The Impact of Packaging and Messaging on Adherence to Malaria Treatment: Evidence from a Randomized Controlled Trial in Uganda*

Jessica Cohen Indrani Saran Elif Yavuz †

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Abstract

The failure of patients to adhere to recommended treatment guidelines is a major driver of widespread pathogen resistance, making diseases like malaria, pneumonia and HIV increasingly difficult and expensive to treat. Currently, Artemisinin Combination Therapies (ACTs) are the only effective treatment remaining for malaria. Although ACTs have a short three-day dosing regimen, over 35 percent of patients do not complete the full course of drugs. We conducted a randomized controlled trial in Central Uganda, with 2,500 households, designed to understand the reasons for poor adherence to the ACT treatment regimen.We also experimented with specially designed packaging and targeted messages to boost adherence. We find that a very strong predictor of adherence is how the patient is feeling (their symptom severity) when they are halfway through the treatment course. We hypothesize that patients who feel better mid-course are assuming their malaria is cured and discontinue treatment. Consistent with this hypothesis, a sticker affixed to standard ACT packaging that informs people that "malaria is not gone until all tablets are finished" significantly (though modestly) increases adherence, particularly for those patients whose symptoms were resolving early. On the other hand, a message designed to discourage saving pills for future malaria episodes had no significant effect on adherence. We also test a common approach to increasing adherence to ACTs in Africa by using

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†Jessica Cohen: Harvard School of Public Health and J-PAL, cohenj@hsph.harvard.edu. Indrani Saran: Harvard School of Public Health, ins289@mail.harvard.edu

specialized packaging that includes pictoral instructions for illiterate patients and information designed to raise patients' confidence in the effectiveness of the medication. While this special packaging increases the cost of ACTs by 10 to 50 percent, we find that it has no significant effect on medication-taking behavior or on comprehension of instructions.

1 Introduction

As with most infectious diseases, the treatment of malaria has both private and public benefits. While the treated patient benefits from no longer suffering from the illness, curing the disease also generates positive externalities by reducing the likelihood that the malaria parasite will be transmitted to other individuals through infected mosquitoes. This is what Gersovitz and Hammer term the "pure infection externality" (2004). However, treatment of malaria also generates negative externalities, by increasing selective pressure on the parasites to develop resistance to the drug and making the drug less effective in the future (Laxminarayan and Weitzman, 2002).[1] The tradeoff between expanding access to antimalarials and preserving their effectiveness has significant implications for morbidity and mortality: lack of access to effective medications is a primary reason why children still die from malaria (Getahun et al., 2010; Stauffer and Fischer, 2003) and the historical emergence of parasite resistance to Chloroquine fueled the rebound in malaria mortality seen in the 1980s and 1990s (Baird, 2005; Murray et al., 2012; Trape, 2001).[2]

We explore this tradeoff in the context of Artemesinin-Combination Therapies (ACTs), currently the first line treatment for malaria, and the only antimalarials that are effective against the parasite. ACTs are a three-day, six dose treatment course for uncomplicated malaria consisting of a fast-acting Artemisinin derivative combined with another slower-acting antimalarial drug. Combining drugs with different modes of action reduces the risk of resistant parasites surviving after being exposed to the drugs (White, 1999).[3] Although ACTs are very effective, they are also five to ten times more expensive than the older anti-malarial drugs such as chloroquine and sulphadoxine-pyrimethamine (SP), to which the malaria parasite has gained substantial resistance(O'Connell et al., 2011). The public benefits of malaria treatment (as well as the credit constraints faced by most households in malaria endemic areas) suggest that the drugs should be subsidized, and indeed most governments provide ACTs

[1] A similar tradeoff occurs when using antibiotics to treat bacterial infections and antivirals to treat viruses.

[2] Trape et al (1998) compare malaria-specific mortality between 1984 and 1995 in three rural regions in Senegal. After the emergence of chloroquine resistance, the risk of malaria death in children 0-9 years old increased 2.1, 2.5 and 5.5 times in the three regions. There is also evidence from Tanzania that the rate of malaria admissions and malaria deaths increased in the 1980s which coincides with the emergence of chloroquine resistance Trape (2001).

[3] Artemisinins are very effective in treating malaria, eliminating approximately 90 percent of parasites within three days (the remaining 10 percent are cleared by the partner drugs, which remain in the blood stream longer) WHO (2010)

free of charge in public sector hospitals and clinics. There have also been efforts to subsidize ACTs in the private sector, which is where many people obtain antimalarial drugs.[4]

While increasing the availability and use of ACTs confers important health and health system benefits, it also raises the probability of resistance developing to the drugs. Resistance to Artemisinin has already been identified in parts of South-East Asia and appears to be spreading (Ashley et al., 2014; Dondorp et al., 2009; Phyo et al., 2012). It is generally acknowledged that widespread resistance to artemisinin would pose a major threat to malaria control efforts across the world as there are currently no alternative anti-malarial drugs that are as effective. (White, 2012).

One way to preserve the effectiveness of ACTs is to increase diagnostic testing, since this can limit the substantial amount of over-treatment with antimalarials that has been documented in Africa (Cohen et al., 2014). Another approach is to ensure that people take the full recommended course of treatment in three days. A sub-therapeutic dose can kill all sensitive parasites while allowing the resistant parasites to survive (i.e. sub-therapeutic doses can "select" for resistance). Clinical studies have found that the cure rate for ACTs is 10-30 percent higher when patients take six doses of the drug instead of four doses(Novartis Pharmaceuticals Corporation, 2013; Makanga et al., 2006).[5] A failure to completely eliminate all parasites increases the likelihood of a recurrence of infection (Beshir et al., 2013; Stepniewska et al., 2010), which is not only harmful for the individual but may also increase the opportunities for resistance (since the parasites are potentially subjected to a second round of selection) (White et al., 2009).

As others have noted, decisions about malaria treatment occur in a very noisy learning environment.(Adhvaryu, 2014; Cohen et al., 2014; Bjorkman-Nyqvist et al., 2013) Using a theoretical framework for the adherence decision, we hypothesize that non-adherence is strongly related to uncertainty about the relationship between symptom severity and the perceived likelihood of being cured as well as the patient's uncertainty about the effectiveness of the medication in curing malaria. In this study, we explore these and other potential

[4]For example, the Affordable Medicines Facility-malaria (AMFm) initiative subsidizes ACTs at the top of the global supply chain so that the subsidized ACTs are available both in the public and private sector (Gelband et al., 2004; Laxminarayan and Gelband, 2009).

[5]Evidence in favor of the three-day dosing regimen also comes from other clinical studies which find that a small percentage of people (5-6%) continue to have parasites on the second day of treatment Muhindo et al. (2014); Das et al. (2013).

reasons for non-adherence to ACTs and generate evidence on interventions that could boost adherence.We conducted a field experiment with approximately 2500 households in Central Uganda in which subsidized ACTs were sold over-the-counter in drug shops with a variety of targeted packaging and messages aimed at improving medication taking. We find that over 35 percent of people who buy subsidized ACTs from drug shops in Uganda fail to complete the full treatment. We also test whether improved drug packaging designs and simple messages about the importance of finishing medication increase the likelihood of adherence. We show that the conventional approach used in a number of African countries to increasing adherence by designing colorful, glossy packages with pictorial instructions is not effective in raising adherence. This is notable not only because this approach is used in so many countries and contexts, but also because it increases the unit cost of ACTs by 10 to 50 percent. On the other hand, people who received an inexpensive sticker affixed to the standard box of drugs with the short message "Malaria is not gone until ALL Tablets are finished" were approximately five percentage points more likely to finish the treatment (an 8 percent increase on the baseline rate of 65 percent) and finished 36 percent more tablets than the control group. We show that this simple targeted message boosts adherence particularly for those patients who began to feel better midcourse and would likely have otherwise discontinued treatment. There is also some evidence that people may be motivated by a desire to save the pills for future malaria episodes. A sticker with a message directly targeting this behavior had a positive but non-significant impact on adherence.

Non-adherence is a major economic and public health concern and is not limited to anti-malarial drugs. In the case of malaria, the cost of research and development for new antimalarial drugs is estimated to be about $180 million a year (PATH, 2013). Patients in the United States who do not complete their prescribed medications are estimated to result in more than $100 billion dollars spent on avoidable hospitalizations (Cutler and Everett, 2010; Osterberg and Blaschke, 2005). Poor adherence to anti-retroviral treatment for humman immunodeficiency virus (HIV) also leads to poor health outcomes and increases the risk of resistance (Mills et al., 2006; Bangsberg et al., 2001, 2003). The growing concern about the spread of bacterial resistance to antibiotics forms a strong parallel to the current threat posed by emerging resistance to artemisinin (President's Council of Advisors on Science and Technology (PCAST), 2014; Center for Disease Control and Prevention, 2013). As with antimalarial medications, the threat of widespread bacterial resistance to antibiotics is exacerbated by in-

appropriate dosing and overuse of the drugs (World Health Organization, 2014). Thus, understanding how to increase patient adherence to recommended treatment regimens is a major policy goal.

Beyond the research on decisions about malaria treatment noted above (Cohen et al., 2014; Adhvaryu, 2014; Bjorkman-Nyqvist et al., 2013), our paper contributes to the economics literature in three main ways. First, we contribute evidence to the literature on treatment-seeking behavior in developing countries, in particular the central role played by the private sector (Banerjee et al., 2004; Leonard and Masatu, 2007; Cohen et al., 2014). Second, we add to the literature on when and what type of information influences people's beliefs and behavior. While some studies find that people respond to information on health risks or returns to education (Jalan and Somanathan, 2008; Madajewicz et al., 2007; Jensen, 2010), others find little impact on behavior when people are provided with information about education quality or prevention of worm infection (Banerjee et al., 2010; Kremer and Miguel, 2007). Finally, we contribute to the literature that explores the problem of increasing access to health products that have positive externalities by subsidizing them, while minimizing wastage of the subsidies by ensuring that people actually make appropriate use these products. (Cohen and Dupas, 2010; Ashraf et al., 2010; Dupas, 2011) Most of this literature examines whether cost sharing can screen for those who need the product most or increase use through a "sunk cost" effect. This study, however, focuses on whether information about the product (in this case the ACT drug) and its attributes can encourage appropriate use.

The remainder of the paper proceeds as follows: Section 2 provides some background on malaria treatment-seeking behavior in this study context and on private sector ACT subsidies. Section 3 provides a theoretical framework highlighting the reasons for non-adherence and how patients may decide whether or not to complete a full treatment course. Section 4 describes in detail our experimental study design and the interventions we tested. In Section 5 we present the results of our intervention, and in Section 6we explore some potential reasons that people don't finish their medications. Section 7 concludes.

2 Background on Malaria Treatment in Africa and the Affordable Medicines Facility-malaria

Malaria remains the cause of roughly 200 million illnesses and 600,000 deaths per year (WHO, 2013). In high endemicity countries like Uganda, malaria is a large burden on the public health system, responsible for nearly 50 percent of all outpatient visits to public clinics(Government of Uganda, 2009). Given increasing parasite resistance to older generations of antimalarials, in 2004 the Government of Uganda – following the recommendations of the WHO – adopted artemisinin combination therapies (specifically, Artemether/Lumefantrine (AL)) as the first-line treatment for uncomplicated malaria Government of Uganda (2006). ACTs are supposed to be available for free in Ugandan public sector hospitals and clinics, but patients often report substantial costs associated with public sector treatment including travel and wait times and ancillary fees for equipment like gloves and syringes and for malaria testing. Stock outs of essential medicines such as ACTs are also common in these settings. Thus, as with many other African countries, the majority of people in Uganda, when struck by a suspected malaria episode, bypass the public health system altogether and buy antimalarial drugs from private clinics and from retail establishments like pharmacies and informal drug shops. While these outlets are considerably more accesible than public sector clinics (closer proximity, open longer hours, etc), they vary widely in the quality of advice and product they make available. A substantial share of antimalarials sold in the private sector are the older, less effective non-artemisinin medications such as chloroquine and Sulfadoxine/pyrimethamine (SP) which are both cheaper than ACTs and likely also more familiar to patients in this region.[6] The variety of medicines available–with their varying efficacy and dosing schedules–lead to considerable confusion among malaria patients about which medicines they should be taking and how to take them (O'Connell et al., 2011; Goodman et al., 2004, 2007).

The majority of suspected malaria episodes are treated based on symptoms, rather than a confirmed diagnosis through blood test. Until recently, WHO guidelines recommended presumptively treating all cases of fever in young children with antimalarials (Government of Uganda, 2005; WHO, 2006; Reyburn, 2010). Despite more recent recommendations to confirm malaria with a blood test prior to initiating treatment, both patients and health workers continue to

[6]The median cost for an adult treatment course of ACTs in Uganda in 2009 was $4.48 compared to a median cost of $0.50 for the equivalent dose of SP O'Connell et al. (2011)

rely on symptomatic diagnosis of malaria much of the time (Hamer et al., 2007; Reyburn et al., 2007). The symptoms of malaria, however, are non-specific and overlap with many other diseases, most notably pneumonia, but also a range of simple viral illnesses. This leads to a substantial amount of uncertainty about the true cause of illness for patients seeking treatment for suspected malaria, and to high rates of over-diagnosis and over-treatment of malaria (Amexo et al., 2004; Harchut et al., 2013; Msellem et al., 2009). Cohen, Dupas and Schaner (2014) find that only 25 percent of older teenagers and adults buying ACTs in drug shops in Western Kenya actually had malaria. The high rates of over-treatment exacerbate confusion over appropriate treatment for malaria as it is difficult to learn about the relative effectiveness of different antimalarial drugs when they are frequently used to treat diseases that are not malaria (Adhvaryu, 2014). The prevalence of counterfeit antimalarials complicates things further (Bjorkman-Nyqvist et al., 2013).

In an effort to address inadequate access to ACTs and to slow resistance to artemisinin, the Affordable Medicines Facility-malaria (AMFm) program was established in 2009 and introduced nationally in seven African countries, including Uganda. The AMFm subsidized the cost of ACTs by 95 percent to first line buyers in the private and public sectors (Laxminarayan and Gelband, 2009; Gelband et al., 2004). The objectives of the AMFm were to reduce malaria mortality and morbidity by encouraging patients to buy ACTs over older, less effective medications and to slow the emergence of artemisinin resistance by "crowding out" artemisinin monotherapies from the market. Initial studies of the pilot phase of the program suggest that it was effective in increasing the availability and use of ACTs (particularly at private for-profit outlets) (Cohen et al., 2013; CHAI, 2008; Fink et al., 2013). However, the increasing availability of ACTs, especially through informal channels, has raised concern that the inappropriate use of ACTs could accelerate parasite resistance and reduce the cost-effectiveness of the subsidy. The field experiment described below was designed to test potential "supporting interventions" for private sector ACT distribution, in order to maintain the benefits in terms of access that private sector ACT subsidies confer, while preserving the effectiveness of these drugs.

3 Theoretical Framework

Figure 1 categorizes some of the many reasons why a person may not complete a malaria treatment course. In this framework, we first distinguish between conscious and non-conscious reasons. Non-conscious reasons include simply forgetting to take pills or not fully understanding how to correctly take the pills. Conscious reasons involve the deliberate decision to discontinue medication. We further break down conscious choices into those made by people who believe, partway through the treatment course, that they still have malaria and those who believe they no longer have malaria. Among those who believe they no longer have malaria, they could discontinue treatment either because they believe they are cured or because they believe their illness was never malaria to begin with. Even if people believe that they still have malaria, they may choose to stop taking the pills anyway. First, some people may believe that the drug is not very effective in treating the disease and decide to seek alternative treatment. Second, they may find it beneficial to save a few pills for a future illness episode. Finally, some people may be deterred from finishing the pills if they experience many unpleasant side effects.

