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Evaluation of SMS reminder messages for altering treatment adherence and health seeking perceptions among malaria care-seekers in Nigeria

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Abstract

In Nigeria, access to malaria diagnostics may be expanded if drug retailers were allowed to administer malaria rapid diagnostic tests (RDTs). A 2012 pilot intervention showed that short message service (SMS) reminder messages could boost treatment adherence to RDT results by 10–14% points. This study aimed to replicate the SMS intervention in a different population, and additionally test the effect of an expanded message about anticipated RDT access policy change on customers' acceptability for drug retailers' administration of RDTs. One day after being tested with an RDT, participants who purchased malaria treatment from drug shops were randomized to receive (1) a basic SMS reminder repeating the RDT result and appropriate treatment actions, (2) an expanded SMS reminder additionally saying that the 'government might allow pharmacists/chemists to do RDTs' or (3) no SMS reminders (i.e. control). Using regression analysis, we estimate intent-to-treat (ITT) and treatment effects on the treated for 686 study participants. Results corroborate previous findings that a basic SMS reminder increased treatment adherence [odds ratio (OR) = 1.53, 95% CI 0.96–2.44] and decreased use of unnecessary anti-malarials for RDT-negative adults [OR = 0.63, 95% CI 0.39–1.00]. The expanded SMS also increased adherence for adults [OR = 1.42, 95% CI 0.97–2.07], but the effects for sick children differed—the basic SMS did not have any measurable impact on treatment adherence [OR = 0.87, 95% CI 0.24–3.09] or use of unnecessary anti-malarials [OR = 1.27, 95% CI 0.32–1.93], and the expanded SMS actually led to poorer treatment adherence [OR = 0.26, 95% CI 0.10–0.66] and increased use of unnecessary anti-malarials [OR = 4.67, 95% CI 1.76–12.43]. Further, the targeted but neutral message in the expanded SMS lowered acceptance for drug retailers' administration of RDTs [OR = 0.55, 95% CI 0.10–2.93], counter to what we hypothesized. Future SMS interventions should show consistent positive results across populations and be attuned to message length and content before initiating a larger messaging campaign.

Key words: Adherence, child health, diagnosis, drug sellers, essential drugs, evidence-based policy, malaria, rational drug use

Key Messages

- A short message service (SMS) reminder message intervention was successfully replicated among a different population of adults in Nigeria seeking treatment for malaria at drug shops, showing that a basic SMS can increase medication adherence after rapid diagnostic test (RDT) malaria testing and suggesting that the resulting effects may be generalizable among adults.
- The basic SMS reminder intervention had no impact on behaviours for caregivers of sick children, suggesting that small informational reminders may not be effective when strong priors underpinning health behaviours exist. The difference in outcomes for children and adults highlights the importance of replicating behavioural interventions in multiple population segments before being scaled and the need for testing different message content for caregivers of children.
- The targeted, but neutral message in the expanded SMS informing participants of the potential expansion of RDTs at drug vendors actually lowered customer acceptance for pharmacists to conduct RDTs. Hence, small differences in message language, even if seemingly neutral, may have unintended consequences.

Introduction

Increasingly, studies that aim to change health behaviours are relying on small interventions that change the choice environment to accomplish behaviour change (Thaler and Sunstein 2008). These interventions, often broadly referred to as 'nudges', do not alter the decision maker's choice set or incentives, but influence the decision maker's behaviour with momentary cues. Examples of nudges include sending people reminders of appointments, placing information on water consumption near public faucets, and changing the order in which choices are presented. In all of these examples, the intervention is modest, but aims to change the salience of one particular decision outcome relative to the others.

Using randomized control trial (RCT) methodology, a series of recent studies have shown that reminders sent via SMS can encourage people to successfully improve health behaviours. Studies find that SMS-based reminders have led to improvements in applying sunscreen (Armstrong *et al.* 2009), remembering to take diabetes drugs (Vervloet *et al.* 2012), following HIV treatment regimens (Pop-Eleches et al. 2011), adhering to asthma treatment (Strandbygaard *et al.* 2010) and birth control pills (Castano *et al.* 2012), getting vaccinated (Stockwell *et al.* 2014), losing weight (Bouhaider *et al.* 2013) and quitting smoking (Whittaker *et al.* 2009). Because the health benefits of such behaviours may accrue well into the future, individuals may fail to follow through on intentions in the present, whether due to lack of attentiveness (Banerjee and Mullainathan 2008; Datta and Mullainathan 2014) or a bias towards alternative choices that may offer more immediate gratification (Strotz 1955; Ainslie 1975; Ainslie 1991; Hoch and Loewenstein 1991; Laibson 1997). Thus, message reminders, when timed correctly, may elevate the saliency of the decision above other distractions, and, depending on the content, may further indicate what the optimal choice should be.

