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# Subsidise the test, the treatment or both? Results of an individually randomised controlled trial of the management of suspected malaria fevers in the retail sector in western Kenya

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## ABSTRACT

**Introduction** In many malaria-endemic countries, the private retail sector is a major source of antimalarial drugs. However, the rarity of malaria diagnostic testing in the retail sector leads to overuse of the first-line class of antimalarial drugs known as artemisinin-combination therapies (ACTs). The goal of this study was to identify the combination of malaria rapid diagnostic test (RDT) and ACT subsidies that maximises the proportion of clients seeking care in a retail outlet that choose to purchase an RDT (RDT uptake) and use ACTs appropriately.

**Methods** 842 clients seeking care in 12 select retail outlets in western Kenya were recruited and randomised into 4 arms of different combinations of ACT and RDT subsidies, with ACT subsidies conditional on a positive RDT. The outcomes were RDT uptake (primary) and appropriate and targeted ACT use (secondary). Participants' familiarity with RDTs and their confidence in test results were also evaluated.

**Results** RDT uptake was high (over 96%) across the study arms. Testing uptake was 1.025 times higher (98% CI 1.002 to 1.049) in the RDT subsidised arms than in the unsubsidised groups. Over 98% of clients were aware of malaria testing, but only 35% had a previous experience with RDTs. Nonetheless, confidence in the accuracy of RDTs was high. We found high levels of appropriate use and targeting of ACTs, with 86% of RDT positives taking an ACT, and 93.4% of RDT negatives not taking an ACT. The conditional ACT subsidy did not affect the RDT test purchasing behaviour (risk ratio: 0.994; 98% CI 0.979 to 1.009).

**Conclusion** Test dependent ACT subsidies may contribute to ACT targeting. However, in this context, high confidence in the accuracy of RDTs and reliable supplies of RDTs and ACTs likely played a greater role in testing uptake and adherence to test results.

## INTRODUCTION

In 2018, an estimated 228 million cases of malaria occurred worldwide, with 93% occurring in the WHO African region. In the same year 259 million rapid diagnostic tests (RDTs) and 214 million ACT treatment courses were delivered by National Malaria Programs.[1] Artemisinin combination therapies (ACTs)—the WHO-recommended first-line therapy for uncomplicated malaria—have played a significant role in reducing global malaria mortality,[2] but their overuse is rampant. Overconsumption of ACTs is an unnecessary drain on scarce public health resources and threatens the future sustainability of publicly funded subsidies. In addition, it puts both present and future patients at risk; inappropriate treatment of a non-malaria illness with an antimalarial increases case fatality rates and contributes to population-wide drug pressure that accelerates the spread of drug resistance.[3–7] To mitigate the risks of overuse, WHO recommends parasitological confirmation by quality-assured microscopy or RDTs for all individuals suspected of malaria, before treatment is started.[8]

In many malaria endemic regions, the private retail sector, including general retailers, drug sellers and pharmacies, is a major source of antimalarials.[9–11] The Affordable Medicines Facility-malaria pilot, which dramatically improved access to quality ACTs through private sector subsidies, led to a significant increase in the affordability and availability of quality-assured ACTs, but may have contributed to overconsumption since it did not include efforts to increase

## Key questions

### What is already known?

- The availability and use of malaria diagnostic tests is uncommon in the private retail sector, despite it being a major source of antimalarial drugs.
- Studies evaluating the use of malaria rapid diagnostic tests (RDTs) in the private retail sector have found highly variable rates of test uptake and adherence to the test result, with many test-negative clients still purchasing artemisinin-combination therapies (ACTs), the recommended antimalarial drug.
- There is some evidence that longer provider training, lower RDT prices and frequent supervision can encourage test uptake and improve adherence.

### What are the new findings?

- When malaria treatment is highly subsidised for a positive test result, we found nearly all participating retail sector clients in Western Kenya purchased RDTs even at the unsubsidised retail price of $0.40.
- We also found high levels of adherence to the test result, with 86% of RDT positives buying (subsidised) ACTs, and 93.4% of RDT negatives not buying (unsubsidised) ACTs.
- Even though only 35% of participants had previous experience with an RDT, most people were confident that both a positive and negative RDT result was correct.