This section focuses, in more detail, on those who make a conscious choice to stop taking the pills. We present a simple model where, in period one, a patient is hit with an illness shock that they believe is malaria and begins taking medication [7] and, in period two, the patient decides whether to finish taking the pills or to stop the treatment. The patient faces a tradeoff between the benefit of being healthy and the costs of adhering to the medication. The tradeoff is mediated by the patient's subjective probability that he/she is still suffering from malaria on the second day of treatment, which we assume depends primarily on the severity of the symptoms the patient experiences on that day.

3.1 Definitions

We begin by defining the following terms:

- s denotes the severity of the symptoms experienced by the patient in period two
- Let $\pi(s)$ be the patient's perceived likelihood that they (continue to) suffer from malaria in period two. We assume that this probability is increasing

[7] We limit all our empirical analyses to those who begin treatment

in the severity of the symptoms experienced by the patient in that period so that $\pi'(s) > 0$

- c is the cost of adhering to the drug treatment. These costs include possible side effects of the drugs, the effort to remember to take the drugs, and the opportunity cost of consuming pills that could otherwise be used to treat future malaria episodes (which is increasing in things such as frequency of malaria infection, distance to the drug shop , etc.). We assume that the cost of adhering to the treatment is the same regardless of whether the person is, in fact, still sick with malaria.[8]

- $U^H$is the utility that a person gets from being healthy (that is, not sick with malaria), while U^S is the utility that a person gets when they are suffering from malaria. We normalize a patient's utility when sick to zero ($U^S = 0$). The utility of being healthy includes factors such as increased productivity and wages as well as the intrinsic value of being healthy.

3.2 Patient Decision-Making

We first consider the case in which the patient knows that the drugs are effective in treating the disease. After having taken the first two or three doses of the medication in period one, the patient has two possible actions in period two $a \epsilon A, N$: (1) Continue to finish all the medications (i.e. adhere to treatment guidelines) $a = A$ or (2) Stop taking the medication (i.e., not adhere to treatment guidelines) $a = N$. The action decision in period two is based on the perceived likelihood of still having malaria that the patient assigns probability π, which is increasing in the severity of the symptoms (s) that the patient is experiencing on that day.

The expected value of adhering (finishing the medication) is denoted as V^A and can be represented as follows:

$$V^A(\pi) = \pi(s)(U^H - c) + (1 - \pi(s))(U^H - c)$$

$$V^A = U^H - c$$

[8]It is possible that those who no longer have malaria will feel less sick and thus find it harder to remember to take the pills. On the other hand, those with malaria could be vomiting and have a difficult time taking the pills. How these costs vary with actual malaria status is hard to predict but this seems like a reasonable simplifying assumption for those types of costs most likely to affect adherence.

The expected value of not adhering is denoted as V^N and can be represented as follows:

$$V^N(\pi) = \pi(s)(U^S) + (1 - \pi(s))(U^H)$$

$$V^N(\pi) = (1 - \pi(s))U^H$$

By finishing the medication, the patient pays the cost$c$ in order to ensure that she will be healthy, regardless of whether or not she still has malaria. If the patient chooses not to finish the medication, she avoids the cost c, but assumes some risk that she is not fully cured of the disease and may continue to suffer from malaria symptoms, either from the current infection or a future recrudescent infection.

The patient will adhere to the treatment if the expected value of adhering to the treatment exceeds the expected value of not adhering to the treatment:

$$V^A(\pi) - V^N(\pi) > 0$$

$$U^H - c - (1 - \pi(s))U^H > 0$$

$$\pi(s) > \tfrac{c}{U^H}$$

This implies that a patient will adhere if the belief that they have malaria (and by extension the severity of symptoms) exceeds some threshold value of c/U^H. Patients are thus more likely to adhere when symptom severity is high, when the costs of adhering are low (few side effects, low value of saved pills, etc.) and when the benefit to being healthy is high (see Figure 2A).

3.3 The Impact of Perceived Drug Effectiveness

We now turn to the case in which the patient is unsure whether the drugs she is taking are effective in treating malaria. We assume that the belief that the drug is effective, denoted $\lambda(s)$, is decreasing in symptom severity on the second day of treatment, where $\lambda^{'}(s) < 0$.

Then the expected utility of adhering $V^A(\pi)$ is as follows:

$$V^A(\pi) = \pi\,(s)\,[\lambda(s)U^H + (1 - \lambda(s))U^S - c] + (1 - \pi\,(s))[U^H - c]$$

$$V^A(\pi) = \pi(s)\lambda(s)U^H + (1 - \pi(s))U^H - c$$

The expected utility of not adhering is the same as in the previous section:

$$V^N(\pi) = (1 - \pi(s))U^H$$

Once again, the patient will adhere to the treatment if the expected value of adhering to the treatment exceeds the expected value of not adhering to the treatment.

$$V^A(\pi) - V^N(\pi) > 0$$

$$\pi(s)\lambda(s)U^H + (1 - \pi(s)U^H) - c - (1 - \pi(s))U^H > 0$$

$$\pi(s)\lambda(s)U^H - c > 0$$

$$\pi(s)\lambda(s) > \frac{c}{U^H}$$

As before, the likelihood of adhering increases with the utility of being healthy and decreases with the cost of adhering. However, since $\pi'(s) > 0$ and $\lambda'(s) < 0$, there is a non-linear relationship between the probability of adhering and the severity of the disease (see Figure 2B). At low severities, people perceive the drug to be very effective, but are less likely likely to believe that they still have malaria and so the expected value of finishing the medication is low. At high severities, people are more likely to believe that they still have malaria, but the perceived probability that the drug is effective is low, so the expected utility of adhering is again low. The expected utility of adhering is therefore maximized at intermediate levels of illness severity on the second day of treatment.

3.4 Impact of Interventions to Increase Adherence

The theoretical framework suggests several packaging-based interventions that could potentially increase adherence. First, one could try to improve patient comprehension of dosing. This should increase the probability of adherence along the entire curve in Figure 2B, but should be particularly effective for illiterate and poorly educated patients. Second, one could try to target the perception that once symptoms disappear, the patient is cured of the disease. As a result, each level of symptom severity would be associated with a higher probability of having malaria, raising the likelihood of adherence, as shown in Figure 2C. This type of intervention should increase adherence rates primarily among people who feel relatively healthy on the second day of treatment (in Figure 2D, it would raise the left side of the curve to get the red curve). Third,

one could target the perception that the drugs are poor quality. In that case, we would expect $\lambda(s)$ to be shifted upwards, so that people believe the drug is more effective for every level of symptom severity. This intervention should increase adherence rates primarily among those who experience severe symptoms on the second day of treatment (in Figure 2D, it should raise the right hand side of the curve to get the blue curve).

Other interventions could address the cost of adhering to the treatment, such as the message we test below targeting the saving of pills for future episodes. This should be especially effective for patients who are poorer or who live further away from the drug shop since they have a greater opportunity cost of consuming the last few pills. Additional interventions such as reminders to reduce the cost of adhering or training for drug dispensers to improve patient knowledge of dosing have potential (Goldberg and Fink, 2014; Marsh et al., 1999, 2004), but are not explored here as they are separate from the packaging of the drug .

4 Study Design and Data Collection

4.1 Experimental Design and Data Collection

The study took place in the district of Luwero, Uganda, located in Uganda's central region, between November 2010 and September 2011.[9] Despite its proximity to the capital city of Kampala (about 68 km), Luwero district is rural and poor, with the majority of households engaged in subsistence farming. Luwero has a high level of malaria endemicity, with an average of over 100 infective bites per person per year (Uganda Bureau of Statistics (UBOS) and ICF Macro, 2010). The study area itself constitutes catchment areas surrounding nine drug shops that were located in and around three small trading centers in the east of the district. Two of the trading centers (Busiika and Zirobwe) each had four participating drug shops, while the third trading center (Wabitungu) had the remaining one. [10]

[9] On May 13, 2011 the Ministry of Health of Uganda confirmed a fatal case of Ebola Haemorrhagic Fever in a 12-year old girl from Luwero District. As a result, the study was halted for approximately a month between May 18, 2011 and June 16, 2011. While surveying and project research stopped during this time, we ensured a steady supply of ACTs at shops during this period. We find no evidemce that this break in study implementation affected adherence rates.

[10] Drug shops were selected from a list of licensed shops provided by the Luwero District Area Drug Inspector. Shops were selected based on shop owner qualifications, length of time the shop had been in business, daily customer traffic and operating days/hours. We selected shops that were well qualified and established and that had sufficient customer traffic to reach

The experimental study design is illustrated in Figure 3. A household census was conducted in catchment areas of roughly 2.5 km (approximately one hour walking distance in each direction) around each shop. In November and December 2010, a team of enumerators traveled to each household in the study area to enroll participants and conduct a baseline survey. Households were then given a Purchase ID card (see Appendix Figure A1), which enabled any of the household members to purchase ACTs at a 95 percent subsidy at any of the selected drug shops. [11] ACTs are priced by dose, with the appropriate dose determined by age, and ranged from 200-800 USH (approximately $0.09-$0.35 at the time of the study; see Appendix Table A1).[12] No restrictions were placed on the number of times the card could be used during the study period and no expiration date was given.[13] 2,641 households and 12,572 individuals were enrolled in the study at baseline.[14]

The objective of the project was to assess the impact of various forms of packaging and messaging of ACTs on adherence (we define this outcome in detail below). To evaluate this, we randomized the type of packaging/messaging households received each time they came to the participating shops to purchase ACTs. The treatment arms were randomly assigned at the shop-day level. That is, an ex-ante schedule was laid out using a random number generator that indicated that Shop 1 got package A on March 1, package B on March 2, and Shop 2 got package C on March 1, etc. Surveyors assigned to each shop brought the control or treatment packs for that particular day with them, and both the study team and shop owners were blinded to the treatment assignment until the day of sale. Prior to the intervention, participating drug shop owners received a training session led by a Ugandan Ministry of Health official on storage and

the desired sample size in a five month period but were not so large that the traffic would be unmanagable for our survey team.

[11] The brand of ACT used was Lumartem, manufactured by Cipla, which is Artemether Lumefantrine.

[12] In December 2010, the exchange rate was roughly 2250 USH per $1 USD.

[13] No restrictions were placed on the number of times the card could be used in order to avoid intra-household rationing. However, the project had a limited budget and could not accomodate excessive purchases caused, for example, by hoarding. Hoarding did not turn out to be a serious problem and our approach to this was informal. In the limited cases in which a household seemed to be purchasing an excessive number of ACT doses (34 households, or 3% of households that purchased an ACT, bought more than 6 doses of ACTs over the course of the study), we would have a surveyor visit the household and inquire about the health of the members, reminding the household head that the cards were only to be used for people in the household who were currently sick. This approach worked very well throughout the study.

[14] This is the same number of households that were found in the census activity. No households refused to participate in the study.

appropriate use of Lumartem, the type of ACT used in this study.[15] Attendants were instructed to follow their normal prescribing protocol for Lumartem and other anti-malarials. If the patient had a study ID card and wanted to purchase Lumartem they were sent to our survey team member, who sat at a table in the shop to check IDs, dispense the Lumartem in the appropriate packaging and administer a short survey, described below.

Adherence was assessed through at home follow-up visits roughly three days after the time of purchase. Lumartem is a six-dose treatment (with the number of pills per dose varying by age (see Appendix Table A1), intended to be taken over three days. The first two doses are to be taken eight hours apart and the remaining doses should be taken every 12 hours, generally in the morning and evening so that the entire course should take 56 hours from initial dose to completion. 75 percent of individuals were randomly assigned ex-ante to receive a follow-up visit at their household to measure adherence.[16] Individuals were not told of the intent to follow up in order to avoid influencing behavior, but informed consent was sought at the time of follow up. The respondent for the follow up survey was the patient if the patient was 18 years old or above and the caregiver if the patient was under the age of 12. If the patient was between the ages of 12 and 18, the patient was interviewed in the presence of the caregiver. 96 percent of people assigned to receive a follow-up survey were successfully reached for a follow-up visit. The follow-up survey was scheduled for 72 hours after the time of the ACT purchase unless this time fell at night, in which case the interview occured first thing on the following morning. The timing was designed so as to allow people sufficient time to have completed their medication while minimizing the risk that they would have already disposed of their blisterpacks. Appendix Figure A2 describes the choice of follow-up window in more detail. Of those who had a completed follow-up survey, 95.6 percent were found within 96 hours from the time of purchase of their ACTs. At the follow-up visit surveyors asked to see the Lumartem that was purchased through the project and recorded the number of pills remaining in the blister pack. Surveyors told participants that they were asking to see the blister pack

[15] We refer to "shop owners" throughout the paper loosely to refer to either the shop owner him/herself or to the shop attendants (who man the shop but might not be owners). All shop personnel were trained on ACT dosing and prescribing.

[16] In early July 2010, we increased the probability of follow up by individual to 85% because we found that we had the survey team capacity to do additional follow up surveys. As this was the last month of the study, it did not increase the overall probability of follow-up among our sample of ACT purchasing households by much. Overall, of the 2517 people purchasing ACTs during the course of the study 76.8% of them were assigned to be followed up with.

for quality control purposes and recorded the batch number on the packaging in their notebook in an attempt to limit any hawthorn effects on adherence. Blister packs were available in 86 percent of cases. At the end of the project, all households were visited for an endline survey and ID cards were collected. Households were informed that a national ACT subsidy program (the AMFm, described above) was now in place and was being scaled up in their area.

4.2 Treatment Arms

Shops were randomized by day into either a control package or one of four treatment packages, shown in Figures 4A-C. There were two main objectives to the study design. The first was to test the status quo approach to promoting adherence through specialized packaging (the "CAPSS Package"). The second was to test whether simple, inexpensive ammendments to the standard packaging could be made to increase adherence. The aim was to test an approach that a pharmaceutical manufacturer could use and implement on a large scale. Because we wanted to test interventions to boost adherence that did not need to be tailored at the national (or sub-national) level, and because Uganda does not have a national language, all of the package types were in English. While many Ugandans do not speak or read much English, 1) the CAPSS Package (which we did not develop) was the current approach to boosting adherence and was already in English and 2) the messages we developed used very simple language with English words that were field tested to be familiar to many Ugandans.

4.2.1 Control Package

The control package in this study was the standard packaging in which Lumartem was sold in Uganda and elsewhere in Africa. The box, shown in Figure 4A, had the name, brand and manufacturer of the medication. Inside the box was a blister pack which grouped the pills by dose and day and a paper insert –similar to what is seen inside most medication boxes in the U.S. and elsewhere – with small print about dosing, side effects, etc.

4.2.2 CAPSS Package and Handout

We refer to the first package as the "CAPSS" package since it was the ACT packaging used in Uganda during the Consortium for ACT Private Sector Subsidy pilot program (run by the Uganda MOH, Medicines for Malaria Venture, PSI

and others). The CAPSS program was a pilot designed to test the feasibility of a private sector ACT subsidy prior to the AMFm.[17] The ACT packaging that was designed for CAPSS (illustrated in Figure 4B) was intended to serve several purposes. First, it differentiated the subsidized private sector ACTs from those in the public sector (which were intended to be free). Second, it served as a form of branding and quality assurance, providing "consumers with the instant recognition that they were purchasing a high quality and effective anti-malarial at an affordable price" Talisuna et al. (2012). Finally, it was designed to encourage correct use of the product, incorporating features like colorful pictorial instructions on how to take the medicine, principally to assist illiterate patients and caregivers in taking the medication correctly. Several messages on the CAPSS package relate directly to adherence, such as: 1) "Complete the full course, even if the child improves. This is important for your child's full recovery.", 2) "Only effective if treatment is completed." and 3) "Do not share this drug." The CAPSS package is very similar to the packaging used for other ACT subsidy programs in Tanzania and in Rwanda (the "Primo" ACT package). [18]

While the potential benefits to this type of specialized packaging are substantial, so are the costs. The CAPSS package, and others like it, add roughly 15-20 cents to the cost of the ACT and are a potential additional source of bottlenecks in the drug supply chain. Because the costs are high, we also tested a packaging type that conveyed the same information content at a significantly lower cost. We created a handout to be distributed with the ACTs that was a simple photocopy of the CAPSS package and wrapped it around the control package when distributing the medication at the drug shop (see Figure 4C). The purpose of this treatment arm was to explore, if the CAPSS packaging was successful at boosting adherence rates, whether the improvement was due mostly to the information and pictoral instructions or whether it was linked also to the product quality and differentiation conveyed by the special, glossy packaging.[19] We refer to this treatment as the CAPSS-Information Only pack.