However, there is growing concern that some of the results of the RCTs lack external validity and may not necessarily be replicable across settings, particularly in light of growing evidence that small differences in message timing and content result in different behavioural outcomes (Sanson-Fisher et al. 2007; Pop-Eleches et al. 2011; Science Exchange 2014). In addition, because behaviour change studies recruit people drawn from distinct populations (either by design or through selection), there is greater need to consider the influence of unobservable study population characteristics and possible heterogeneity in the pathways through which behavioural interventions may be working.

Recognizing the importance of replicability and concerns over the external validity of RCT interventions, we attempt to replicate a previous study focusing on malaria diagnosis and treatment, which examined patients' use of artemisinin-based combination therapy (ACTs) after having been given a malaria rapid diagnostic test (RDT) when purchasing anti-malarial treatments at retail drug shops in Nigeria (Modrek *et al.* 2014). The previous study took place in an urban and peri-urban area in Oyo State, among the wealthiest and most educated states in Nigeria (Nigeria and ICF International 2012), and included only adults. The results suggested that sending a SMS reminder regarding a person's diagnostic test result improved adherence to the recommend treatment course by 10–15% points. The study also documented that customers preferred RDTs to be made available at hospitals and clinics, but not at drug retailers, such as patent and proprietary medicine vendors (PPMVs, colloquially referred to as 'chemists') or pharmacies. In particular, when participants were asked which places could be trusted to provide RDTs, the overwhelming majority (77%) indicated hospitals or clinics, followed by diagnostic laboratories (18%); only 4% trusted pharmacies and 1% named PPMVs (Isiguzo *et al.* 2014).

However, the extent of over- and mis-treatment of malaria in Nigeria (Uzochukwu *et al.* 2014; Isiguzo *et al.* 2014) has prompted policymakers in to consider expanding access to malaria diagnostics by allowing drug retailers to administer RDTs as part of new guidelines for integrated management of paediatric illnesses (Ministry of Health 2012; WHO and UNICEF 2012) and malaria (NMCP 2011). Drug retailers are particularly important for increasing access (Beyeler *et al.* 2015) as 77% of fever episodes among children (NPC and ICF International 2013) and 35–55% of adults seeking malaria treatment (Uguru *et al.* 2009; Onwujekwe et al 2011) first seek care at these types of shops. However, demand for diagnosis is also low as very few individuals seek testing before purchasing anti-malaria drugs (Isiguzo *et al.* 2014; Liu *et al.* 2015; Prach *et al.* 2015). Thus, message reminders for malaria treatment adherence after RDT diagnosis were first developed to reinforce behaviour change (i.e. away from presumptive treatment) and appropriate treatment behaviours in accordance with the diagnostic result (Modrek *et al.* 2014). Further, given the policy consideration, understanding the acceptability of RDTs given by drug retailers is another important outcome that could be shaped by appropriate messaging.

To further understand how reminder messages could be used to change presumptive treatment behaviours and improve treatment adherence for malaria, we conducted an intervention trial testing

different reminder messages as part of a larger study of malaria diagnosis and treatment at privately owned pharmacy and PPMVs conducted in Nasarawa State, Nigeria (see Liu *et al.* 2015). This study was designed to directly build on our previous study in Oyo State (Isiguzo *et al.* 2014, Modrek *et al.* 2014) in three specific ways: (1) replicate the SMS reminder intervention that was piloted within a specific urban, adult population in a more generalizable setting (including rural areas), (2) expand the study population to include children and (3) test the effect of expanded message content that adds language about anticipated policy change for RDT availability on customers' acceptance of drug retailers' administration of RDTs. The overarching objective was to identify message content and frames that would both encourage treatment adherence across the general population and increase awareness of RDT diagnostic capabilities among frequented drug shop vendors in anticipation of policy change.

Methods

Study area and sample selection

The study was conducted in the Karu Local Government Area of Nasarawa State in the North Central geopolitical zone of Nigeria. Located along the main road from the adjacent capital city, Abuja, the string of communities in Karu are densely populated and growing fast due to a commercial scene that attracts many migrants, surrounded by rural agricultural areas (UN-Habitat 2012).

In August–September 2013, all drug shops in Karu were enumerated, producing a complete listing of 747 shops: 569 PPMVs and 178 pharmacies. A description of the selection criteria for choosing shops for inclusion into the study is published elsewhere (Liu *et al.* 2015). Briefly, 117 shops from the list were purposively selected to participate in the study based on antimalarial drug stocking information collected during enumeration and in-person visits to shops during peak business hours (typically 3–8 pm) that indicated higher volumes of customers seeking treatment for malaria. Two shops declined to participate.