### What do the new findings imply?

- High levels of ACT subsidies conditional on a positive RDT result could improve the targeting of ACTs in the retail sector.
- Public health messaging about the importance of malaria testing, and about the reliability of RDTs, appears to have increased confidence in malaria RDTs and may contribute to test uptake and adherence.
- Further expanding access to RDTs in the retail sector will require evaluating approaches that allow retail sector providers to take ownership of testing and RDT supply.

parasitological testing of people suspected of having malaria.[12–14] In 2015, 44% of all donor-funded ACTs consumed world-wide were distributed through the retail sector where studies have shown that between 65% and 91% of ACTs dispensed for malaria are purchased by people without malaria.[15–18] Malaria diagnostic testing is uncommon in the retail sector; fewer than 1 in 10 suspected cases are tested.[15] In the absence of parasitological testing, distinguishing fevers due to malaria from those due to other causes is not possible based on clinical presentation alone, and most fevers in malaria-endemic areas are assumed to be malaria-associated. As a result, presumptive treatment is prevalent in the retail sector and targeting ACTs to individuals with malaria infection is poor.

Malaria RDTs, which have excellent sensitivity and specificity and are simple enough to be used by trained laypersons,[19] could expand the reach of diagnostics into the retail sector and help improve the rational use of antimalarials.[20] For RDTs to improve the targeting of ACTs sold in the retail sector, consumers need to both choose to get tested *and* purchase ACTs according to the test result. These behaviours likely depend on the relative costs of testing and treatment and on people's perceptions about the likelihood their illness is malaria and the accuracy of the test.[21]

In this study, we set out to identify the combination of RDT and ACT subsidies out of four subsidy levels that maximises the proportion of clients at retail medicine outlets that choose to purchase an RDT, and subsequently use ACTs appropriately. We designed an individually randomised experiment which varied both the price of the RDT and the ACT while making the ACT subsidy conditional on a positive RDT. We also examined participants' familiarity with RDTs, their confidence in test results, and their perceptions about the prevalence of malaria fevers to understand the value they may place on a test to differentiate between malaria and non-malaria illnesses. We hypothesised that ACT subsidies that are conditional on the client receiving a malaria positive test can increase the uptake of malaria testing in the retail sector and improve ACT targeting, but that the effect will be related to the price of the RDT.

## METHODS

The study was carried out in a random sample of twelve retail outlets in two subcounties of rural western Kenya. Both subcounties have a similar malaria burden, predominantly Plasmodium falciparum with perennial transmission. About 50% of the health facilities are public, while the rest are either private or faith based.[22] A 2016 ACT watch survey showed that 70.6% of all antimalarials were distributed through the private sector, with 37% being through unregistered pharmacies,[23] and that 27.2% of all antimalarials were non-artemisinin-based. The RDT availability in retail outlets was 16% and 9.5% in the registered and unregistered outlets, respectively. Median RDT price in the private sector was $1.00; median ACT cost was $1.31 (adult) and $0.5 (child). At the time of the study, there were no RDT or ACT subsidies in the study area.

The study population comprised any individual presenting to the outlet with a malaria-like illness on randomly selected days. Children >1 year of age were eligible if they were physically present and accompanied by a parent or legal guardian. Any individual with signs of severe illness requiring immediate referral, those who had taken an antimalarial in the preceding 7 days or had a positive malaria test in the last 14 days and those with a prescription from a facility or medical provider were excluded from the study. Pregnant women were enrolled and offered an RDT but were advised to seek treatment in a health facility where accurate dating of the pregnancy would be done, and appropriate treatment administered.

A sampling frame of all eligible retail outlets in the study area was developed. The outlets included in the sampling were: (1) located within the study area; (2) stocked quality assured ACTs; (3) registered with the Kenya Pharmacy and Poisons Board and (4) willing to participate by

selling ACTs at the subsidised price for study participants with a positive RDT. From this roster of eligible outlets, 10 were randomly selected and enrolled in the study. Two of these outlets withdrew before the end of the study and were replaced by two other eligible outlets.