[17] The CAPSS study took place between August 2007 and May 2010 in five districts. CAPSS was completed six months before this study took place and was not in (or near) Luwero district.

[18] See, for example, http://www.mmv.org/sites/default/files/uploads/docs/events/access/AccessSymp2007/Karema_Rwanda_Providing_subsidized_ACT.pdf and http://www.pmi.gov/news/stories-from-the-field/stories-from-the-field---detail/proper-treatment-of-malaria-made-easier-with-primo

[19] It is also possible that differences between the CAPSS package arm and the CAPSS handout arm could be due simply to the information content if the handout often got thrown away or misplaced. We show below that this does not appear to be a major driver of our results.

4.2.3 Simple Messages: "Malaria is Not Gone Until..." and "Don't Save Pills..."

We also tested simple, targeted messages to promote adherence delivered via stickers attached to the control packaging, an approach that is used to encourage patients to finish their medications when prescribed antibiotics Morris and Halperin (1979) [20]. The first sticker was designed to address non-adherence based on the belief that the illness is cured when symptoms have improved or resolved. It said "Malaria is NOT gone until ALL tablets are finished". The second sticker message aimed to discourage the saving of pills for the next malaria episode and internalize the externality associated with non-adherence. It said "Finish ALL tablets. Saving tablets for later can be harmful for malaria control in your community." Both stickers were yellow and placed in the front and center of the box of medicines[21].

4.3 Survey Tools and Measurement

Surveys were conducted at four points through the study period: at baseline, at the point of ACT purchase, several days after ACT purchase ("follow up") and at study endline. The baseline survey was conducted in the home with the female head of household and collected information about demographics and malaria treatment and prevention activities. The ACT purchase survey was a very short survey administered at the shop with the patient or with the caretaker if the patient was a young child. The survey primarily concerned the severity of the symptoms that the patient was currently experiencing. These were elicited using a picture of a ladder scale which had numbers from 0 to 10 with each "step" representing increased levels of illness (see Appendix Figure A3) and pictures at the top and bottom representing feeling very well or feeling very poorly. The patient had to indicate the severity of the symptoms by pointing to a number of the scale. In addition, the patient was also asked to estimate, using the same 0-10 scale, how certain they were that the illness they were experiencing was, in fact, malaria. In 71 percent of ACT purchases for patients over age 12, the patient was at the shop and could answer these questions for themselves.

[20] See, for example, http://www.knowledgeisthebestmedicine.org/index.php/en/know_your_healthcare_team/auxiliary_labels and https://www.vacrxplus.com/Product/1281/Antibiotic-Finish-All-Medication

[21] An additional treatment arm was also included in the study with a sticker that provided the actual (non-subsidized) price of the medicines. However, due to budgetary reasons, this treatment had to be phased out before we obtained a reasonable sample size. We control for this treatment arm in all analyses but do not present the results.

The follow-up surveys took place at the households of patients who were ex-ante randomly assigned to be followed up with and who purchased ACTs approximately three days prior. The main purpose of this survey was to determine whether the patient had completed their medications by counting the number of pills remaining in the blisterpack as described above. The follow-up survey also included questions about the day and approximate time the patient took each dose of the drug, their overall feeling of sickness each day while taking the medication (using the ladder scale described above), and their current level of symptoms.

At the end of the data collection period, field officers visited each of the participating households and informed participants the study was ending. At this time, field officers collected the Purchase ID Card and asked a few more questions about their knowledge and beliefs about malaria treatment and their understanding of the dosing instructions on the packages used in this study. The enumerators also discussed the benefits of adhering to treatment regimens with the household members, as well as the dangers of non-adherence.

Our primary outcome is a binary measure of adherence which we define as having no remaining pills in the blisterpack at the time of the follow-up survey. In the 14 percent of cases where the blisterpack was not seen, we relied on the patient or caregiver's report on the number of pills remaining. This definition of adherence is standard in the literature, with the majority of studies using a combination of pill counts and self-reports in order to measure adherence (Bruxvoort et al., 2014; Banek et al., 2014). [22][23]

[22]Some studies include measures of "probably adherent" and "probably non-adherent" for adherence that is based on self-reports Fogg et al. (2004); Depoortere et al. (2004). However, for the sake of simplicity, we rely on a binary measure of adherence for our main results and present additional analyses limited to those who showed their blisterpack as a robustness check. A few studies rely on biological assays of the drug or medical event monitoring system (MEMS) containers in order to measure adherence, however these are generally more costly and difficult to implement in practice Shwe et al. (1998); Bell et al. (2009); Na-Bangchang et al. (1997); Twagirumukiza et al. (2010). On the other hand, relying on self-reports alone is likely to over-estimate the level of adherence Thirumurthy et al. (2012).

[23]While a few studies include the timing of the doses taken in the definition of adherence, they vary widely in how they define appropriate timing of the dose. Some studies only take into account whether the correct number of doses were taken each day Depoortere et al. (2004), while other studies use windows of 1-4 hours around the correct time as determined by the dosing regimen and the timing of the first dose Lemma et al. (2011); Kabanywanyi et al. (2010); Twagirumukiza et al. (2010). Since there is little consensus on how to determine whether a dose was taken at the correct time, we do not include timing of the dose in our definition of adherence. Moreover, since the timing of when the doses were taken depend on patient recall, they may be inaccurate and subject to recall bias Das et al. (2012). Finally, conditional on completing a full treatment course in the appropriate total amount of time, it is unclear how much the timing of doses matters from a public health or private health perspective, barring a case in which a patient took an excessive number of pills too quickly.

We also look at the number of doses and tablets remaining as additional outcomes of the intervention. Any improvement in the intensive margin is likely to still be beneficial both in treating the disease and in minimizing the likelihood of the development of resistance by reducing the number of parasites (Stepniewska et al., 2010). Those who did not start taking the medication (34 people or 1.8 percent of all people who were assigned to a follow-up survey) are dropped from the analysis. Assuming the patient did indeed have malaria, the parasites were not exposed to the drug, and, therefore, were not under selective pressure to develop resistance to the drug (White, 2004).

5 Results

We begin our discussion of results with a description of the uptake of ACTs sold through the program and some basic characteristics of the sample as well as balance across treatment arms. In Section 5.1 we present basic results on adherence and medication taking behavior in the sample. We then present visual evidence and regression adjusted estimates of impact. In all of the main analysis, we limit the analysis to an individual's first purchase, since the impact of a particular package type could change if the individual experienced a different type of package previously.[24] Eighty-one percent of all ACT purchases are first purchases. We also drop the 32 ACT purchases where no medication was taken at all (i.e. the entire treatment course was remaining) and the 68 people who were found for follow-up after the 96 hour window. Below we explore the robustness of our results to this sample definition.

We run regressions of the following form in our analysis:[25]

In a pilot conducted for this study in another nearby district, we explored the possibility of "over-dosing" by conducting follow-up visits on the second day after starting medication. We found no evidence that patients mistakenly take the entire course of ACTs too quickly.

[24] We could also include second ACT purchases for individual's who first purchase was the control pack and remain consistent but for simplicity, we restrict the analysis in the main results section to first purcahses only. The robustness analysis explores all ACT purchases.

[25] At project rollout, we had a fifth treatment arm exploring the impact of subsidies for ACTs on adherence and included this arm in the random assignment for the first two weeks of the project. For budgetary reasons–and since the arm was not strictly related to packaging–we had to drop it from the study. Rather than throwing out the observations in this arm, we include a dummy variable indicating treatment assignment to this arm and do not present the results since the experiment was clearly not powered to detect an impact. We also have a cross-cutting treatment arm in which a fraction of study participants (randomly assigned ex-ante) were tested for malaria at the time of ACT purchase. We explore the impact of the testing in another paper and do not present those results here. Those results are available upon request. In this paper, we include a dummy variable in all specifications indicating whether a person was offered a malaria test and all interactions between being offered a test

$$y_{isd} = \beta_0 + \beta_1 CAPSS_{sd} + \beta_2 CAPSS - INFO - ONLY + \beta_3 "MALARIA - NOT - GONE" - MESSAGE_{sd} + \beta_4 "DONT - SAVE - PILLS" - MESSAGE_{sd} + \sigma_{shop} + \delta_{day} + \epsilon_{isd}\text{i}$$

where y_{isd} is the outcome for person i who bought an ACT at shop s on day d. Outcomes include a binary adherence measure equal to one if all medication is completed at the time of follow up and zero otherwise, a "tablets left" variable measuring the number of tablets remaining in the blister pack and a "doses left" variable which is the number of tablets remaining divided by the appropriate number of tablets to be taken by age group per dose. We also include shop (σ_{shop}) and day (δ_{day}) fixed effects. Standard errors are clustered by shop since that was the level of random assignment, but we also present standard errors and p-values based on the wildbootstrap procedure described in Cameron et al. (2008) in Table A2.

5.1 Uptake of ACTs, Sample Characteristics and Balance

Over the period of the study in which ACTs were available for purchase, 42 percent of households (16 percent of individuals) purchased at least one treatment course of ACT using their ID card. The mean number of ACTs purchased per household (individual) was 1.33 (.278). We do not see much evidence for hoarding: 92 percent of study participants who ever purchased an ACT, purchased only one or two over the course of the study. Just over 60 percent of ACT purchases were for children in the three lower age/dose categories (under 12 years old), while nearly 40 percent were for the highest dose category, including individuals ages 12 and older. We see no significant differences across treatment arms in the number of ACT purchases per household or individual, or in the percent of adult doses purchased (Table 2, Panel C). Although there are some significant differences across treatment arms in the mean age of the patient (Table 2, Panel C), the differences in magnitude are small.

Sample characteristics and balance across treatment arms are shown in Table 2. Columns (1) and (2) include data from the entire sample of ACT purchasers and demonstrate balance across a range of characteristics for those who were and were not randomly assigned to be followed up with. The differences between

and the packaging treatment arms to absorb the effect of the testing and present the main impact of the packaging arms themselves.

those who were followed up with and those who were not are small and are insignificant for all but two variables.

Columns (3) - (9) explore characteristics and balance across treatment arms for the analysis sample. We were successful in interviewing the female head of household roughly 91 percent of the time. On average, female household heads had 7.3 years of education and their spouses had about 8.6; 42 percent of them said they could read a letter written in English (Table 2, Panel A).

Roughly 70 percent of households have had a member with suspected malaria in the past month and about 64 percent of household members slept under a net the night before the survey. 65 percent of people had heard of ACTs at baseline, just under 60 percent said that ACTs were their preferred antimalarial and 54 percent said they thought it was the most effective antimalarial drug (Table 2, Panel D).

Among the people who sought outside treatment for a previous episode of malaria (which almost everyone did), nearly 25 percent first sought care at a drug shop, while 46 percent first sought care at a private hospital or clinic. Only 17 percent received a confirmed diagnosis of malaria using microscopy or an RDT and roughly 52% of those who took medicines to treat the disease took ACTs (Table 2, Panel E)

While there are some significant differences in these characteristics between treatment arms and the control group, for most of the arms, only one or two variables are significant (which is to be expected) and the differences are all modest in magnitude. Only the "Don't Save Pills" treatment group has more notable differences from the control group–they appear somewhat more educated and literate and report less burden of malaria in their household, but they are also less likely to own a mobile phone and other assets and are less knowledgeable about ACTs (and less likely to have used them to treat a previous episode of malaria) so some of these results may simply be due to chance.

5.2 Overall Adherence Behavior

The overall adherence rate was 64 percent in our analysis sample (and 64.7 percent in the completely unrestricted sample). There is virtually no association between the age of the patient and the likelihood of adherence in our sample. This is somewhat surprising because we might expect adherence to decline with the age of the patient for two main reasons. First, infants and young children are much more at risk of serious consequences of sub-therapeutic malaria treat-

ment than adults. Second, the treatment course is more cumbersome for older patients, who have to take four pills per dose twice a day. The mean number of pills remaining overall was 2.45 and the mean among those who were not adherent was 6.6. Since the number of pills required varies with age, it can be more instructive to consider how many doses were left. The mean number of doses left was .9 overall and 2.4 among those who did not adhere. This means that, among those who did not complete their medication, they had on average between a day and a day and a half of the three-day treatment left. We measured the percent of people that took each dose at approximately the correct time of day and find that adherence is high for the first two doses (94 percent and 89 percent) and then falls steadily (between 8-11 percent percentage points) with each subsequent dose (data not shown).When we include proper timing in the definition of adherence (as is standard in the medical literature), the overall adherence rate falls from 64 percent to 52 percent.

5.3 Impact of Packaging and Messaging on Adherence

5.3.1 Graphical Evidence

We start by presenting a simple graphical analysis of the impact of packaging on adherence. For each treatment arm, we present two figures. The figure on the left plots the treatment coefficients (and 95 percent confidence intervals) from a regression in the form of Equation 1, but with a series of dummy variables for outcomes indicating "zero doses left" (i.e. full adherence), "one or fewer doses left", "two or fewer doses left", etc. The figure on the right shows the coefficient on tablets remaining instead. Graphical evidence of a positive treatment impact would be seen in the coefficients for a treatment arm lying above zero.

Figure 5 shows the impact of CAPSS packaging relative to the control for doses and tablets remaining. The figure suggests that there is no impact of CAPSS on medication taking, as the coefficients are close to zero, although the confidence intervals are very wide. We also do not see evidence that the "CAPSS Information Only" arm increases adherence (Figures 6). The point estimates are negative though quite noisy. Taken together, these results are suggestive that the current approach to promoting adherence through specialized packaging is not effective at improving medication taking.

The impact of the "Malaria is not gone until..." message on adherence is presented in Figure 7. While the difference in the probability of having five or fewer doses remaining does not appear to be affected by the message, the impact

increases in magnitude and statistical significance as doses left decrease (and as tablets left decrease, see Fig 7B), suggesting that the message leads to improvements in medication taking at the later stages of the treatment course. On the other hand, Figure 8 shows no clear impact of the "Don't Save Pills" message on adherence. While the point estimates on adherence by dose and tablet are positive–with a similar pattern of increasing impact as doses/tablets decline–the confidence intervals are wide and include a range of impact estimates.

5.3.2 Regression Estimates and Robustness

Regression estimates based on Equation 1 are presented in Table 3. Column (1) presents coefficient estimates of the impact of the various treatment arms on adherence. As seen in the figures, the CAPSS and "CAPSS Information Only" arms have insignificantly negative impacts on adherence, while the "Malaria is not gone until..." message and "Don't save pills..." message have positive effects on adherence, though only the "Malaria is not gone until..." message is statistically significant. The "Malaria is not gone until..." message increases adherence by 5.5 percentage points (8.5 percent), relative to the mean of 64.3 percent adherence in the control group. While the effect on overall adherence is modest, the magnitude of its effect on the number of pills remaining is more substantial. The "Malaria is not gone until..." sticker reduces the number of doses remaining by .21, a 26 percent decrease in remaining doses (Column 4), and reduces the number of tablets remaining by .768, a 36 percent reduction in remaining tablets (Column 7). The "Don't save pills..." message has a smaller postive (and insignificant) impact on doses/tablets remaining and the CAPSS and CAPSS-Information packages once again appear to, if anything, increase the number of doses/tablets remaining, though the results are not statistically significant.