From October to December 2013, 741 participants were enrolled at 91 drug shops (37 pharmacies and 54 PPMVs) acting as recruitment sites. A survey researcher trained on interviewing techniques and performing RDTs approached customers as they exited the drug store and enrolled willing, non-pregnant adults that had just purchased malaria treatment for him- or herself or an accompanying sick child (child must have been present at the time). While seeking written consent (assent for adolescents), the participant or caregiver of a sick child was informed that if they qualified, they or the sick child would be offered an RDT and would be compensated for their time with a small mobile phone credit of 200 Naira (~US$1.20) for participating in the interview. Customers meeting the eligibility criteria were not found at the remaining 24 shops participating as recruitment sites (7 pharmacies, 17 PPMVs) on the days that surveyors were posted there.

Customer survey

Two surveys were conducted: one at the time of enrolment and testing (baseline) and one 4 days after the initial encounter via telephone (follow-up). At baseline, the eligible and enrolled participant was offered a RDT. Regardless of agreement to have a RDT administered, all participants were interviewed using a standard survey instrument that captured background sociodemographics, symptoms experienced and care-seeking actions taken for the current episode of suspected malaria; modules relating to perceptions of RDTs were skipped for those participants ($n = 2$) who did not agree to have an RDT administered.

Towards the end of the survey, the participant was provided with the result of his or her test and was also given standard treatment advice according to their RDT result. If the participant tested positive for malaria, he/she was told that the positive result suggested the presence of malaria and that an anti-malarial drug should be taken. To ensure that RDT-positive individuals had a quality-assured anti-malarial drug, a course of ACTs was provided for free and participants were instructed to take it according to dosing instructions, and to save the anti-malarials that they had just purchased at the shop for their next episode of suspected malaria. If the RDT test was negative, the participant was told that the negative result indicated the absence of malaria and that the anti-malarial drugs they purchased were not needed. Regardless of the test result, all participants were referred to local clinics and hospitals where they could seek care if their condition was not malaria, or if their illness became worse.

After being given their test result and treatment instructions, participants were asked a series of questions regarding their perceptions of the RDT experience. This included asking two questions about participants' agreement about who the government should allow to conduct RDTs: respondents could answer 'yes' or 'no' to (1) 'Should the government allow chemists to do the malaria RDT for people?' and (2) 'Should the government allow pharmacists to do the malaria RDT for people?'

At the conclusion of the baseline interview, contact information was collected to facilitate later follow-up. All participants were told to expect a short 5–10 min follow-up phone call in 4 days to check on their illness status and that they would be compensated with a small phone credit of 100 Naira (~US$0.60) for taking the call.

Four days after the baseline survey, an interviewer called participants and conducted a phone survey to obtain information on the state of their health and the drugs they had used. Participants were asked a series of questions about each drug recorded at baseline: whether or not s/he had taken any of the drug, when s/he began taking it, whether or not the entire dose was completed, and if not completed, reason for not completing the dosage regimen. Questions regarding perceptions of the RDT experience were asked again verbatim.

SMS reminders

One day after having a RDT administered, participants in the overarching RDT acceptability study were randomized to either (1) receive a basic SMS reminder repeating the RDT result and appropriate treatment actions as had been done in the prior Oyo State study (see Modrek *et al.* 2014), (2) receive an expanded SMS reminder that additionally indicated that the 'government might allow pharmacists/chemists to do RDTs' or (3) a control arm that did not receive any SMS reminders. A 1-day lag was chosen to coincide with when most individuals would be taking the second dose of their anti-malarial drug if they had followed proper dosage instructions. At this point, individuals suffering from malaria may be feeling better as a result of the first dose and may stop taking additional doses. Thus, the message timing was primarily aimed at encouraging RDT-positive individual to complete the full treatment course, and secondarily to reinforce to RDT-negative individuals that they should not be taking any anti-malarials. For participants in the two intervention arms, the messages were RDT result-specific, as outlined in Table 1. The same message was sent to each participant once in English and once in Hausa (the dominant language for the local tribal groups). The basic content of the message repeated the advice given by the study surveyor at the time of testing and was meant to be purely informational. In the second expanded SMS intervention arm, an additional sentence about the policy change

Table 1. SMS reminders

Intervention arm	RDT-positive	RDT-negative
Basic SMS	*RDTs confirm malaria status. Your RDT was POSITIVE. Please take Coartem.*	*RDTs confirm malaria status. Your RDT was NEGATIVE. Do not take malaria drugs.*
Expanded SMS	*RDTs confirm malaria status. Government might allow pharmacists/chemists to do RDTs. Your test was POSITIVE. Please take Coartem.*	*RDTs confirm malaria status. Government might allow pharmacists/chemists to do RDTs. Your RDT was NEGATIVE. Do not take malaria drugs.*