Potential participants were approached by the research assistants, present in each of the 12 outlets, as they sought services at the outlets. Those reporting fever or malaria-like symptoms in the preceding 24 hours were informed of the study and invited to participate. Those consenting to the study were administered a questionnaire to obtain information on symptoms, medications taken before coming to the outlet and familiarity with malaria diagnostic tests. We also asked participants their beliefs about malaria and testing. For example, we asked participants the likelihood that a hypothetical adult fever was malaria and that the likelihood that their own (or their child's) illness was malaria. For those who had heard of RDTs, we asked the likelihood that a hypothetical positive and hypothetical negative RDT result was correct. Participants' beliefs about malaria and testing were asked using a 5-point Likert Scale ranging from 'Not Possible' to 'Absolutely sure'. In order to simplify the presentation of these results we combine the responses at the two ends of the range so that we have three possible answers: 'Not Possible/Unlikely', '50–50' and 'Likely/Absolutely sure'.

Participants were then offered a scratch card with masked arm assignment, which randomised them to one of four study arms in a 1:1:1:1 ratio, each arm with a different combination of two different RDT prices and two different conditional ACT prices using a 2×2 factorial design to yield the four study arms (online supplemental table 1). The consumer RDT price was either \$0.2 (50% subsidy) or \$0.4 (no subsidy) while the ACT was either free (100% subsidy) or between \$0.1 and \$0.4 depending on the dosing (67% subsidy). On scratching the card, they were invited to purchase a malaria test as per the revealed arm. Those willing to be tested had the RDT performed by the research assistant and the results explained to them. The WHO prequalified CareStart Malaria HRP2 RDT with a sensitivity of 98% and a specificity 97.5%[24] was used. Once they (or their child) were tested, and the results were given to the participant, we asked them to estimate the likelihood their RDT result was correct. Those with a positive test could present the test cassette and the scratch card to the shopkeeper in exchange for a discounted ACT as per the arm assignment (table 1). No ACT discount was offered for individuals with a negative test or those without a test. The final treatment decision was recorded for all study participants as they left the outlet. The research assistants who performed the RDTs dispensed the RDT discounts to the clients and also reimbursed the shops for the discounted ACTs daily.

The primary outcome for the study was testing uptake, namely the customer's choice to purchase an RDT before purchasing medicine. Using the 2×2 factorial design we evaluated the effect of RDT subsidy (two levels: 50% vs 0% subsidy) and of conditional ACT subsidies (two levels: 100% vs 67% subsidy) on the primary outcome of testing uptake. The secondary outcomes were appropriate ACT use and targeted ACT use (defined as taking an ACT if positive or not taking if negative, either among all individuals with an RDT or among all participants, respectively). Individuals without a test result are excluded from the definition of appropriate ACT use and are included only in the denominator when defining targeted ACT use.

The target sample size of a total of 832 participants provided at least 80% power to detect each of the anticipated main effect sizes (online supplemental table 2). This was based on a two-sample Z-test for proportions each at alpha=0.0167 (based on a Bonferroni correction to the overall alpha level of 0.05 to account for three hypothesis tests—two main effects and the interaction).

The primary outcome was analysed within the modified Poisson generalised estimating equations framework to account for clustering by retail outlet with finite sample correction due to the small number of outlets.[25] The log and identity links were used to estimate relative (ie, risk ratios) and absolute effects (ie, risk differences), respectively, using effect coding. Using the alpha allocation principle, the main effect of each subsidy was evaluated with a prespecified significance level of 0.02 and the interaction effect with a prespecified significance level of 0.01. As a consequence, CIs for the main effects and interactions were summarised with 98% and 99% confidence levels of confidence, respectively. Results from the unadjusted, fully adjusted, and the parsimonious model identified by Beaulieu and O'Meara[26] were reported. The fully adjusted model includes gender and age of the patient, occupation and education level of the patient or guardian, household size and wealth. The parsimonious model only includes wealth. Secondary outcomes and individuals' beliefs about malaria and testing were assessed descriptively, with inference provided only for a comparison of ACT-based outcomes according to ACT subsidy levels.

### Patient and public involvement

The patients or the public were not involved in the design, or conduct, or reporting of the study.

### Trial registry

The trial was registered as clinical trial NCT03810014 at clinicaltrials.gov.