The remaining columns of Table 3 are robustness checks. The main analysis uses the first ACT purchase by individual. This may not be sufficiently restrictive, however, if another individual in that person's household purchased an ACT from the study in the past and received a different type of packaging. Since information flows easily within the household, we explore the robustness of our results to limiting the sample to only first ACT purchases by household. These results are presented in Columns (2), (5) and (8). The other robustness check we conduct restricts the sample to only those who showed their blister pack at the follow-up visit (Columns, (3), (6) and (9)). Our impact estimates

are largely consistent across this range of specifications. The “Malaria is not gone until...” message always has a positive effect on adherence and negative effect on doses/tablets remaining, with coefficient estimates for the impact on adherence ranging from .055 to .092. In the specification in which we restrict the sample to the people who showed blister packs–arguably, the sample with the most reliable information–the "Malaria is not gone until..." message is found to significantly increase adherence by 7.7 percentage points (12.6 percent) and the CAPSS package actually leads to a significant reduction in adherence by 7.4 percentage points.

Appendix Table A2 presents several additional robustness checks, including our main impact estimates with wild bootstrapped standard errors, with fixed effects for households, controls for wealth quintile and with the sample of all ACT purchases (i.e. not limited to first purchases). We find similar impacts as in the main analysis. The “Malaria is not gone until...” message increases adherence rates by 5.5-11.2 percentage points and is generally statistically significant. The CAPSS package seems to reduce adherence rates but the coefficients are not statistically significant.

6 Mechanisms

We find that the “Malaria is not gone until...” message was the only intervention that was moderately successful in raising adherence rates. In this section, we present an explanation for the comparative effectiveness of this intervention, and also examine some of the reasons why the other treatments failed to increase adherence compared to the standard control package. In both cases, we draw upon the theoretical framework outlined in Section 3 and examine the degree to which our data supports the predictions of our model.

6.1 Symptom Severity

Our first main result is that the “Malaria is not gone until...” message, which was designed to target the misperception that malaria is cured as soon as the symptoms of malaria disappear, raised adherence rates by 5.5 percentage points. As shown in Table 4, approximately 22 percent of people said that they stopped taking the medication because they felt better while another 11 percent of non-adherents said that that it was because they thought they were no longer ill with malaria. Moreover, people who didn’t finish their medication were 20

percentage points more likely than those who adhered to say that they were cured of malaria on the second day of treatment.

The theoretical model suggests that if the message worked through the intended mechanism, this treatment should be particularly effective in increasing adherence rates for those who had few symptoms of malaria on the second day of treatment. In the follow-up survey we asked people how sick they felt on each of the three or four days since they started taking the medication. Specifically, they were shown a ladder with a scale of 0-10 and asked to indicate how they felt on each day. The top of the scale (10) indicated the "worst feeling of illness", while the bottom of the scale (0) implied that they were in perfect health (see Appendix Figure A3 for an example of the scale). Figure 9 plots the adherence rates for the control group and the "Malaria is not gone until..." treatment group by the severity of illness the patient experienced on the second day of treatment. As predicted by the model, adherence in the control group is increasing strongly with symptom severity on day two, with the probability of adherence increasing by 20 percentage points as symptom severity goes from zero (perfect health) to eight (quite sick). Further, as predicted, adherence rates for the "Malaria is not gone until..." treatment group are substantially higher (nearly 20 percentage points) than the control group among those who felt relatively healthy on the second day of treatment.

Regression estimates of the relationship between second-day illness severity and adherence confirm the graphical evidence. In the control group, each additional "unit" of illness severity on the 10-point scale is associated with a 3.6 percentage point increase in the likelihood of being adherent (Table 5, Column 1). However, when we interact illness severity on the second day of treatment with a dummy for the "Malaria is not gone until..." treatment group, the coefficient is negative and of almost the same magnitude as the coefficient on "Illness Severity on Second Day" indicating that the effect of symptom severity on adherence is nearly removed by this treatment.[26] This suggests that the intervention convinced patients to complete the treatment when they would have otherwise stopped because they felt better and thought that they were cured.

[26] We find similar evidence using the *change* in illness severity between the first two days but the effects are smaller and not statistically significant (data not shown).

6.2 Drug Effectiveness

Our model also predicts that, for people who do not have strong priors about the effectiveness of the drugs, adherence rates have a non-linear relationship with illness severity on the second day of treatment. Patients who are uncertain about the quality of the drug, and who still feel very sick after a few doses, may conclude that the drug isn't very effective and stop taking the pills. On the other hand, people who have heard of ACTs are are more likely to believe that they just need to continue taking the medication in order to feel better. Figure 10 provides evidence in support of this model. Among people who hadn't heard of ACTs at baseline (approximately 32 percent of people who bought an ACT) , both high and low levels of illness severity on the second day of treatment are associated with lower adherence rates. However, among people who had heard of ACTs, there is no drop in adherence at high levels of illness severity on the second day of treatment[27].

An important feature of the CAPSS package is the glossy, colorful packaging which is intended to convey that the drugs are of higher quality and, therefore, more likely to be effective in treating the disease. Our second main result is that the CAPSS package fails to substantially increase adherence rates compared to the control package. Moreover, we do not find evidence that the CAPSS package differentially increases adherence rates among those who are not familiar with ACTs (Table 5, Column 2). This suggests that the CAPSS package was not successful in changing people's perceptions about the quality of the drug.

6.3 Saving Pills for a Future Malaria Episode

One of the primary costs of finishing the medication is the opportunity cost of consuming pills that could otherwise be used to treat a future malaria episode. If this was an important factor driving non-adherence, we would expect that those who are wealthier, or who live closer to the drug shop, are more likely to finish their medication since they face lower costs in using the pills for the current illness.

[27] We see a similar pattern if we look, instead, at people who at baseline said that, if money were no object, they would prefer to take ACTs (compared to those who didn't), or at people who said that they believed ACTs were the most effective drug for treating malaria in adults (compared to those who mentioned other drugs). While the latter is perhaps the most direct measure of beliefs about effectiveness, we don't have this variable for the entire sample–only for the sample who mentioned ACTs as a drug they have heard of. All of these measures yield similar results.

We constructed an asset index as a measure of the wealth of the patient. Figure 11A shows that there is a positive relationship between wealth and adherence in the control group. We find that those who are of the richest quintile are approximately 12 percentage points more likely to be adherent than those who are of the poorest quintile, even when we control for education (Table 5, Column 3). We also find that adherence falls with distance to the shop for distances up to 1.5 kilometer, but beyond that, adherence actually increases with distance (Figure 11B). This may be because, in the case that the disease is not fully cured, the costs of seeking additional treatment increase with distance. Both these graphs suggest that a desire to save pills may be an important reason for not completing the medication.

The "Don't save pills..." message specifically emphasizes the harm that results from saving pills ("Finish ALL tablets. Saving tablets for later can be harmful for malaria control in your community.") and is, therefore, intended to reduce the opportunity cost of consuming the pills. Figure 11 suggests that the "Don't save pills..." message does increase adherence rates relative to the control pack but the effect is not statistically significant and does not seem to do so differentially among the poor or those who live further away from the drug shop (Table 5, Columns 3 and 4). Thus, while there is some evidence that the desire to save pills may be a motivation for stopping treatment, the "Don't save pills..." message does not seem to be effective in counteracting that tendency.

6.4 Understanding Dosing Instructions

One reason people may fail to complete their malaria treatment on time is that they may not fully understand how and when to correctly take the drugs, resulting in pills remaining at the time of the follow-up survey.[28] At the follow-up survey, 57 percent of non-adherents said that they were still continuing treatment (Table 4). If these respondents were being truthful, this suggests that understanding of dosing instructions may be major a factor limiting adherence. However, we also find that 89 percent of patients (across all pack types) took the first two doses, with the correct number of pills per dose, at approximately the correct time. This implies that, at least in this study, knowledge of dosing instructions is not the major factor limiting adherence rates. Consistent with this, we do not find that those who can read English, or those who have more

[28] Approximately 95 percent of follow-up surveys were done between 70 and 96 hours. If all doses of the ACT treatment are taken at the correct time, a single treatment course should be completed in 56 hours.

education, have significantly higher adherence rates (data not shown) [29].

The CAPSS pack and the CAPSS-Information packs, which both included pictorial instructions and visual cues to demarcate dosing (see Figures 4B and 4C), were designed to increase people's understanding of how to correctly take the drugs, particularly among those who are illiterate. We find no impact on either of these packs on adherence rates. Moreover, evidence from our endline survey suggests that the CAPSS packages are not very effective in increasing people's understanding of how to take the medication (Appendix Table A3).

Overall these results suggest that a lack of knowledge about the ACT dosing regimen is unlikely to be the primary factor limiting adherence rates in this study context since most people correctly take the first couple of doses. Moreover, the CAPSS and the CAPSS-Information packs do not seem to be any better than the control pack in improving people's understanding of how to correctly take ACTs.

7 Conclusion

The focus of most interventions to improve medication adherence is on chronic, long-term treatments (McDonald et al., 2002; Haynes et al., 2008). However, sub-optimal adherence to short-course therapies such as antimalarial drugs and antibiotics not only makes it less likely that the disease is cured, but also encourages the development of pathogen resistance to the treatment. Currently, the only large scale, patient-directed attempt to increase adherence to the ACT dosing regimen is to add pictorial instructions to enhance comprehension of dosing guidelines. Often, the packaging is also glossy and colorful to convey the high quality of the drugs. This packaging is typically used in branded, "social marketing" campaigns distributing ACTs. Our first main result is that this standard approach is not effective in increasing the likelihood that people will finish their medication. This is of particular importance because this type of package can significantly add to the cost of the drugs and create disruptions in the drug supply chain. It is important to note that social marketing campaigns also have the objective of increasing uptake of products. We cannot speak to whether or not the CAPSS pack and those like it are successful in encouraging

[29] While the instructions given at the shop may have been insufficient, it is likely that they were the best instructions patients would get in this context. This is because our shop attendants were provided with special training in ACT administration, were among the largest and most professional shops in these areas, and were working side by side with our study team throughout the project.

uptake, only on whether they improve adherence.

Other efforts to improve adherence to treatments (both for short and long-term therapies) have included monetary incentives (Volpp et al., 2009; Kimmel et al., 2012), shopkeeper training (Marsh et al., 1999, 2004), patient counseling (Munoz et al., 2014; Lauwo et al., 2006), verbal instructions to the patient (Okonkwo et al., 2001), text message reminders (Pop-Eleches et al., 2011; Goldberg and Fink, 2014) and special reminder pill packaging (McDonald et al., 2002; Haynes et al., 2008). These treatments have had varying impacts in different contexts and none have been consistently effective across all contexts, likely because there is still a lack of clear evidence on why people stop taking their medications (Bruxvoort et al., 2014).

The interventions tested in our study also did not dramatically increase adherence rates, highlighting further the difficulty in encouraging people to finish their treatment. We did, however, find that a simple sticker on the box with a message that emphasizes the importance of completing the medication for curing the disease is moderately succesful in increasing adherence rates. In contrast to the CAPSS package, the additional cost of adding this sticker to the box is miniscule. Thus, these types of stickers are likely to be a more cost-effective way of increasing the percentage of people who finish their medications. This approach may be more effective in countries with a national language, since this raises the likelihood that people understand the message (although we find no relationship between english literacy and adherence in our sample).

Although most of the interventions we tested did not increase adherence rates, our study was also designed to better understand the reasons why people fail to complete their medications. People have to contend with several different sources of uncertainty when deciding whether to continue to take the medication: whether the illness they are suffering from is actually malaria, whether the drugs are effective, and when they are fully cured of the disease. There are also subconscious factors that may drive non-adherence such as forgetting to take the pills and simply not knowing how to take the drugs correctly.

Our results suggest that the primary factor influencing adherence rates is the symptoms that people experience and the interaction of the severity of these symptoms with people's beliefs about the effectiveness of the drugs. We find that people who feel substantially better after a few doses of the drug are less likely to complete their medication. This effect is moderated in the group that received the "Malaria is not gone until..." Message, suggesting that people were stopping because they thought that they were cured of malaria once they felt

healthy. We also find that patients who had not heard of ACTs, and who feel very sick on the second day of treatment, are less likely to finish their medication. This may be because they interpret the persistence of strong malaria symptoms as a sign that the drugs are not effective in treating the disease. Consistent with this explanation, people who know of the superior effectiveness of ACTs show no decline in adherence at high illness severities.

Surprisingly, given the fact that malaria is much more prevalent among young children, we find little effect of age on the likelihood of completing medication. Moreover, while people seem to have some trouble understanding the dosing instructions on the packages, most people take the first few doses of the drug correctly which indicates that knowledge and understanding of the treatment regimen is likely not the major factor limiting adherence. In addition, we do not find that the CAPSS or CAPSS-Information packages enhance understanding of dosing instructions compared to the standard control package.

These results suggest that any intervention that is succesful in increasing adherence rates will need to convince people that they cannot rely on their symptoms alone when evaluating whether they still have the disease. In addition, increasing awareness about the effectiveness of ACTs may be a promising way to boost adherence rates. One way to do this is to ensure that people only take ACTs for confirmed cases of malaria since inappropriate use of the drug can contribute to the perception that it is not very effective (Adhvaryu, 2014). This is not entirely straightforward since many people do not comply with the results of a negative test for malaria (Cohen et al., 2014). As part of this study, we randomly offered a subsample of patients a test for malaria at the time of ACT purchase. 174 people tested negative for malaria on the randomly offered test and 98 percent of them decided to still buy the drugs. The relationship between malaria testing and adherence is important given the prominence that diagnostics is gaining in global malaria control strategy (WHO, 2010; Perkins and Bell, 2008). We explore this in a companion paper.

While our interventions had small impacts on adherence, they did help shed some light on why people may be stopping their medication and what types of interventions might be successful in increasing adherence rates. Further research to better understand how people's beliefs about malaria illness and treatment are formed may enhance our understanding of why they are so difficult to change.