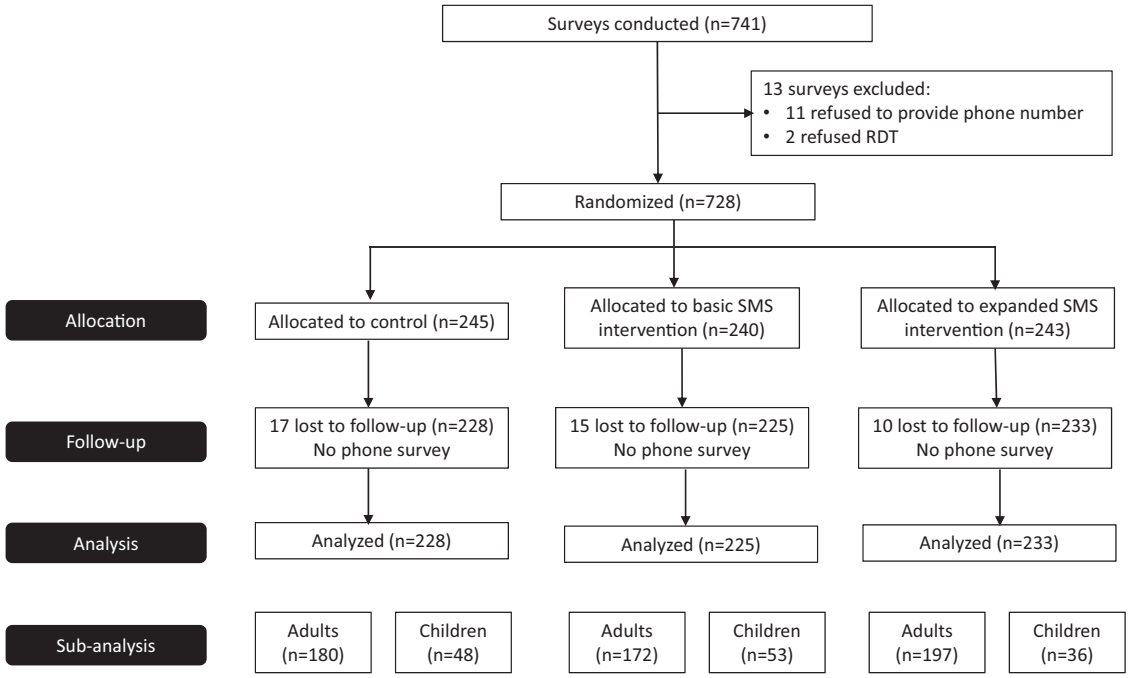

Figure 1. Data exclusion flow diagram

under consideration was added, 'Government might allow pharmacists/chemists to do RDTs'. The addition of this phrase was motivated by findings from our previous pilot study in Oyo State which found that few respondents trusted pharmacies and PPMVs to provide RDTs, but overwhelmingly trusted hospitals and clinics (Isiguzo *et al.* 2014). This phrase was developed in consultation with local research staff and experts at a social marketing non-governmental organization specializing in health promotion who advised that the content was legally accurate and that the mention of 'government' had neither a negative nor a positive connotation. The phrase was also pre-tested in different languages to ensure accuracy of translation.

To ensure that none of the survey staff would know which participants were chosen to receive the SMS, the study manager, who did not have any interaction with participants, randomly assigned surveys into the treatment groups after the surveys were returned to the study office each day. The protocol for treatment assignment entailed assigning consecutive surveys to one of the intervention or control arms on the day of the baseline survey, replicating the randomization procedure from the previous study (Modrek *et al.* 2014).

Participants

Figure 1 shows the number of participants who were enrolled, randomized and followed-up through the SMS intervention. Of 741 enrolled participants, all of whom completed the baseline survey, 13 participants were excluded from the analysis either because they did not provide a phone number ($n = 11$) or refused to allow a RDT to be administered ($n = 2$). The remaining 728 participants were randomized to one of three arms. A total of 686 (94.2%) participants were followed-up for the phone survey, which includes 549 (80.0%) adults and 137 (20.0%) children under the age of 18.

Based on the results of the 2012 study conducted in Oyo State (Modrek *et al.* 2014), the sample size was chosen to have 80% power to detect a 14.3% point difference in treatment adherence with a two-tailed significance test and 95% confidence.

Outcome measures

We examined four outcomes as a result of the SMS intervention:

1. Followed treatment advice (i.e. complied with the RDT result): Coded as 1 for either RDT-negative participants who reported not taking any anti-malarial drugs or RDT-positive participants who reported that they took an anti-malarial drug.[1]
2. Took anti-malarial drug (i.e. did not comply with the RDT result): Restricted to participants who were RDT-negative, and coded as 1 if an anti-malarial drug was taken.
3. Took symptom drug: Coded as 1 if a non-anti-malarial drug purchased to treat symptoms (i.e. 'symptom drug') was taken, restricted to those that had purchased a symptom drug. Because the SMS reminders entailed only instructions for anti-malarial drugs and not other types of drugs that may have been

purchased for symptomatic relief, this measure is included to assess the validity and specificity of the participant response to the message content.