## RESULTS

The study was conducted between 28 March 2018 and 30 October 2019, capturing the different malaria transmission seasons in the region. A total of 842 participants were recruited and randomised to the study. Six were pregnant and therefore not eligible for the ACT subsidy and information on the medicines purchased after testing was missing for five participants. Therefore, the primary analysis of testing uptake was performed using 836 participants, excluding pregnant women, and the secondary

**Table 1** Participants characteristics by treatment arm (for n=836 participants included in the primary analysis)

| | Arm 1: 50% RDT subsidy and 100% ACT subsidy | Arm 2: 50% RDT subsidy and 67% ACT subsidy | Arm 3: RDT no subsidy and 100% ACT subsidy | Arm 4: RDT no subsidy and 67% ACT subsidy | Total |
|---|---|---|---|---|---|
| | (n=210) | (n=211) | (n=213) | (n=202) | (n=836) |
| Patient age (years) | | | | | |
| Median (Q1, Q3) | 30.0 (16.0 to 43.0) | 31.0 (15.0 to 45.0) | 30.0 (11.0 to 45.0) | 28.5 (11.0 to 45.0) | 30.0 (13.0 to 45.0) |
| Household size | | | | | |
| Median (Q1, Q3) | 5.0 (3.0 to 7.0) | 5.0 (3.0 to 6.0) | 4.0 (3.0 to 6.0) | 5.0 (3.0 to 6.0) | 5.0 (3.0 to 6.0) |
| Patient age in years % (n) | | | | | |
| 0–5 | 10.5% (22) | 12.8% (27) | 12.7% (27) | 12.4% (25) | 12.1% (101) |
| >5 to <18 | 15.7% (33) | 14.2% (30) | 20.2% (43) | 19.8% (40) | 17.5% (146) |
| 18 to <35 | 34.3% (72) | 28.0% (59) | 21.6% (46) | 27.2% (55) | 27.8% (232) |
| 35+ | 39.5% (83) | 45.0% (95) | 45.5% (97) | 40.6% (82) | 42.7% (357) |
| Patient gender % (n) | | | | | |
| Female | 43.8% (92) | 49.0% (103) | 45.5% (97) | 47.5% (96) | 46.5% (388) |
| Male | 56.2% (118) | 51.0% (107) | 54.5% (116) | 52.5% (106) | 53.5% (447) |
| Missing | (0) | (1) | (0) | (0) | (1) |
| Highest level of education completed % (n) | | | | | |
| <Primary or none | 21.0% (44) | 16.1% (34) | 19.7% (42) | 19.3% (39) | 19.0% (159) |
| Complete primary | 41.9% (88) | 32.2% (68) | 34.7% (74) | 33.2% (67) | 35.5% (297) |
| Complete secondary | 37.1% (78) | 51.7% (109) | 45.5% (97) | 47.5% (96) | 45.5% (380) |
| Occupation % (n) | | | | | |
| Farming | 19.5% (41) | 23.8% (50) | 24.9% (53) | 19.8% (40) | 22.0% (184) |
| Unemployed | 17.6% (37) | 15.2% (32) | 13.6% (29) | 17.3% (35) | 15.9% (133) |
| Formally employed | 13.3% (28) | 17.6% (37) | 15.0% (32) | 10.4% (21) | 14.1% (118) |
| Self-employed | 42.9% (90) | 41.4% (87) | 39.4% (84) | 45.5% (92) | 42.3% (353) |
| Informal employment | 6.7% (14) | 1.9% (4) | 7.0% (15) | 6.9% (14) | 5.6% (47) |
| Missing | (0) | (1) | (0) | (0) | (1) |
| Wealth: lower 40th percentile % (n) | | | | | |
| >40th percentile | 56.9% (119) | 61.9% (130) | 60.3% (126) | 60.7% (119) | 60.0% (494) |
| 0–40th percentile | 43.1% (90) | 38.1% (80) | 39.7% (83) | 39.3% (77) | 40.0% (330) |
| Missing | (1) | (1) | (4) | (6) | (12) |

Age is for the sick individual and education level is for respondents over the age of 18 (either the sick individual or the parent/guardian for minor participants). Q1 and Q3 correspond the 25th and 75th percentile, respectively.
ACT, artemisinin-combination therapy; RDT, rapid diagnostic test.

analysis on ACT consumption conditional on test results was based on the 831 participants with complete drug purchasing information (figure 1).