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Table 1: Loss to Follow-Up Across Treatment Groups

	Mean in Control Group	CAPSS	CAPSS-Information Only	"Malaria is NOT gone until…" message	"Don't Save Pills..." Message	F-Test {P-value}: All Treatments Jointly Equal to Zero	F-Test {P-value}: All Treatments Jointly Equal to Each Other	Obs
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Follow Up Completed	0.963	0.000	0.019	0.010	-0.045**	2.846*	3.209*	1933
	(0.188)	[0.017]	[0.019]	[0.013]	[0.019]	{0.097}	{0.083}	
Follow Up Completed in 96 hours or less	0.925	-0.010	0.022	-0.014	-0.045**	3.038*	1.756	1933
	(0.264)	[0.029]	[0.025]	[0.022]	[0.014]	{0.085}	{0.233}	
Blisterpack was available at Follow-Up Survey	0.865	-0.078***	0.032**	0.001	0.029	9.641***	12.201***	1856
	(0.342)	[0.021]	[0.010]	[0.022]	[0.029]	{0.004}	{0.002}	

Notes: Data Source is Follow-Up Survey, sample is all people assigned to a follow-up survey. Column 1 shows the mean in the control group and Columns 2-5 shows the coefficient on the dummies for each treatment pack. The regressions include shop and day fixed effects. Standard deviations of the mean are in parentheses and standard errors of the coefficient (clustered at the shop) are in square brackets. Column 6 shows the f-statistic of a joint test that all the treatment coefficients are equal to zero while column 7 shows the f-statistic of a joint test that all the treatments are equal to each other. The p-values of the f-statistics are in curly braces. *** p<0.01 ** p<0.05 * p<0.10

Table 2. Baseline Summary Statistics

	All ACT Purchases		First Purchases Assigned to Follow-Up							
	Mean Among Those Not Assigned to Follow-Up	Coefficient on Assigned to Follow- Up	Mean in Control Group	CAPSS	CAPSS-Information Only	"Malaria is NOT gone until..." Message	"Don't Save Pills…" Message	P-Value: Test of All Treatments Jointly Equal to Zero	P-Value: Test of All Treatments Jointly Equal to Each Other	Obs
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
A. Characteristics of Female Household Head										
Age (Years)	34.340	-2.424**	32.687	0.085	-1.339	-0.350	-0.324	{0.526}	{0.463}	1548
	(12.893)	[0.840]	(11.501)	[0.678]	[0.918]	[0.884]	[1.226]			
Female	0.918	0.005	0.913	0.024	0.038**	0.023	-0.008	**{0.099}**	**{0.100}**	1556
	(0.275)	[0.021]	(0.283)	[0.031]	[0.012]	[0.029]	[0.009]			
Reads English	0.464	-0.061	0.420	0.054	-0.011	-0.009	0.061**	{0.126}	{0.156}	1549
	(0.499)	[0.039]	(0.494)	[0.038]	[0.023]	[0.041]	[0.023]			
Years of Education (Among Those Who Reported Some Education)	7.649	-0.315	7.310	0.248	0.026	-0.076	0.548***	**{0.024}**	**{0.055}**	1426
	(3.021)	[0.319]	(2.975)	[0.195]	[0.284]	[0.252]	[0.161]			
Years of Spouse/Partner Education (Among Those with Some Education)	8.958	-0.497	8.630	0.038	-0.122	0.097	-0.241	{0.810}	{0.827}	1145
	(3.066)	[0.353]	(3.220)	[0.368]	[0.198]	[0.412]	[0.205]			
B. Household Characteristics										
Household Size	5.937	0.067	5.966	0.041	0.510**	0.428*	-0.021	**{0.060}**	**{0.046}**	1556
	(2.580)	[0.220]	(2.777)	[0.287]	[0.214]	[0.194]	[0.165]			
Has Electricity	0.192	-0.020	0.162	0.010	-0.011	0.003	-0.006	{0.975}	{0.931}	1543
	(0.394)	[0.034]	(0.369)	[0.023]	[0.019]	[0.018]	[0.034]			
Owns Mobile Phone	0.826	-0.019	0.802	-0.005	-0.012	-0.000	-0.051*	{0.184}	{0.359}	1545
	(0.379)	[0.018]	(0.399)	[0.026]	[0.023]	[0.027]	[0.025]			
C. ACT Purchases										
Number of ACT Purchases per Individual	1.464	-0.034	1.230	-0.014	0.007	-0.051	-0.001	{0.403}	{0.309}	1556
	(0.695)	[0.026]	(0.481)	[0.051]	[0.046]	[0.049]	[0.049]			
Age (Years)	15.111	-1.540**	15.448	-0.186	-1.803	-2.076	0.028	**{0.030}**	**{0.017}**	1538
	(17.488)	[0.500]	(17.347)	[1.179]	[1.385]	[1.133]	[1.022]			

% of Adult Dose Purchases (Aged 12 years and above)	0.404	-0.036	0.414	0.030	-0.032	-0.002	0.019	{0.665}	{0.532}	1546
	(0.491)	[0.026]	(0.493)	[0.048]	[0.049]	[0.040]	[0.047]			
D. Health Behaviors and Knowledge										
Member of Household had Malaria in the last 30 days	0.673	0.038	0.725	-0.075	0.011	-0.072	-0.091**	**{0.029}**	{0.210}	1556
	(0.470)	[0.045]	(0.447)	[0.042]	[0.025]	[0.044]	[0.035]			
Slept under Bednet Last Night	0.614	0.063	0.638	0.026	0.021	0.027	0.033	{0.876}	{0.981}	1467
	(0.487)	[0.046]	(0.481)	[0.030]	[0.033]	[0.051]	[0.034]			
Heard of ACTs (Coartem/Lumartem/Lonart/AL)	0.682	0.005	0.647	0.008	-0.033	-0.068	-0.055	{0.462}	{0.412}	1556
	(0.466)	[0.023]	(0.479)	[0.040]	[0.047]	[0.047]	[0.041]			
Prefer Taking ACTs	0.638	-0.011	0.582	-0.019	-0.049	-0.014	0.030	{0.497}	{0.447}	1363
	(0.481)	[0.042]	(0.494)	[0.036]	[0.049]	[0.042]	[0.034]			
Believe ACTs are the Most Effective Drug	0.629	-0.021	0.542	-0.019	0.012	-0.028	0.029	{0.701}	{0.704}	1420
	(0.484)	[0.022]	(0.499)	[0.025]	[0.053]	[0.054]	[0.050]			
E. Previous Treatment-Seeking Behavior										
Sought Treatment at Drug Shop	0.296	-0.059	0.250	0.002	0.017	0.073	0.005	{0.632}	{0.721}	513
	(0.457)	[0.041]	(0.434)	[0.076]	[0.119]	[0.062]	[0.069]			
Sought Treatment at Private Hospital Or Clinic	0.389	0.041	0.455	-0.038	-0.048	-0.077	-0.035	{0.802}	{0.974}	513
	(0.489)	[0.066]	(0.500)	[0.111]	[0.105]	[0.063]	[0.092]			
Received Confirmed Diagnosis (Microscopy or RDT)	0.219	0.006	0.169	0.098	0.009	-0.010	0.029	{0.585}	{0.620}	510
	(0.415)	[0.035]	(0.376)	[0.079]	[0.066]	[0.066]	[0.074]			
Used ACT (Among Those Taking Medicine	0.506	0.053	0.521	-0.068	-0.142	-0.034	-0.149*	**{0.019}**	**{0.030}**	389
	(0.501)	[0.090]	(0.502)	[0.089]	[0.082]	[0.075]	[0.070]			

Notes: Data Source is Baseline Survey. Column 2 shows the coefficient on those assigned to the follow-up survey with the SE in square brackets. Column 3 shows the mean in the "analysis sample": first purchases of ACTs followed up within 96 hours . Columns 4-7 show the coefficients on dummies for each of the treatment groups with the SE (clustered at the shop) in square brackets. The regression includes controls for whether an RDT was offered, shop fixed effects and standard errors clustered by shop. Column 8 shows the f-statistic of whether all the treatment coefficients are jointly equal to 0. Column 9 shows the f-statistic for a test of whether all of the treatments coefficients are jointly equal to one another. The p values on the f-statistics are in curly braces
*** p<0.01, ** p<0.05 and * p<0.01

Table 3. Impact of Packaging and Messaging on Adherence and Medication Taking

	Dependent Variable is:								
	Adherence (Completed All Medication)			Number of Doses Remaining			Number of Tablets Remaining		
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
A. CAPSS	-0.027	0.028	-0.074**	0.048	-0.029	0.174*	0.229	-0.133	0.641
	(0.040)	(0.072)	(0.026)	(0.122)	(0.225)	(0.092)	(0.434)	(0.827)	(0.366)
	[0.514]	[0.711]	[0.021]	[0.704]	[0.899]	[0.097]	[0.613]	[0.876]	[0.118]
B. CAPSS INFO ONLY	-0.052	-0.018	-0.048	0.292	0.268	0.307	1.011	1.025	1.049
	(0.058)	(0.074)	(0.053)	(0.180)	(0.315)	(0.188)	(0.641)	(0.933)	(0.673)
	[0.396]	[0.817]	[0.395]	[0.143]	[0.419]	[0.142]	[0.153]	[0.304]	[0.158]
C. "MALARIA IS NOT GONE UNTIL…." MESSAGE	0.055*	0.092	0.077**	-0.208*	-0.254	-0.253*	-0.768*	-1.041	-0.982**
	(0.026)	(0.068)	(0.030)	(0.110)	(0.246)	(0.119)	(0.361)	(0.701)	(0.380)
	[0.065]	[0.213]	[0.035]	[0.095]	[0.331]	[0.066]	[0.066]	[0.176]	[0.033]
D. "DON'T SAVE PILLS…" MESSAGE	0.045	0.067	0.051	-0.086	-0.088	-0.084	-0.478	-0.740	-0.525
	(0.057)	(0.086)	(0.052)	(0.112)	(0.225)	(0.118)	(0.431)	(0.812)	(0.414)
	[0.456]	[0.457]	[0.360]	[0.466]	[0.706]	[0.494]	[0.299]	[0.388]	[0.240]
Mean of Dependent Variable	0.643	0.608	0.609	0.789	0.908	0.879	2.114	2.326	2.334
P-value: A = B = C = D = 0	0.024	0.471	0.006	0.010	0.106	0.005	0.005	0.044	0.003
R-squared	0.156	0.225	0.203	0.159	0.222	0.201	0.211	0.268	0.255
Number of Observations	1354	719	1159	1350	716	1159	1350	716	1159
First Individual ACT Purchases Only	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes
First Household ACT Purchases Only	No	Yes	No	No	Yes	No	No	Yes	No
Only Those who Showed Blister Pack	No	No	Yes	No	No	Yes	No	No	Yes

Notes: All Regressions Control for Shop and Day Fixed Effects, whether an RDT was offered, and an interaction between each pack type and a dummy for whether an RDT was offered. Regressions with remaining tablets as an outcome also include dosage group fixed effects. Standard errors are in parentheses and clustered by shop. p values are in square brackets. Those who did not start taking their medication and who were found after 96 hours are dropped from the analysis. *** p<0.01 ** p<0.05 * p<0.1

Table 4. Self-Reported Reasons For Remaining Pills

Reasons	Percentage of Non-Adherents
Still Continuing Treatment	56.1%
Felt Better	21.7%
No Longer Ill With Malaria	10.8%
Saving Pills for Next Malaria Episode	3.87%
Felt Worse/Didn't Get Better	0.86%
Too Many Side Effects	0.86%
Forgot to Finish Them	0.65%
Other	5.16%

Notes: Data Source is Follow-Up Survey. Only people who did not finish taking their pills were asked why they did not finish. Responses were not prompted but were pre-coded in the questionnaire.

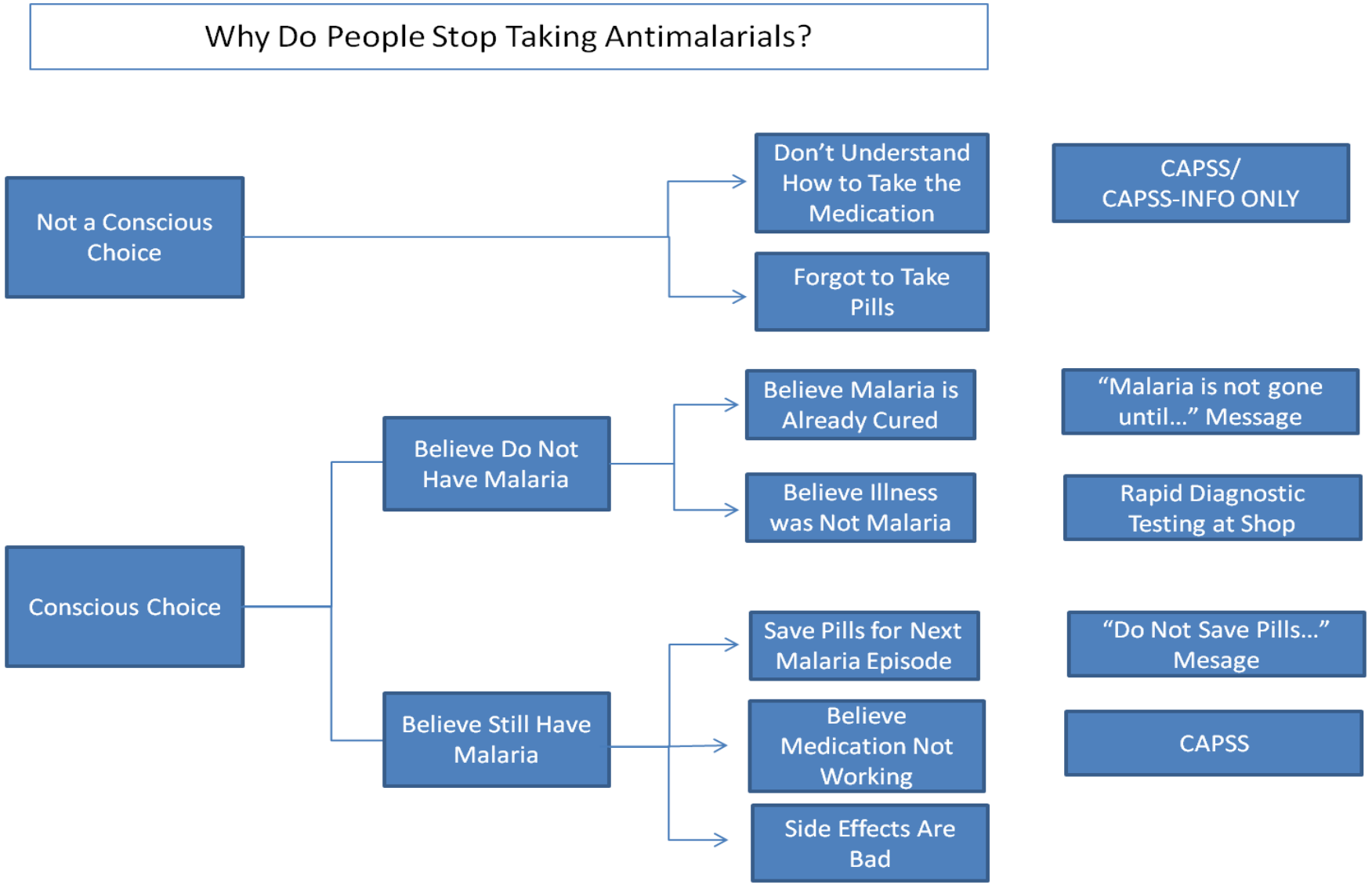
Table 5: Evidence on Mechanisms

	Dependent Variable: Adhered			
	(1)	(2)	(3)	(4)
CAPSS	0.013	-0.030	-0.074	-0.031
	(0.099)	(0.030)	(0.144)	(0.038)
	[0.896]	[0.352]	[0.623]	[0.441]
CAPSS - Info Only	-0.016	-0.027	0.022	0.006
	(0.073)	(0.043)	(0.103)	(0.042)
	[0.836]	[0.545]	[0.833]	[0.892]
"Malaria is NOT gone until..." Message	0.157*	0.034	0.134	0.064**
	(0.068)	(0.032)	(0.101)	(0.024)
	[0.051]	[0.314]	[0.219]	[0.026]
"Don't Save Pills…" Message	0.082	-0.003	0.071	0.036
	(0.061)	(0.041)	(0.087)	(0.039)
	[0.213]	[0.944]	[0.439]	[0.386]
Illness Severity on Second Day of Treatment	0.036***			
	(0.009)			
	[0.005]			
CAPSS X Illness Severity	-0.013			
	(0.020)			
	[0.538]			
CAPSS Information X Illness Severity	-0.007			
	(0.014)			
	[0.620]			
"Malaria is NOT gone until..." X Illness Severity	-0.033*			
	(0.016)			
	[0.076]			
"Don't Save Pills…" X Illness Severity	-0.017			
	(0.014)			
	[0.257]			
Haven't heard of ACTs		-0.089*		
		(0.045)		
		[0.085]		
CAPSS X Haven't Heard of ACTs		-0.024		
		(0.081)		
		[0.776]		
CAPSS Info X Haven't Heard of ACTs		-0.059		
		(0.091)		
		[0.536]		
"Malaria is NOT gone until…" X Haven't Heard of ACTs		0.037		
		(0.093)		
		[0.701]		
"Don't Save Pills…" X Haven't Heard of ACTs		0.087		
		(0.064)		
		[0.209]		
Wealth Quintile			0.041***	
			(0.009)	
			[0.002]	
CAPSS X Wealth Quintile			0.016	
			(0.041)	
			[0.700]	
CAPSS Info X Wealth Quintile			-0.023	
			(0.031)	
			[0.484]	