4. Increased agreement that chemists or pharmacists 'should be allowed to do RDTs': Coded as 1 if the participant changed from disagreement at baseline to agreement during follow-up for either question about chemists or pharmacists.

Statistical analysis

Descriptive analyses compared sample characteristics between intervention groups to assess the randomization across arms.

For each of the outcomes (1–4), we then estimate an ITT effect of the different SMS reminders first without any controls, and then adjusted for observable characteristics that were not balanced across groups after randomization. We assess any differential effects of the SMS reminders between sick adults treating him- or herself and sick children (under 18 years of age) under the care of someone else. This is operationalized as an interaction of the intervention group indicator with an indicator for the participant being a sick child. Lastly, we estimate the 'treatment effect on the treated' for the full sample by excluding individuals or caregivers in the intervention arms who were supposed to have received the SMS, but reported that they did not read it. This last analysis fully adjusts for any differences in observable characteristics resulting from the sample restriction (i.e. between those who did and did not read the SMS). All analyses for binary outcomes were estimated using logistic regressions with standard errors clustered by recruitment site to account for potential autocorrelation amongst customers attending the same site.

Ethical approval

Ethical approval was obtained from the first author's institute and corresponding agency in Nigeria. This trial is registered under ISRCTN12605216.

Results

Sample characteristics

The sample characteristics measured at baseline for each of the intervention arms are summarized in Table 2. The intervention and control groups were substantially different in terms of marital status. Nearly 70% ($n = 158$) of participants in the control group were married, compared with only 58.9% ($n = 133$) and 58.4% ($n = 136$) among the general SMS and expanded SMS arms. We control for marital status to adjust for this difference in all subsequent analyses. Between 14.9% ($n = 34$) and 18.9% ($n = 44$) of participants were RDT-positive across arms, and this was not statistically significantly different.

ITT effects

Estimates of the 'ITT' effect for all outcomes are similar between model specifications that do (regression-adjusted) and do not (unadjusted) control for unbalanced covariates, and statistical significant levels do not substantively change (see Table 3).

For the first outcome of following the treatment advice, regression-adjusted estimates (controls for unbalanced sample covariates, i.e. marital status), there is some evidence that participants who received the basic SMS were more likely to follow the correct treatment advice [OR = 1.490, 95% CI 0.963–2.306, $P = 0.074$] compared with the control group (a relative risk of 9.3%).

Table 2. Sample characteristics at baseline by study arm

Variable	Control		Intervention			
	$N = 228$		Basic SMS $N = 225$		Expanded SMS $N = 233$	
	Mean	CI	Mean	CI	Mean	CI
Age (in years)	33.579	(32.266–34.892)	32.804	(31.561–34.048)	31.854	(30.649–33.059)
Male	0.557	(0.49–0.623)	0.621	(0.553–0.684)	0.545	(0.479–0.61)
Married	0.695	(0.63–0.754)	0.589	(0.522–0.654)	0.584	(0.518–0.649)
Education						
Less than primary	0.044	(0.021–0.079)	0.053	(0.028–0.091)	0.039	(0.018–0.073)
Primary	0.162	(0.117–0.217)	0.124	(0.084–0.175)	0.147	(0.104–0.2)
Secondary	0.439	(0.373–0.506)	0.449	(0.383–0.516)	0.442	(0.376–0.508)
More than secondary	0.355	(0.293–0.421)	0.373	(0.31–0.44)	0.372	(0.31–0.438)
Muslim	0.132	(0.091–0.182)	0.156	(0.111–0.211)	0.159	(0.114–0.212)
Currently employed	0.706	(0.642–0.764)	0.693	(0.629–0.753)	0.670	(0.605–0.73)
Buying for a sick child	0.211	(0.159–0.269)	0.236	(0.182–0.297)	0.155	(0.111–0.207)
Sick child is male	0.610	(0.543–0.673)	0.652	(0.585–0.714)	0.608	(0.542–0.671)
Shop location						
Urban	0.399	(0.335–0.466)	0.422	(0.357–0.49)	0.472	(0.407–0.538)
Peri-urban	0.417	(0.352–0.484)	0.396	(0.331–0.463)	0.326	(0.266–0.39)
Rural	0.184	(0.136–0.241)	0.182	(0.134–0.239)	0.202	(0.152–0.259)
Chemist (ref: pharmacy)	0.531	(0.464–0.597)	0.524	(0.457–0.591)	0.545	(0.479–0.61)
Wealth						
Poorest	0.175	(0.128–0.231)	0.178	(0.13–0.234)	0.193	(0.144–0.25)
Poorer	0.202	(0.152–0.26)	0.196	(0.146–0.253)	0.206	(0.156–0.264)
Middle	0.232	(0.179–0.293)	0.196	(0.146–0.253)	0.202	(0.152–0.259)
Richer	0.197	(0.148–0.255)	0.227	(0.174–0.287)	0.185	(0.137–0.24)
Richest	0.193	(0.144–0.25)	0.204	(0.154–0.263)	0.215	(0.164–0.273)
RDT-positive	0.149	(0.106–0.202)	0.156	(0.111–0.21)	0.189	(0.141–0.245)

95% confidence intervals (CI) in parentheses.