Randomisation to the four arms overall and by outlet was approximately balanced in terms of participant characteristics. Overall, the differences in characteristics among the four treatment arms were negligible (table 1). Nearly 70% of participants were adults (>18 years) and 46.5% were female. Further characteristics are summarised in table 1.

Prior to randomisation, we found that a large percentage of people recognised that not all febrile illnesses are malaria with only 55% saying that an adult fever was 'very likely/absolutely sure' to be malaria and 60% saying the same about their own/ their child's illness (table 2, Panel B). We found that almost all participants (98%) were already aware of malaria testing, but only 48% were aware of RDTs specifically and only 35% had previous experience with RDTs (table 2, Panel A). Despite this, we find high confidence in RDTs (among those who were aware of them), with 91% saying a hypothetical positive malaria test was 'very likely/absolutely sure' to be correct and 84% saying the same about a hypothetical negative malaria RDT result. We found similar beliefs across all four treatment arms (online supplemental table 3).

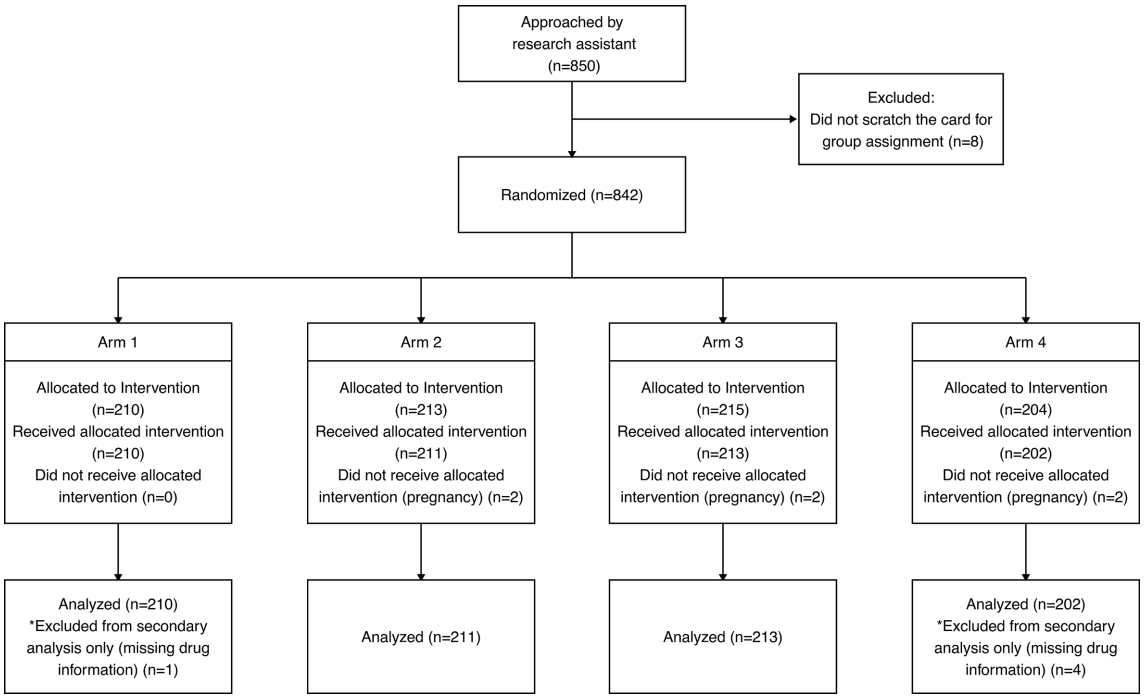


**Figure 1** CONSORT flowchart for flow of individuals through four treatment arms. Arm 1: 50% RDT subsidy and 100% ACT subsidy; Arm 2: 50% RDT subsidy and 67% ACT subsidy. Arm 3: RDT no subsidy and 100% ACT subsidy; Arm 4: RDT no subsidy and 67% ACT subsidy. ACT, artemisinin-combination therapy; RDT, rapid diagnostic test.

### RDT testing

The proportion of participants choosing to pay for an RDT before purchasing medicine was overall very high (97.8%) and similar across the four arms (table 3). The proportion receiving a test was slightly higher in the two arms where an RDT subsidy was provided. Among the tested participants, 21.3% had a positive result. Overall, 85% said that their RDT result was 'very likely/absolutely sure' to be correct (table 2, Panel B) and we found no differences in these beliefs by treatment arm (online supplemental table 3).