"Malaria is NOT gone until…" X Wealth Quintile			-0.031	
			(0.030)	
			[0.331]	
"Don't Save Pills…" X Wealth Quintile			-0.019	
			(0.032)	
			[0.575]	
Distance to Closest Drug Shop (km)				0.031
				(0.027)
				[0.286]
CAPSS X Distance to Shop (km)				-0.009
				(0.058)
				[0.882]
CAPSS Info X Distance to Shop (km)				-0.074
				(0.066)
				[0.290]
"Malaria is NOT gone until…" X Distance to Shop (km)				-0.044
				(0.032)
				[0.204]
"Don't Save Pills…" X Distance to Shop (km)				-0.021
				(0.034)
				[0.561]
R-squared	0.171	0.166	0.175	0.162
Number of Observations	1346	1351	1285	1344
Mean of Dependent Variable	0.667	0.665	0.668	0.667

Notes: All regressions include shop and day fixed effects. Those who were offered an RDT and those who didn't start their medication were dropped from the analysis. Illness Severity is Measured on a 10-point scale. Standard Errors Clustered by shop are in parentheses. P values are in square brackets. *** p<0.01, ** p<0.05 *p<0.01

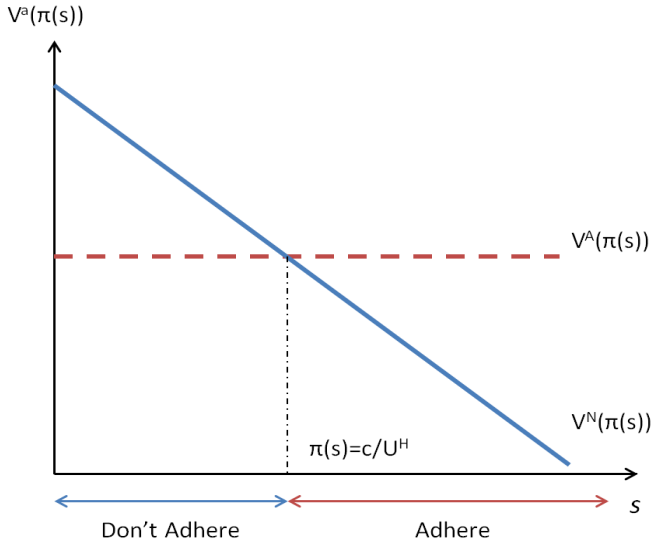
Figure 1: Conceptual Framework of Reasons People May Stop Taking Medications



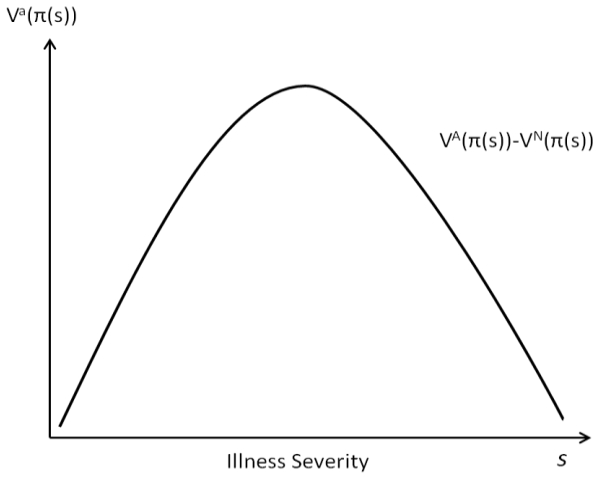
Notes: This is a conceptual framework of some of the reasons that we hypothesize people may not complete their medications and how the interventions tested in this study may affect adherence

Figure 2: Theoretical Impact of Interventions

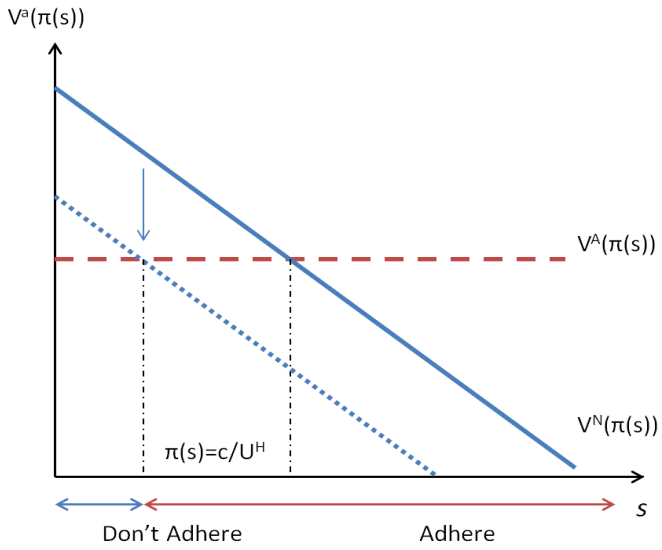
A. Believe ACTs Are Effective



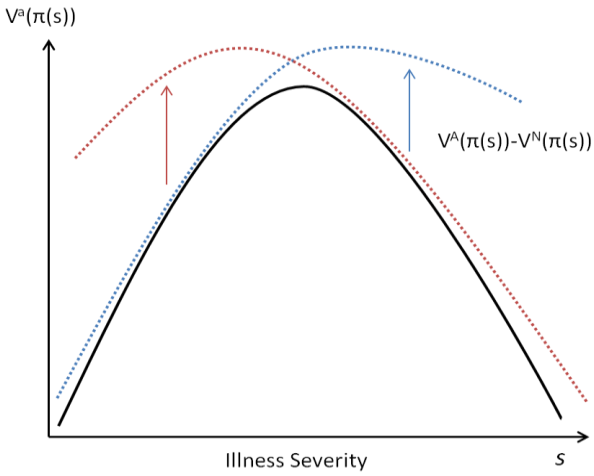
B. Uncertain About ACT Effectiveness



C. Intervention Targeting Beliefs About Being Cured

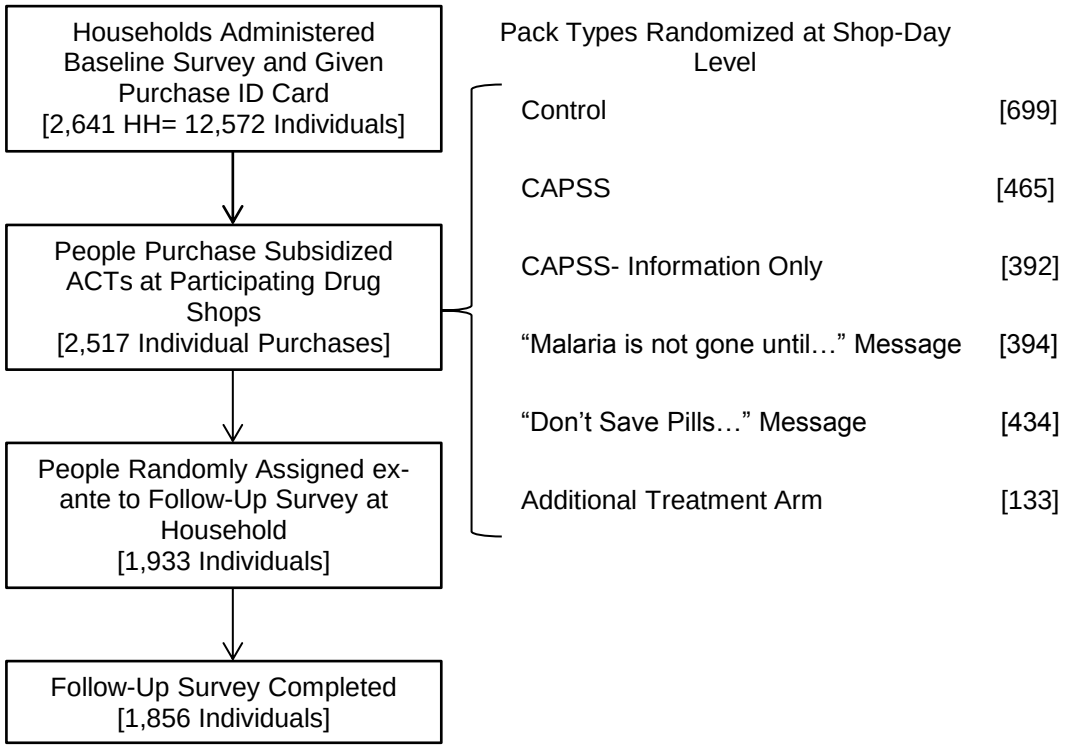


D. Interventions to Increase Adherence



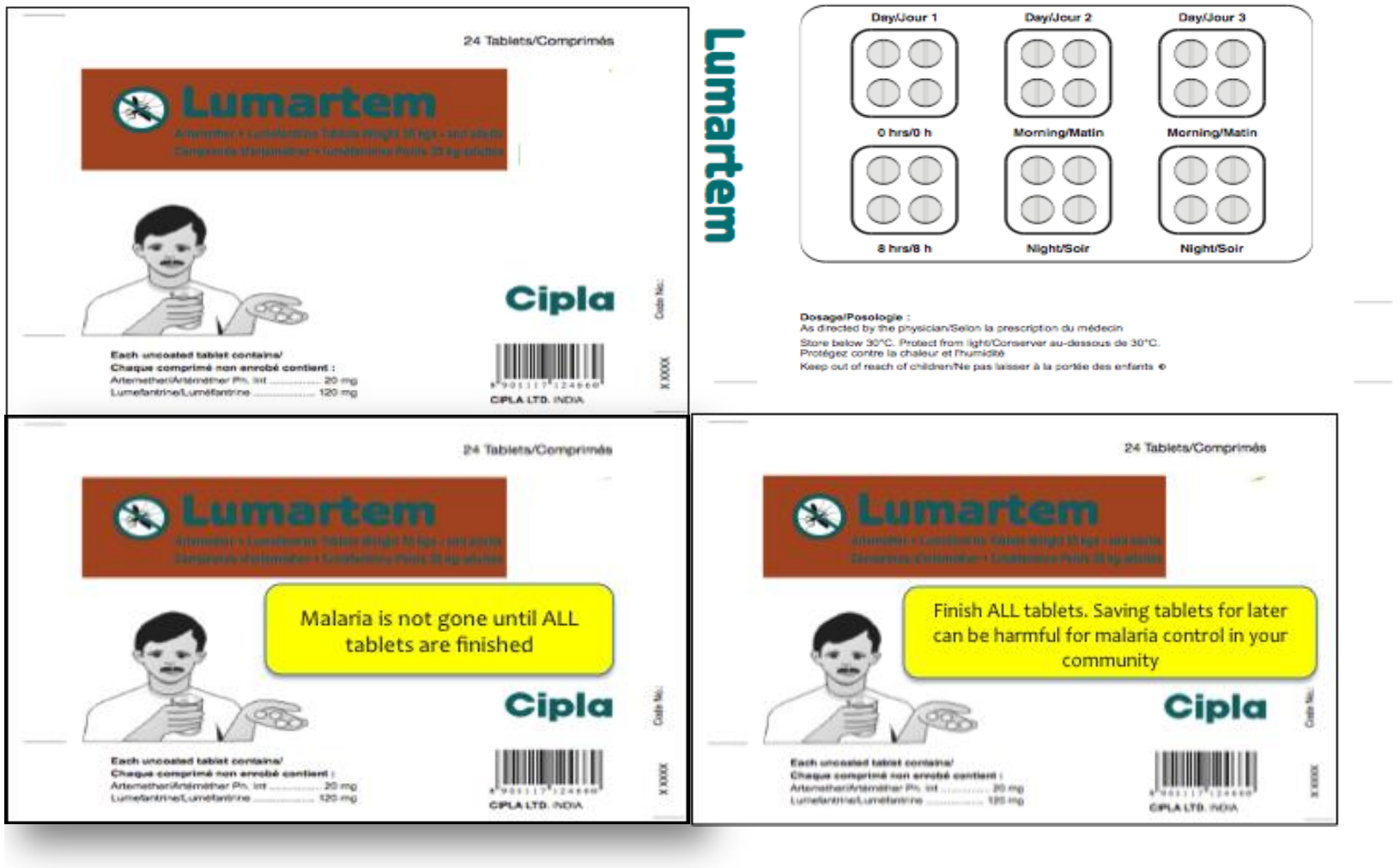
Notes: s is the severity of the illness experienced on the second day of treatment. π(s) is the perceived probability that the person is still suffering from malaria. V^A is the value of adhering (finishing the medication) and V^N is the value of not adhering (stopping the medication). U^H is the utility of being healthy and c is the cost of adhering. We normalize the utility of being sick U^S to equal 0.

Figure 3. Experimental Design and Attrition: Number of ACT Purchases Per Study Arm



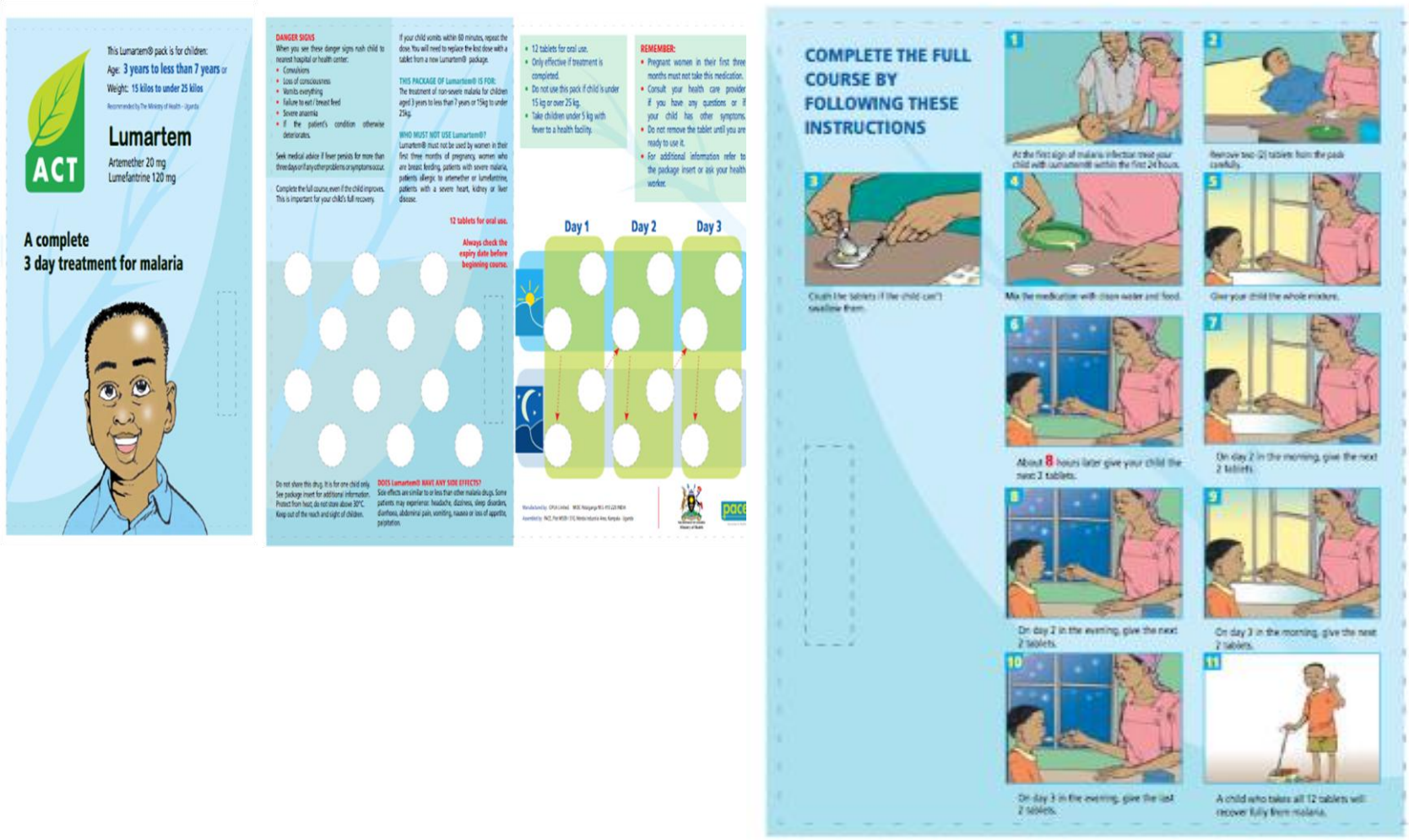
Notes: The "Additional Treatment Arm" is not discussed in this paper since it had to be dropped over the course of the study due to budgetary reasons. As a result, we do not have sufficient sample size to detect any treatment effects. People could buy ACTs multiple times during the course of the study period