Table 3. Estimated effect of the intervention's 'ITT'

Outcome			Unadjusted			Adjusted				
Study arm	*n*/*N*	%	OR	(95% CI)	*P* value	OR	(95% CI)	*P* value	Pr(Y = 1)	(95% CI)
Followed treatment advice										
Control	170/228	74.6	1.000			1.000			0.740	(0.680–0.801)
Basic SMS	182/225	80.9	1.444	(0.941–2.216)	0.093	1.490	(0.963–2.306)	0.074	0.809	(0.764–0.855)
Expanded SMS	176/233	75.6	1.053	(0.747–1.486)	0.767	1.107	(0.781–1.568)	0.569	0.759	(0.715–0.804)
Took anti-malaria drug[a]										
Control	58/194	36.9	1.000			1.000			0.306	(0.236–0.376)
Basic SMS	43/190	27.4	0.686	(0.440–1.068)	0.095	0.662	(0.422–1.040)	0.073	0.226	(0.173–0.280)
Expanded SMS	56/189	35.7	0.987	(0.677–1.439)	0.947	0.928	(0.632–1.362)	0.701	0.290	(0.235–0.345)
Took symptom drug										
Control	92/104	88.5	1.000			1.000			0.884	(0.817–0.952)
Basic SMS	93/106	87.7	0.933	(0.381–2.285)	0.880	0.931	(0.373–2.325)	0.879	0.877	(0.820–0.934)
Expanded SMS	98/107	91.6	1.420	(0.561–3.594)	0.459	1.411	(0.558–3.564)	0.467	0.915	(0.865–0.965)
Increased agreement that PPMVs or pharmacist "should be allowed to do RDTs"										
Control	30/215	12.0	1.000			1.000			0.139	(0.077–0.202)
Basic SMS	22/209	7.7	0.725	(0.389–1.353)	0.313	0.735	(0.389–1.388)	0.342	0.106	(0.061–0.152)
Expanded SMS	18/220	4.7	0.550	(0.292–1.034)	0.063	0.559	(0.293–1.067)	0.078	0.083	(0.048–0.118)

95% confidence intervals (CI) in parentheses. All standard errors are clustered by recruitment site.

[a]Restricted to RDT-negative participants.

Participants sent the expanded SMS were also slightly more likely to take the correct treatment, but this was not statistically different than the control group [OR = 1.107, 95% CI 0.781–1.568, $P = 0.569$]. The corresponding estimated probabilities for following the treatment advice according to the RDT result was 80.9% for the basic SMS group and 75.9% for the expanded SMS group compared with 74.0% in the control group.

When restricted to only those who were RDT-negative (Outcome 2), there is some evidence that participants sent the basic SMS were less likely to take an anti-malarial drug [OR = 0.662, 95% CI 0.422–1.040, $P = 0.073$] compared with the control group.

There were no differences detected for Outcome 3, taking drugs for symptomatic relief resulting from either the basic [OR = 0.931, 95% CI 0.373–2.325, $P = 0.879$] or expanded SMS [OR = 1.411, 95% CI 0.558–3.564, $P = 0.467$] message when regression-adjusted.

For Outcome 4, participants sent the expanded SMS message were less likely to increase agreement for chemists or pharmacists to administer RDTs compared with the control group [OR = 0.550, 95% CI 0.292–1.034, $P = 0.078$]; no effect was found for the basic SMS.

Heterogeneous ITT effects between children and adults

Estimated ITT effects are different for sick children compared with adults (summarized in Table 4). When including an interaction term between intervention group and an indicator for the sick person being a child, the effects of both types of SMS reminders reduced the likelihood of following the treatment advice (Outcome 1, Column 1). While the interaction estimate for the basic SMS is negative and not statistically significant [OR = 1.474, 95% CI 0.675–3.219, $P = 0.829$], the effect of the expanded SMS for children indicates that caregivers were much less likely to follow the treatment advice for sick children [OR = 0.262, 95% CI 0.104–0.661, $P = 0.005$] compared with adults treating themselves. For adults, the expanded SMS increased the likelihood of following the treatment advice by an amount [OR = 1.418, 95% CI 0.973–2.066, $P = 0.069$] that is similar to the estimated effect for adults for the basic SMS [OR = 1.528, 95% CI 0.959–2.435, $P = 0.074$]. Adults who received the basic SMS or the expanded SMS were more likely to follow the correct treatment advice [OR = 1.47, 95% CI 1.026–2.101, $P = 0.036$; combined SMS results not shown in tables].

