdawalla, Darius, Neeraj Sood, and Dana Goldman. 2006. "HIV breakthroughs and risky sexual behavior." *The Quarterly Journal of Economics*, 1063–1102.

- Makanga, Michael, and Srivicha Krudsood. 2009. "The clinical efficacy of artemether/lumefantrine (Coartem®)." *Malaria Journal*, 8(Suppl 1): S5.
- PMI. 2006. "Angola: President Malaria Initiative: Country Action Plan FY06-Angola." Luanda, Angola: CDC/USAID Angola.
- Seban, Juliette, Josselin Thuilliez, and Vincent Herbreteau. 2013. "Possession of bed nets in Haut-Katanga (DRC): Prevalence-elastic behaviour or performance of health care system delivery?" *Health & Place*.

7 Figures and Tables





Table 1:	Descriptive	Statistics
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	2006-2007			2011							
	Obs	Mean	Std. Dev.	Min	Max	(Dbs	Mean	Std. Dev.	Min	Max
ITN Use (Child level)	1,503	0.20027	0.4003327	0	1	7,	,558	0.277	0.447	0.000	1.000
ITN ownership (Household level)	1,503	0.420	0.494	0	1	7,	,558	0.453	0.498	0.000	1.000
ACT use (Province average)	1,503	0.029	0.035	0.000	0.076	7,	,558	0.216	0.132	0.012	0.500
Exposure (Cohort level)	1,500	0.404	0.270	0.143	1	7,	,499	1.000	0.000	1	1
Wealth Quintiles (1-5, Household level)	1,503	2.557	1.361	1	5	7,	,558	3.312	1.365	1	5
Age (in months, Child level)	1,503	34.874	16.785	0	59	7,	,558	29.441	17.304	0	59
Female (Child level)	1,503	0.509	0.500	0	1	7,	,558	0.502	0.500	0	1
Mother education (Child level)	$1,\!495$	0.725	0.607	0	3	7,	,558	0.792	0.669	0	3
Urban (Household level)	1,503	0.424	0.494	0	1	7,	,558	0.358	0.479	0	1
Malaria Prevalence (Province , based on RDTs)	1,503	0.239	0.177	0.000	0.850	7,	,558	0.118	0.124	0.000	0.667

Notes: All children are fully exposed in the 2011 survey. There are 18 provinces in Angola.

	(1)	(2)	(3)	(4)
	Full Sample	Full Sample	Households with an ITN	Households with an ITN
$Exposure_{ict} \times ACT_{jt}$	-2.086***	-2.711**	-4.026***	-5.187*
	(0.409)	(0.949)	(0.879)	(2.566)
ACT_{jt}	2.257***	-	4.174***	-
	(0.498)		(1.032)	
$Exposure_{ct}$	0.166	-	0.382	-
	(0.177)		(0.369)	
Wealth	0.000	0.000	0.000	0.000
	(0.000)	(0.000)	(0.000)	(0.000)
Age	-0.002**	-0.002	-0.006**	-0.006
	(0.001)	(0.002)	(0.002)	(0.004)
Female	0.016**	0.016^{**}	0.032**	0.033**
	(0.007)	(0.007)	(0.014)	(0.014)
Mother Educational Level	0.036***	0.035***	0.078***	0.077***
	(0.007)	(0.006)	(0.013)	(0.013)
Urban	-0.009	-0.010	-0.017	-0.027
	(0.025)	(0.027)	(0.048)	(0.051)
Provincial Malaria Prevalence	-0.151	-	-0.354**	-
	(0.088)		(0.129)	
$Age_{ict} \times ACT_{jt}$	0.000	-0.005	0.004	-0.005
	(0.002)	(0.010)	(0.004)	(0.024)
ITN Ownership	0.572***	0.573***	-	-
	(0.014)	(0.015)		
δ_c	Yes	Yes	Yes	Yes
δ_j	Yes	Yes	Yes	Yes
δ_t	Yes	Yes	Yes	Yes
δ_{ct}	No	Yes	No	Yes
δ_{cj}	No	Yes	No	Yes
δ_{jt}	No	Yes	No	Yes
R2	0.464	0.479	0.085	0.131
Observations	8991	8991	4019	4019

Table 2: ITN Use: Main results

Notes: Asteriks *, ** and *** denote statistical significance indicate significance at the 10, 5 and 1% level. Standard errors (in brackets) and tests are robust to intra-province correlation (there are 18 provinces in Angola). All regressions also include the transmission season when the child was interviewed. Full sample includes all households. Regression (3) and (4) only include Households with an ITN.