Figure 4A. Standard ACT Pack Used in Control Group with Messages



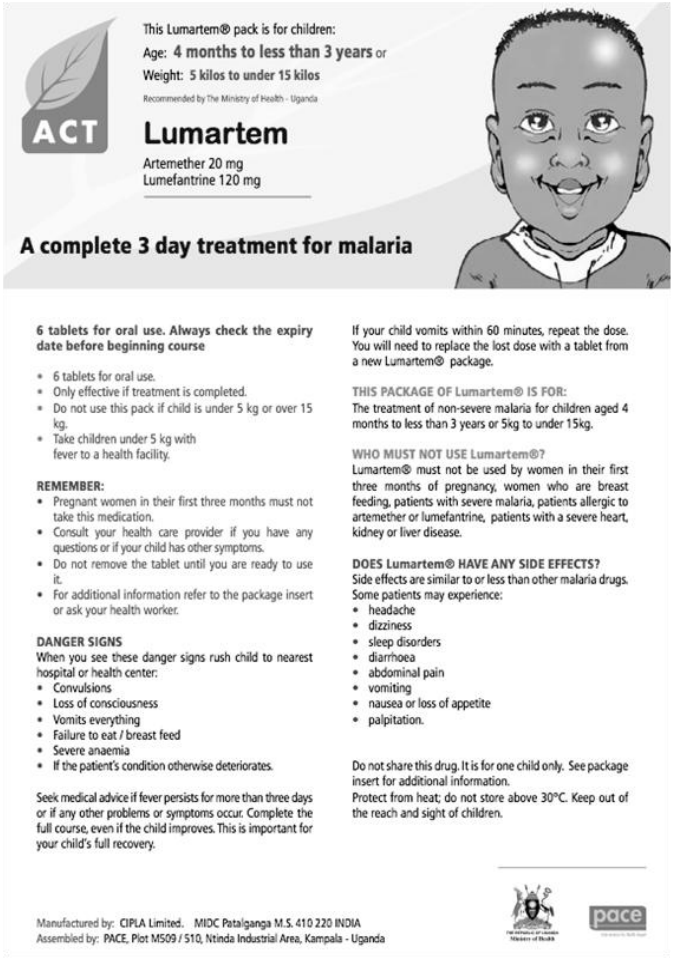
Notes: The top panel indicates the box (left) and the blisterpack inside the box (right) of the standard ACT pack that was used in the Control Group. The bottom panel shows the "Malaria is not gone until..." Message (left) and the "Don't Save pills..." Message (Right) affixed to the box

Figure 4B. CAPSS Package and Blisterpack



Notes: The pack shown here is for ages 3-7 years although the packages for the other dosage groups is similar (but generally a different color). The blisterpack (left) is inside the package and has pictures of the sun and the moon to indicate timing of the doses

Figure 4C. CAPSS Information Pack



This Lumartem® pack is for children:
Age: **4 months to less than 3 years** or
Weight: **5 kilos to under 15 kilos**
Recommended by The Ministry of Health - Uganda

ACT

Lumartem
Artemether 20 mg
Lumefantrine 120 mg

A complete 3 day treatment for malaria

6 tablets for oral use. Always check the expiry date before beginning course

- 6 tablets for oral use.
- Only effective if treatment is completed.
- Do not use this pack if child is under 5 kg or over 15 kg.
- Take children under 5 kg with fever to a health facility.

REMEMBER:
- Pregnant women in their first three months must not take this medication.
- Consult your health care provider if you have any questions or if your child has other symptoms.
- Do not remove the tablet until you are ready to use it.
- For additional information refer to the package insert or ask your health worker.

DANGER SIGNS
When you see these danger signs rush child to nearest hospital or health center:
- Convulsions
- Loss of consciousness
- Vomits everything
- Failure to eat / breast feed
- Severe anaemia
- If the patient's condition otherwise deteriorates.

Seek medical advice if fever persists for more than three days or if any other problems or symptoms occur. Complete the full course, even if the child improves. This is important for your child's full recovery.

If your child vomits within 60 minutes, repeat the dose. You will need to replace the lost dose with a tablet from a new Lumartem® package.

THIS PACKAGE OF Lumartem® IS FOR:
The treatment of non-severe malaria for children aged 4 months to less than 3 years or 5kg to under 15kg.

WHO MUST NOT USE Lumartem®?
Lumartem® must not be used by women in their first three months of pregnancy, women who are breast feeding, patients with severe malaria, patients allergic to artemether or lumefantrine, patients with a severe heart, kidney or liver disease.

DOES Lumartem® HAVE ANY SIDE EFFECTS?
Side effects are similar to or less than other malaria drugs. Some patients may experience:
- headache
- dizziness
- sleep disorders
- diarrhoea
- abdominal pain
- vomiting
- nausea or loss of appetite
- palpitation.

Do not share this drug. It is for one child only. See package insert for additional information.
Protect from heat; do not store above 30°C. Keep out of the reach and sight of children.

Manufactured by: CIPLA Limited. MIDC Patalganga M.S. 410 220 INDIA
Assembled by: PACE, Plot M509 / 510, Ntinda Industrial Area, Kampala - Uganda

pace

COMPLETE THE FULL COURSE BY FOLLOWING THESE INSTRUCTIONS

1 At the first sign of malaria infection treat your child with Lumartem® within the first 24 hours.

2 Remove one (1) tablet from the pack carefully.

3 Crush the tablet if the child can't swallow it.

4 Mix the medication with clean water and food.

5 Give your child the whole mixture.

6 About **8** hours later give your child the next tablet.

7 On day 2 in the morning, give the next tablet.

8 On day 2 in the evening, give the next tablet.

9 On day 3 in the morning, give the next tablet.

10 On day 3 in the evening, give the last tablet.

11 A child who takes all 6 tablets will recover fully from malaria.

Notes: This was a black and white copy of the instructions given in the CAPSS pack. This paper was wrapped around the standard ACT box used in the Control Group

Figure 5: Doses and Tablets Remaining for CAPSS Packs

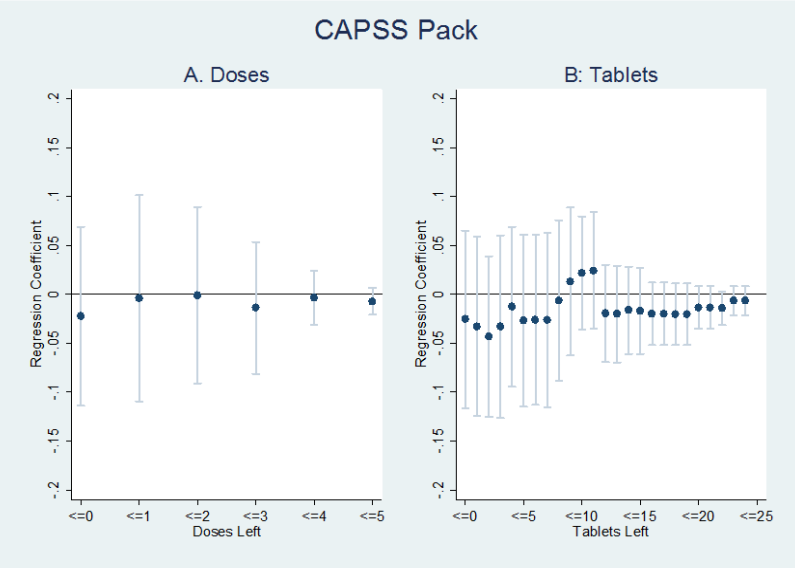
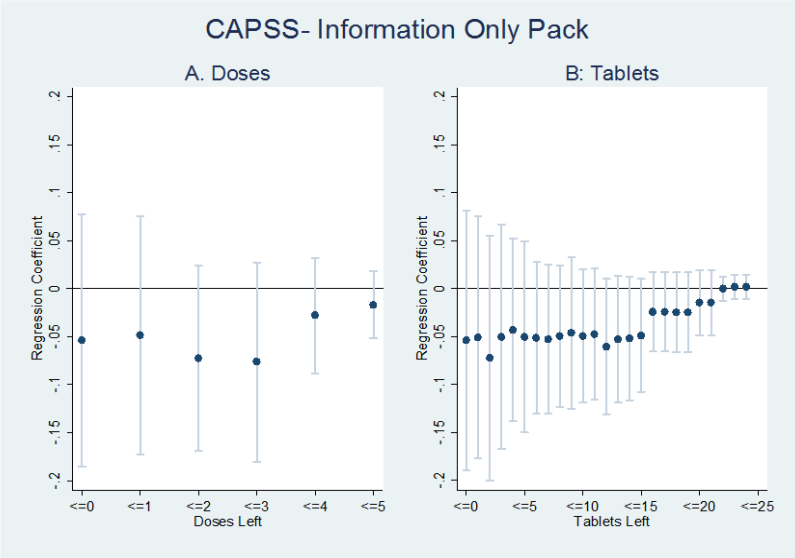


Figure 6: Doses and Tablets Remaining for CAPSS-Information Only Packs



Notes: Figures plot regression coefficients of the impact of the treatment (compared to the control) on the cumulative probability of each dose (Panel A) or of each tablet (Panel B) remaining with 95% confidence intervals. The regressions control for shop and day fixed effects, whether an RDT was offered, and interactions of each pack type with a dummy for the offer of an RDT. Regression with tablets remaining also include dosage fixed effects. Standard errors were clustered at the shop level.

Figure 7: Doses and Tablets Remaining for "Malaria is NOT gone until…" Message

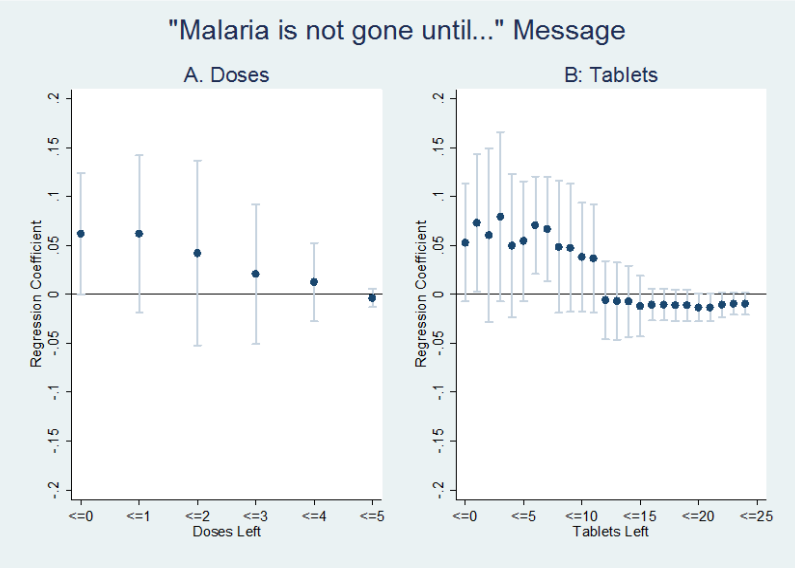
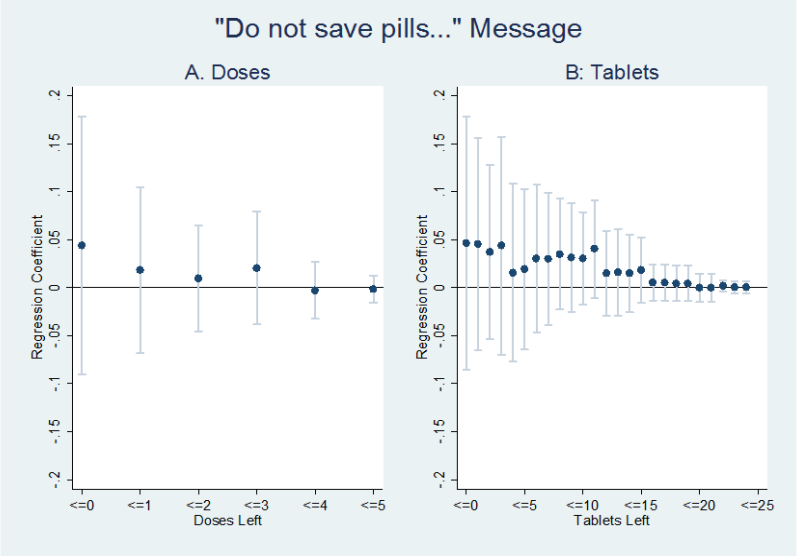
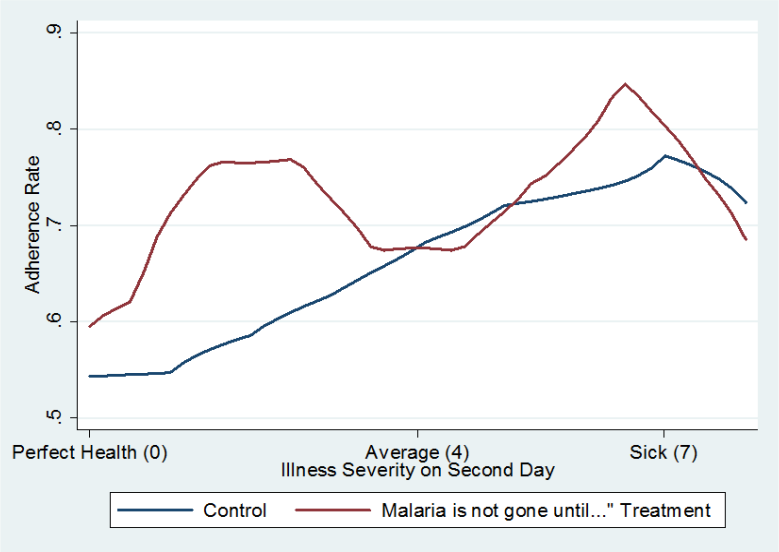


Figure 8: Doses and Tablets Remaining for "Don't save pills…" Message



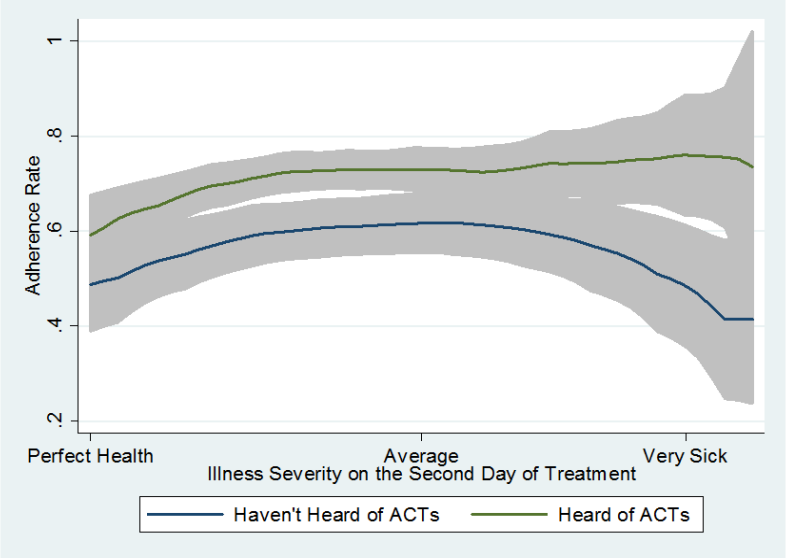
Notes: Figures plot regression coefficients of the impact of the treatment (compared to the control) on the cumulative probability of each dose (Panel A) or of each tablet (Panel B) remaining with 95% confidence intervals. The regressions control for shop and day fixed effects, whether an RDT was offered, and interactions of each pack type with a dummy for the offer of an RDT. Regression with tablets remaining also include dosage fixed effects. Standard errors were clustered at the shop level.