Regression results for the effect of treatment arm are summarised in table 4. Regression results for the covariates are summarised in online supplemental table 4 and online supplemental table 5. There was no evidence of a significant interaction effect of RDT and conditional ACT subsidies on the absolute scale with 0.01 Type 1 error rate

**Table 2** Knowledge and beliefs about malaria and RDTs

| (A) Knowledge/Awareness of malaria testing | | | | | |
|---|---|---|---|---|---|
| | % (n) | Obs | | | |
| Know about malaria diagnostic testing (RDT and/or microscopy) | 98.0% (818) | 835 | | | |
| Heard of RDTs | 47.1% (387) | 805 | | | |
| Experience with RDTs | 34.9% (283) | 811 | | | |
| **(B) Beliefs about malaria and testing** | | | | | |
| | Not possible/Unlikely | 50–50 | Likely/Absolutely sure | Don't know | Obs |
| | % (n) | % (n) | % (n) | % (n) | |
| Adult fever is malaria | 5.5% (46) | 26.1% (218) | 54.6% (456) | 13.8% (115) | 835 |
| Own/child illness is malaria | 3.1% (26) | 23.8% (199) | 59.7% (499) | 13.4% (112) | 836 |
| Hypothetical negative RDT result correct | 7.0% (27) | 7.5% (29) | 84.0% (325) | 1.6% (6) | 387 |
| Hypothetical positive RDT result correct | 2.8% (11) | 5.7% (22) | 90.7% (351) | 0.8% (3) | 387 |
| Belief own RDT result correct | 4.7% (38) | 7.6% (62) | 85.1% (693) | 2.6% (21) | 814 |

Beliefs were asked using a 5-point Likert Scale ranging from 'Not Possible' to 'Absolutely sure'. We combined the responses at the two ends of the range so that we have three possible answers: 'Not Possible/Unlikely', '50–50' and 'Likely/Absolutely sure'. Beliefs about a hypothetical negative/positive RDT result being correct were only asked of people who had heard of RDTs.
RDT, rapid diagnostic test.

Table 3 Sample proportions (% (n)) for testing and treatment outcomes and behaviour by treatment arm

| | Arm 1: 50% RDT subsidy and 100% ACT subsidy | Arm 2: 50% RDT subsidy and 67% ACT subsidy | Arm 3: No RDT subsidy and 100% ACT subsidy | Arm 4: No RDT subsidy and 67% ACT subsidy | Total |
|---|---|---|---|---|---|
| | (n=210) | (n=211) | (n=213) | (n=202) | (n=836) |
| RDT uptake | 98.6% (207) | 100.0% (211) | 96.2% (205) | 96.5% (195) | 97.8% (818) |
| Negative | 85.0% (176) | 78.2% (165) | 75.1% (154) | 76.4% (149) | 78.7% (644) |
| No ACT | 94.9% (166) | 93.9% (155) | 93.5% (144) | 91.0% (132) | 93.4% (597) |
| ACT | 5.1% (9) | 6.1% (10) | 6.5% (10) | 9.0% (13) | 6.6% (42) |
| Missing | (1) | (0) | (0) | (4) | (5) |
| Positive | 15.0% (31) | 21.8% (46) | 24.9% (51) | 23.6% (46) | 21.3% (174) |
| No ACT | 22.6% (7) | 13.0% (6) | 7.8% (4) | 15.2% (7) | 13.8% (24) |
| ACT | 77.4% (24) | 87.0% (40) | 92.2% (47) | 84.8% (39) | 86.2% (150) |
| Appropriate ACT use | 92.2% (190) | 92.4% (195) | 93.2% (191) | 89.5% (171) | 91.9% (747) |
| No RDT uptake | 1.4% (3) | 0.0% (0) | 3.8% (8) | 3.5% (7) | 2.2% (18) |
| No ACT | 100.0% (3) | NA | 50.0% (4) | 71.4% (5) | 66.7% (12) |
| ACT | 0.0% (0) | NA | 50.0% (4) | 28.6% (2) | 33.3% (6) |
| Targeted ACT use | 90.9% (190) | 92.4% (195) | 89.7% (191) | 86.4% (171) | 89.9% (747) |

Appropriate ACT=(# of participants taking ACT if positive or not taking ACT if negative)/(# of participants who had an RDT test), excluding the missing ACT behaviours.
Targeted ACT use=(# of participants taking ACT if positive or not taking ACT if negative)/(# of all participants including those without a test), excluding the missing ACT behaviours.
ACT, artemisinin-combination therapy; RDT, rapid diagnostic test.