	(1)	(2)	(3)	(4)
	Wealth score \leq median	Wealth score \leq median & ITN Sample	Wealth score \geq median	Wealth score \geq median & ITN Sample
$Exposure_{ict} \times ACT_{jt}$	3.505	2.925	-10.863***	-17.878***
	(5.981)	(10.424)	(1.362)	(2.276)
Wealth	0.000	0.000	0.000	0.000
	(0.000)	(0.000)	(0.000)	(0.000)
Age	-0.002	-0.007	-0.009*	-0.004
	(0.002)	(0.006)	(0.004)	(0.007)
Female	0.013	0.036	0.006	0.023
	(0.009)	(0.021)	(0.014)	(0.018)
Mother Educational Level	0.045***	0.117***	0.034**	0.056***
	(0.012)	(0.028)	(0.015)	(0.015)
Urban	-0.009	-0.010	-0.017	-0.027
	(0.025)	(0.027)	(0.048)	(0.051)
$Age_{ict} \times ACT_{jt}$	0.000	0.002	0.008	-0.012
	(0.015)	(0.039)	(0.020)	(0.037)
δ_c	Yes	Yes	Yes	Yes
δ_j	Yes	Yes	Yes	Yes
δ_t	Yes	Yes	Yes	Yes
δ_{ct}	Yes	Yes	Yes	Yes
δ_{cj}	Yes	Yes	Yes	Yes
δ_{jt}	Yes	Yes	Yes	Yes
R2	0.511	0.248	0.104	0.104
Observations	4498	1615	4493	2404

Table 3: Heterogeneous effects (wealth score)

Notes: Asteriks *, ** and *** denote statistical significance indicate significance at the 10, 5 and 1% level. Standard errors (in brackets) and tests are robust to intra-province correlation (there are 18 provinces in Angola). All regressions also include the transmission season when the child was interviewed. Full sample includes all households. Regressions (2) and (4) only include Households with an ITN.

	(1)	(2)	(3)	(4)
	$\mathrm{Pre}\ \mathrm{Mal} \leq \mathrm{median}$	$\label{eq:pre_main} \mbox{Pre Mal} \leq \mbox{median} \ \& \ \mbox{ITN} \ \mbox{Sample}$	${\rm Pre~Mal} \geq {\rm median}$	$\label{eq:pre_matrix} \mbox{Pre Mal} \geq \mbox{median \& ITN Sample}$
$Exposure_{ict} \times ACT_{jt}$	-0.728	-1.773	-5.739***	-5.811***
	(1.172)	(3.393)	(1.393)	(1.562)
Wealth	0.000**	0.000*	0.000***	0.000
	(0.000)	(0.000)	(0.000)	(0.000)
Age	0.005*	0.011**	-0.005	-0.013**
	(0.002)	(0.005)	(0.003)	(0.005)
Female	0.018	0.032	0.014	0.040
	(0.010)	(0.019)	(0.012)	(0.028)
Mother Educational Level	0.033***	0.076***	0.088***	0.085***
	(0.010)	(0.020)	(0.017)	(0.018)
Urban	-0.031	-0.069	-0.042	-0.009
	(0.030)	(0.063)	(0.046)	(0.056)
$Age_{ict} \times ACT_{jt}$	-0.028***	-0.065***	0.008	0.025
	(0.008)	(0.018)	(0.017)	(0.032)
δ_c	Yes	Yes	Yes	Yes
δ_j	Yes	Yes	Yes	Yes
δ_t	Yes	Yes	Yes	Yes
δ_{ct}	Yes	Yes	Yes	Yes
δ_{cj}	Yes	Yes	Yes	Yes
δ_{jt}	Yes	Yes	Yes	Yes
R2	0.472	0.119	0.145	0.183
Observations	4481	2133	4510	1886

 Table 4: Heterogeneous effects (pre-exposure provincial malaria prevalence)

Notes: Asteriks *, ** and *** denote statistical significance indicate significance at the 10, 5 and 1% level. Standard errors (in brackets) and tests are robust to intra-province correlation (there are 18 provinces in Angola). All regressions also include the transmission season when the child was interviewed. Full sample includes all households. Regressions (2) and (4) only include Households with an ITN.

	(1)	(2)	(3)	(4)
	Full Sample	Full Sample	Households with an ITN	Households with an ITN
2010				
$Exposure_{ict} \times ACT_{jt}$	0.005	0.095**	0.009	0.335***
	(0.041)	(0.036)	(0.092)	(0.114)
R2	0.463	0.479	0.081	0.132
Observations	8991	8991	4019	4019
2001				
$Exposure_{ict} \times ACT_{jt}$	0.120	-0.412	0.143	-0.525
	(0.195)	(0.549)	(0.384)	(1.293)
R2	0.463	0.479	0.081	0.131
Observations	8991	8991	4019	4019
δ_c	Yes	Yes	Yes	Yes
δ_j	Yes	Yes	Yes	Yes
δ_t	Yes	Yes	Yes	Yes
δ_{ct}	No	Yes	No	Yes
δ_{cj}	No	Yes	No	Yes
δ_{jt}	No	Yes	No	Yes

Table 5: Fake intervention (2001 and 2010 instead of 2006)

Notes: Asteriks *, ** and *** denote statistical significance indicate significance at the 10, 5 and 1% level. Standard errors (in brackets) and tests are robust to intra-province correlation (there are 18 provinces in Angola). All regressions also include the transmission season when the child was interviewed. Full sample includes all households. Regressions (3) and (4) only include Households with an ITN.

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