Figure 9. Adherence Rates By Illness Severity on Second Day of Treatment



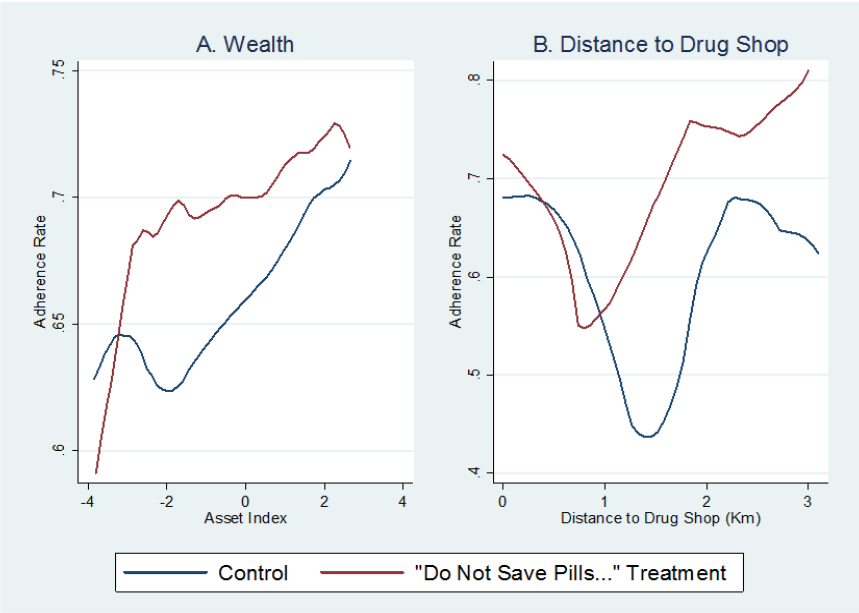
Notes: Graphs are of a smooth local polynomial kernel weight regression of adherence on illness severity on the second day of treatment. Illness severity was measured on a 10-point scale with larger numbers indicating increasing levels of sickness. Illness levels 9 and 10 are not included because there are very few observations at those severity levels

Figure 10: Impact of Interaction between Illness Severity and Knowledge of ACTs on Adherence



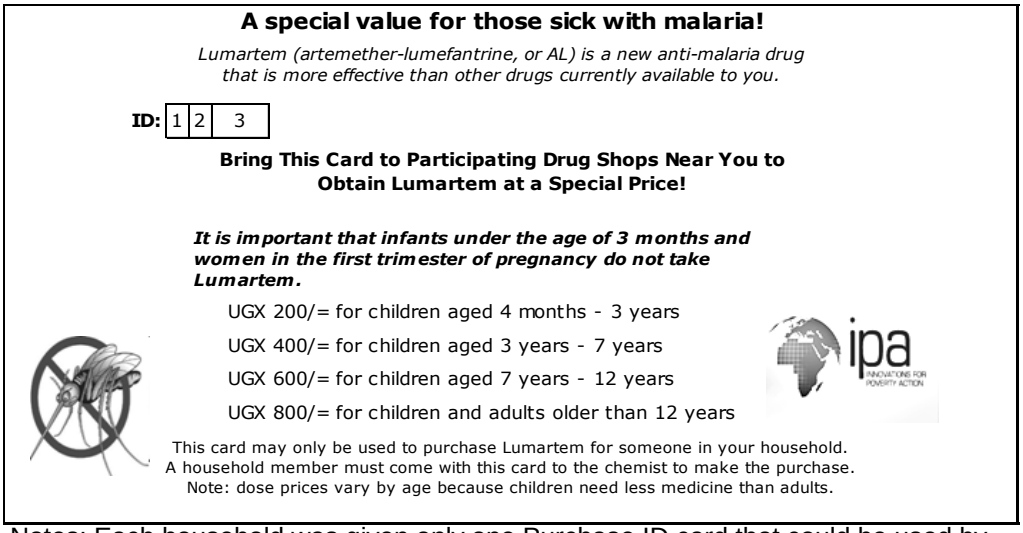
Notes: Smoothed Local Polynomial Regression results of Adherence on Illness Severity on the Second Day of Treatment. Information on knowledge of ACTs is from the Baseline Survey while illness severity and adherence rates are from the follow-up survey. The grey shaded areas indicate the 95% confidence intervals

Figure 11: Adherence Rates by Wealth and Distance to Drug Shop



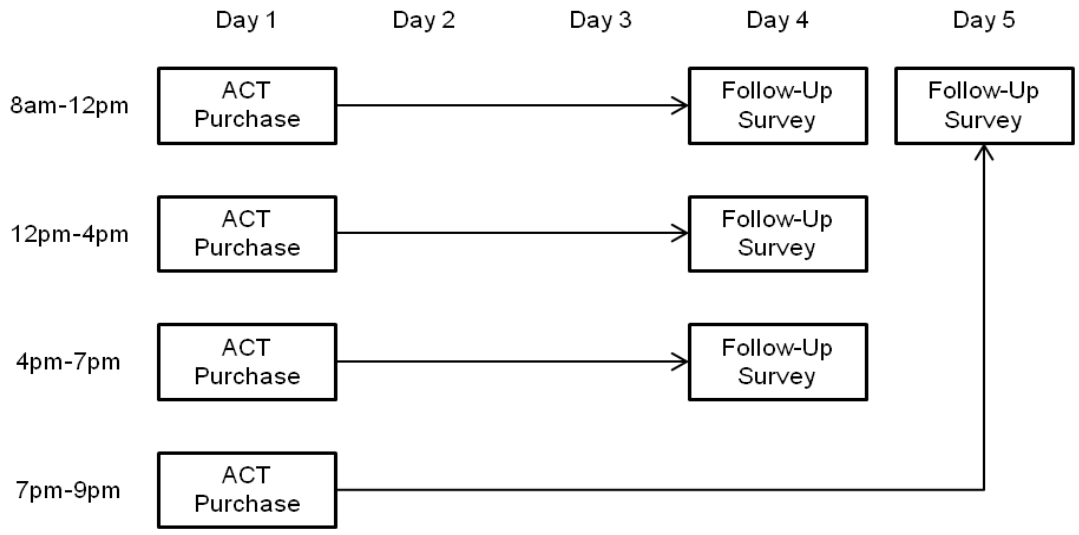
Notes: Smoothed Local Polynomial Regression Results of Adherence Rates and Assets (Panel A) and Distance to Drug Shop (Panel B). Asset and Distance information is from the Baseline survey

Appendix Figure A1. Purchase ID Card



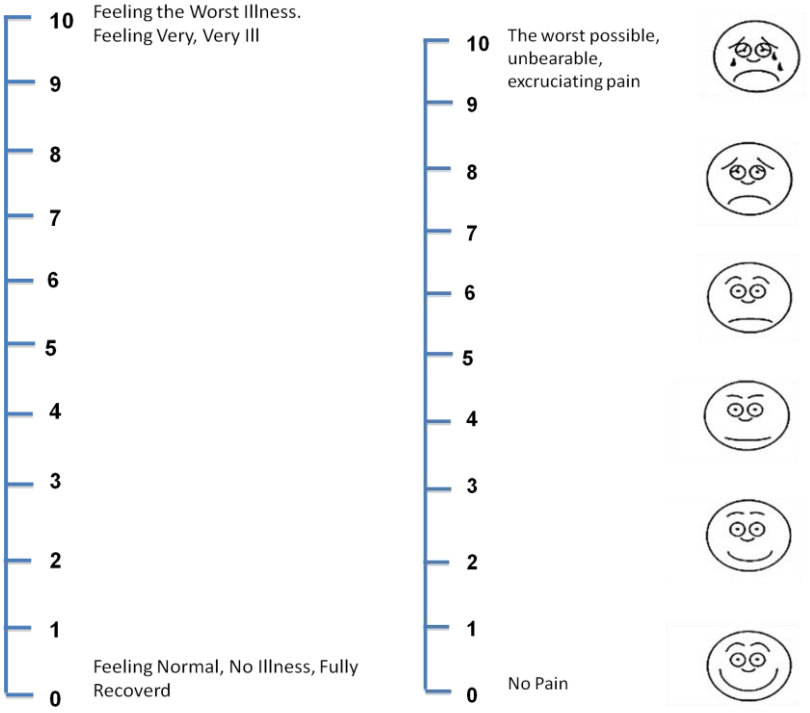
Notes: Each household was given only one Purchase ID card that could be used by any member of the household as many times as they needed. The Purchase ID was used to link the drug shop and follow-up surveys for individuals to the baseline information for the household

Appendix Figure A2. Timing of Follow-Up



Notes: The follow-up survey was planned for 72 hours after the time of the ACT Purchase. If people purchased ACTs after 7pm in the evening, the follow-up was scheduled for approximately 85 hours later, that is the following day at 8am in the morning

Appendix Figure A3. Ladder Scales



Notes: Similar scales were used to gauge severity of other symptoms such as fever, pain and fatigue. The scales were also used to help people estimate the probability that they had malaria at the time of ACT purchase

Appendix Table A1: Dosing Regimen and Prices of ACTs

Dosage Groups	Number of Pills Per Dose	Dosing Schedule	Number of Treatment Days	Subsidized Price (USH)	Subsidized Price (USD)
4 months- 3 years	1	2 X Day	3 Days	200	0.09
3 years-7 years	2	(Morning		400	0.17
7 years-12 years	3	and		600	0.26
12 years and above	4	Evening)		800	0.35

Notes: The exchange rate in December 2010 was approximately 2250 USH to $1 USD

Appendix Table A2: Robustness Checks on the Impact of Packaging and Messaging on Adherence and Medication Taking

	Dependent Variable is:											
	Adherence (Completed All Medication)				Number of Doses Remaining				Number of Tablets Remaining			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
A. CAPSS	-0.027	-0.055	-0.009	-0.033	0.048	0.076	0.056	0.224	0.229	0.257	0.397	0.202
	(0.045)	(0.141)	(0.036)	(0.038)	(0.221)	(0.342)	(0.097)	(0.340)	(0.544)	(1.154)	(0.521)	(0.360)
	[0.546]	[0.695]	[0.816]	[0.413]	[0.828]	[0.824]	[0.581]	[0.530]	[0.674]	[0.824]	[0.468]	[0.591]
B. CAPSS INFO ONLY	-0.052	0.005	-0.041	-0.036	0.292	0.087	0.278	0.937	1.011	0.335	0.935	0.575
	(0.073)	(0.145)	(0.060)	(0.036)	(0.220)	(0.303)	(0.169)	(0.606)	(0.733)	(0.903)	(0.550)	(0.544)
	[0.476]	[0.971]	[0.510]	[0.348]	[0.184]	[0.775]	[0.138]	[0.160]	[0.168]	[0.711]	[0.127]	[0.322]
C. "MALARIA IS NOT GONE UNTIL…" MESSAGE	0.055**	0.112	0.060*	0.062**	-0.208*	-0.359	-0.224*	-0.835**	-0.768*	-1.207	-0.505	-0.713*
	(0.022)	(0.130)	(0.030)	(0.020)	(0.124)	(0.308)	(0.098)	(0.294)	(0.438)	(0.901)	(0.363)	(0.330)
	[0.012]	[0.388]	[0.077]	[0.015]	[0.094]	[0.244]	[0.051]	[0.022]	[0.080]	[0.181]	[0.201]	[0.063]
D. "DON'T SAVE PILLS…" MESSAGE	0.045	0.051	0.039	0.059	-0.086	0.080	-0.043	-0.389	-0.478	-0.475	-0.281	-0.616
	(0.068)	(0.124)	(0.055)	(0.044)	(0.112)	(0.320)	(0.111)	(0.417)	(0.467)	(0.944)	(0.465)	(0.385)
	[0.510]	[0.677]	[0.497]	[0.219]	[0.442]	[0.803]	[0.710]	[0.378]	[0.306]	[0.615]	[0.563]	[0.148]
Mean of Dependent Variable	0.651	0.609	0.645	0.657	0.757	0.879	0.788	0.751	1.720	2.334	2.092	1.958
P-value: A = B = C = D = 0	0.107	0.878	0.088	0.001	0.267	0.668	0.027	0.003	0.186	0.563	0.004	0.004
R-squared	0.156	0.853	0.174	0.126	0.159	0.877	0.172	0.128	0.211	0.868	0.220	0.186
Number of Observations	1354	1159	1286	1700	1350	1159	1282	1696	1350	1159	1282	1696
Wild Bootstrap Standard Errors	Yes	No	No	No	Yes	No	No	No	Yes	No	No	No
Household Fixed Effects	No	Yes	No	No	No	Yes	No	No	No	Yes	No	No
Controls for Wealth Quintile	No	No	Yes	No	No	No	Yes	No	No	No	Yes	No
Redemptions	First	First	First	All	First	First	First	All	First	First	First	All

Notes: All regressions control for day fixed effects, whether an RDT was offered and for interactions with each pack type and a dummy for whether an RDT was offered. Except for the regression with HH fixed effects, regressions also include shop fixed effects. First redemptions are at the individual level. Regressions with tablets as an outcome also include dosage fixed effects. Those who didn't start taking their medication and who were found after 96 hours are dropped. Standard errors are in parentheses and clustered by shop. p values in square brackets. *** p<0.01, **p <0.05 * p<0.10

Appendix Table A3.Understanding of Dosing Instructions on Control Pack and CAPSS Pack

	A. Control Pack (Adult Dose)		
	Number of Days	Number of Pills Per Dose	Time of Day
Correct	33.6%	61.1%	46.1%
Wrong	19.1%	35.0%	35.3%
Didn't Mention It	44.3%	0.86%	15.7%
Don't Know	2.97%	2.97%	2.93%

	B. CAPSS Pack (Adult Dose)		
	Number of Days	Number of Pills Per Dose	Time of Day
Correct	33.4%	60.0%	46.3%
Wrong	18.1%	36.7%	35.8%
Didn't Mention It	46.0%	0.86%	15.5%
Don't Know	2.45%	2.50%	2.46%

Notes: Data Source is Endline Survey. Respondents were all female heads of household. The surveyor showed the respondent each adult dose package (Control and CAPSS) and asked her to say how she would take the medication. Responses were not prompted. "Didn't Mention It" is for people who didn't mention that particular aspect of the dosing regimen