(estimate: −0.7%; 99% CI −3.6% to 2.3%; table 4). Furthermore, the interaction effect was not significant in any of the fitted models, regardless of scales (absolute or relative) and adjustment for covariates. The RDT subsidy resulted in 2.5 percentage point increase (98% CI 0.2% to 4.8%; table 4) in the proportion of testing uptake after adjusting for the full set of prespecified covariates, averaged across the price levels of ACTs. On the relative scale, testing uptake was 1.025 times higher (98% CI 1.002 to 1.049; table 4) in the RDT subsidised groups than in the unsubsidised groups, averaged across the price levels of ACTs. The conditional ACT subsidy did not affect the RDT test purchasing behaviour (risk ratio: 0.994; 98% CI 0.979 to 1.009; risk difference: −0.6%; 98% CI −2.2% to 0.9%; table 4).

Table 4 Modified Poisson model estimates of the effect of RDT and conditional ACT subsidies on testing uptake on the absolute scale using RDs and on the relative scale using RR

| | | Model | | |
|---|---|---|---|---|
| Predictor | Effect measure | Unadjusted | Adjusted (parsimonious) | Adjusted (full) |
| RDT subsidy | Risk Differences (98% CI) | 2.9% (−0.4% to 6.1%) | 2.5% (−0.5% to 5.5%) | 2.5% (0.2% to 4.8%) |
| | Risk Ratios (98% CI) | 1.030 (0.995 to 1.065) | 1.026 (0.995 to 1.058) | 1.025 (1.002 to 1.049) |
| Conditional ACT subsidy | Risk Differences (98% CI) | −0.9% (−2.4% to 0.6%) | −0.8% (−2.6% to 1.0%) | −0.6% (−2.2% to 0.9%) |
| | Risk Ratios (98% CI) | 0.991 (0.976 to 1.007) | 0.992 (0.974 to 1.010) | 0.994 (0.979 to 1.009) |
| Interaction between RDT and ACT subsidies | Risk Difference (99% CI) | −0.7% (−3.6% to 2.3%) | – | −0.6% (−2.8% to 1.6%) |
| | Risk Ratios (99% CI) | 0.993 (0.964 to 1.024) | – | 0.994 (0.972 to 1.017) |

The reported average main and interaction effects of RDT and conditional ACT subsidies are approximations of risk ratios due to the nature of log link. Unadjusted model included the main effects of the RDT and conditional ACT subsidies and their interaction to match the 2×2 factorial design. Effect coding was used so that main effects of each subsidy level can be interpreted averaged over the levels of the other subsidy. Fully adjusted model includes age (of patient), gender (of patient), education level (of patient or guardian if patient <18 years), occupation (of patient or guardian if patient <18 years), household size, wealth, and main and interaction effects of RDT and conditional ACT subsidies. Only the main effects and wealth was included in the parsimonious model identified by Beaulieu and O'Meara.[26] For main effects, 98% CIs were used and 99% CI for the interaction effect to match the prespecified alpha allocation of 0.02 each for main effects and 0.01 for the interaction effect.
RD, risk difference; RR, risk ratio.

### ACT consumption

93.4% of participants who had a negative RDT result did not purchase an ACT; the proportion was similar in each of the treatment groups (table 3). Eighty-six per cent of the participants who had a positive test result purchased ACT. However, that proportion varied from 77.4% in the arm with both RDT and conditional ACT subsidies to 92.2% in the arm with only conditional ACT subsidy. No clear pattern of ACT consumption among the untested was observed, given only 18 participants did not purchase the RDT test. Appropriate and targeted ACT use are summarised by treatment arm in table 3 and by ACT subsidy level in online supplemental table 6). There is no evidence of an impact of either subsidy level on these outcomes.