Similarly, when restricted to only RDT-negative participants (Outcome 2, Column 2), the odds of being given an anti-malarial drug was over four times higher for sick children in the expanded SMS group compared with all others [OR = 4.670, 95% CI 1.755–12.432, $P = 0.002$].

No differences between adults and children were detected in taking drugs for symptomatic relief (Outcome 3, Column 3) or for increased agreement for chemists or pharmacists to do RDTs (Outcome 4, Column 4).

These estimated differences in treatment outcomes between sick adults and children are graphically displayed in Figure 2, which shows the resulting predicted probabilities from ITT regression estimates. Children in the expanded SMS group were only ~59% likely to be given the correct treatment according to the RDT result compared with 80% or more among the children in the basic SMS and control groups. These differences are largely driven by the 57% likelihood of RDT-negative children within the expanded SMS arm to still be given an anti-malarial than RDT-negative children in other groups. Among adults, participants in both intervention arms were ~80% likely to follow the correct treatment compared with only ~73% among the control group.

Treatment effect on the treated

Table 5 presents the estimate of the treatment effect on the treated when the sample is restricted to only participants or caregivers who reported reading the SMS ($n = 453$; 66.5% of the full sample). Note that all regressions control for marital status, education, religion, employment status and recruitment shop type, characteristics that were significantly different between participants who did and did not read the SMS as additional precaution for sources of confounding. Overall, estimated effects of the SMS reminders increased in magnitude. Participants reading both the basic [OR = 2.215, 95% CI 1.313–3.736, $P = 0.003$] and expanded [OR = 1.733, 95% CI 1.058–2.840, $P = 0.029$] SMS were more likely to follow the treatment advice (Outcome 1) compared with the control group.

Table 4. Estimated 'ITT' effects for adults and children

	(1) Followed treatment advice	(2) Took anti-malaria drug[a]	(3) Took symptom drug	(4) Increased agreement that PPMVs or pharmacists "should be allowed to do RDTs"
Control (reference)	1.000	1.000	1.000	1.000
Basic SMS	1.528	0.627	0.962	0.863
	(0.959–2.435)	(0.392–1.001)	(0.368–2.514)	(0.425–1.752)
	[0.074]	[0.051]	[0.936]	[0.684]
Expanded SMS	1.418	0.728	1.215	0.615
	(0.973–2.066)	(0.485–1.093)	(0.461–3.199)	(0.296–1.278)
	[0.069]	[0.126]	[0.694]	[0.193]
Adult (reference)	1.000	1.000	1.000	1.000
Child	1.474	0.874	3.138	1.084
	(0.675–3.219)	(0.396–1.931)	(0.360–27.387)	(0.477–2.463)
	[0.330]	[0.739]	[0.301]	[0.848]
Basic SMS × Child	0.870	1.272	0.535	0.443
	(0.244–3.093)	(0.319–5.073)	(0.035–8.274)	(0.091–2.153)
	[0.829]	[0.733]	[0.654]	[0.313]
Expanded SMS × Child	0.262	4.670		0.551
	(0.104–0.661)	(1.755–12.432)		(0.104–2.932)
	[0.005]	[0.002]		[0.485]
Observations	681	569	292	639

95% confidence intervals (CI) in parentheses; *P*-values in brackets. All regressions control for marital status; standard errors are clustered by recruitment site.
[a]Restricted to RDT-negative participants.

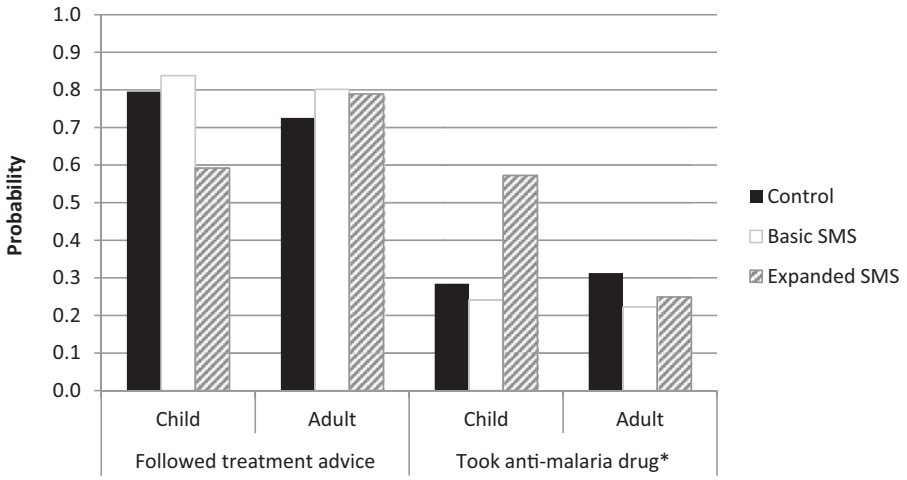

Figure 2. Predicted probabilities for treatment outcomes by study arm. *Restricted to RDT-negative participants.