## DISCUSSION

With retail outlets being the preferred initial point of care for many fevers in malaria endemic areas, access to parasitological testing is necessary to improve rational use of ACTs. Providing access could improve malaria case management in places like Kenya where RDT testing has not been formally introduced in the retail sector. We find that nearly all clients seeking treatment at a retail outlet were willing to purchase a malaria diagnostic test, even at unsubsidised prices. In addition, we document high adherence to test results among both malaria-positive and malaria-negative clients.

Previous studies of RDT implementation in retail outlets have shown that uptake of testing is, among other factors, sensitive to the relationship between the price of the test and the price of the ACT[21 27 28] As the price of the RDT relative to that of the ACT increases, testing rates drop.[29] The absolute price of the ACT is also important; low ACT prices encourage its uptake even without a test or with a negative test, whereas high ACT prices can encourage the use of other less effective drugs.[21] We tested a targeted ACT subsidy whereby individuals with a positive test had access to a lower price for their ACT. Those without a test or with a negative test were required to pay the higher, market price. This differential pricing of ACTs is likely responsible for the high degree of test adherence in our study, although we did not see a significant difference in adherence between those with a partial ACT subsidy and those receiving a free ACT. We found that, somewhat surprisingly, 11 clients who tested positive for malaria did not take an ACT even when it was made available to them for free. This may be because they preferred other drugs over ACTs.

RDT uptake was higher in our study than in previous studies where clients paid fees for testing. Several factors likely contribute both to uptake of RDTs and adherence to results, including test availability, prior experience with testing, perceived skill and training of the tester and an uninterrupted supply of RDTs and ACTs.[10 30–34] Here, RDTs were supplied by the study, thus ensuring a stable supply. The retail outlets were required to ensure ACT availability as a prerequisite for participation. The intact supply chain may have contributed to the high observed uptake. The extent to which we would find similar results if the outlet retailer performed the RDT likely depends on the relationship between the existing client and the retailer and the extent to which the client trusts the retailers' motives and skills.[35]

We also find very high levels of confidence in RDTs. Previous studies have shown that both health workers and patients have low confidence in RDTs, particularly when the test result is negative.[19 36–43] Our own previous work in western Kenya found that only 35% of people believed a negative malaria test result was 'very likely' to be correct.[44] Clients in this study expressed high confidence in the accuracy of malaria RDTs, both when asked in a hypothetical scenario and when asked about their own RDT result. Furthermore, a significant proportion of respondents (~45%) expressed uncertainty about the cause of fever, indicating a high value of testing in guiding treatment decisions. These results are consistent with our finding that most participants chose to purchase an RDT to confirm their diagnosis. High confidence in their own specific RDT result is in line with the high levels of appropriate ACT use we observed in this study. Our results suggest that public health messaging about the importance of confirming a malaria diagnosis via a test, and about the reliability of RDTs, has been effective in changing people's beliefs and encouraging appropriate treatment behaviours. These changes may allow lower levels of RDT subsidy without compromising uptake. We tested high levels of ACT subsidies given that studies have shown that uptake of ACTs is very sensitive to the price of the drug. By making the subsidy conditional on a positive test result, we ensure that the subsidy is only used for those who need the drug.[27]

The study had several limitations. This was a pilot involving a small number of outlets. Second, the testing was performed by the research team who were stationed at the retail outlets. A scalable model requires the testing be done by the staff at the retail outlets as part of their routine tasks. The study also supplied the RDTs; thus, we could not evaluate the ideal supply chain. Additionally, we investigated only four subsidy levels and did not include an arm with no subsidies, though previous studies have shown that testing levels are not ideal when neither ACTs nor RDTs are not subsidised.[45] Overall, the study demonstrated high uptake of RDT testing in the retail outlets irrespective of the subsidy level, and high ACT targeting, indicating retail sector clients' willingness to pay for testing and to adhere to the test result.

## CONCLUSION

In conclusion, conditional ACT subsidies following a positive RDT may contribute to ACT targeting in the retail sector. However, in this context, high confidence in the accuracy of RDTs along with reliable supplies of RDTs and ACTs, likely also contributed to high testing uptake

and adherence to test results. A larger scale deployment of the strategy, with retail outlets taking responsibility for RDT supply and testing will shed light on the scalability of this approach.

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