This corresponds to a lower likelihood of taking anti-malarial drugs among RDT-negative participants (Outcome 2) for the basic SMS group [OR = 0.427, 95% CI 0.249–0.732, $P = 0.002$] and for the expanded SMS group [OR = 0.589, 95% CI 0.347–1.002, $P = 0.051$].

Estimated effects of SMS reminder messages on taking drugs for symptomatic relief (Outcome 3) and increasing agreement for chemists or pharmacists to administer were not significantly different.

Discussion

In this study, we replicate a previous RCT intervention for reinforcing proper malaria treatment behaviour and find that a SMS reminder is again effective in increasing adherence to RDT results (Outcomes 1 and 2) and decreasing use of unnecessary ACTs for RDT-negative adults (Outcome 3). The basic SMS was directly aimed at replicating our previous findings in a more representative area and in a sample that included children. First, among adults, the previous study found a 10–14% point increase in treatment adherence in Oyo State as a result of the basic SMS, with higher differences estimated when the off-protocol timing of the message was controlled for (Modrek et al 2014). However, in this study, the effect of the basic SMS among adults was only a 7.6 % point increase in treatment adherence (see Figure 1), a smaller effect size that, relative to the sample size, renders this study somewhat underpowered, but nonetheless shows a directionality that is consistent with previous results. Further, this estimate effect size is similar to the overall effect sizes measured by Raifman *et al.* (2014) in a similar text message reminder trial for antimalarial treatment adherence in Ghana.

We also find that the text message that included more information on intended government expansions of availability of RDTs for commonly accessed drug retailers increased adherence to RDT

Table 5. Estimated "treatment effect on the treated"

	(1) Followed treatment advice	(2) Took anti-malaria drug[a]	(3) Took symptom drug	(4) Increased agreement that PPMVs or pharmacists "should be allowed to do RDTs"
Control (reference)	1.000	1.000	1.000	1.000
Basic SMS	2.215	0.427	1.718	0.713
	(1.313–3.736)	(0.249–0.732)	(0.383–7.698)	(0.313–1.624)
	[0.003]	[0.002]	[0.480]	[0.420]
Expanded SMS	1.733	0.589	1.470	0.526
	(1.058–2.840)	(0.347–1.002)	(0.342–6.317)	(0.233–1.188)
	[0.029]	[0.051]	[0.605]	[0.122]
Observations	453	389	203	422

95% confidence intervals (CI) in parentheses; *P*-values in brackets. All regressions control for marital status, education, religion, employment status, and recruitment shop type; standard errors are clustered by recruitment site.

[a]Restricted to RDT-negative participants.

results for adults by the same amount as the basic SMS. In other words, the additional message content did not have any differential impact on treatment behaviour over the shorter message, but resulted in better adherence compared with those who did not receive any reminder among adults. Further, neither the basic nor expanded text message had an effect on non-antimalarial drug treatment behaviour (Outcome 3), indicating that the message subject focusing on anti-malarial drugs was appropriately targeted. However, these results contrast with the findings by Raifman *et al.* (2014) and for studies of antiretroviral treatment adherence for HIV (Pop-Eleches *et al.* 2011) in which longer messages resulted in no effect at all. The difference in results related to message length may be due to differences in the number of times the messages were repeated. In our study, the reminder message was only sent at one point in time, whereas the messages in Raifman *et al.* (2014) were sent every 12 h. This suggests that message fatigue, in addition to timing and content, may be an important consideration and should be explored when designing automated message reminders.

Our results were very different for sick children—the basic SMS had essentially no impact on adherence to RDT results or use of unnecessary ACTs, and the expanded SMS actually led to poorer adherence to RDT results with a substantial increase in use of unnecessary ACTs. This unexpected result highlights the importance of testing message content on different target audiences as perceptions may vastly differ and result in unintended effects. While the expanded SMS message content was aimed at influencing perceptions of drug retailers for providing a new service—performing malaria diagnostics—it adversely affected treatment behaviour among caregivers. Meanwhile, perceptions of drug retailers administering RDTs (Outcome 4) actually declined.

We posit several different possible explanations for the different responses in treatment adherence to the SMS messages between children and adults, which have also recently been shown in a similar trial conducted in Ghana (Raifman *et al.* 2014). First, this difference may result from a higher perceived severity of malaria in children and differences in care-seeking behaviour for oneself compared with a sick child. Children have a much higher risk of contracting malaria (Warrell and Gilles 2002), have longer durations of sickness that may require care (Warrell and Gilles 2002), and have a much higher case fatality rate than adults (WHO 2013). Given the seriousness of a child malaria case, there may be more reluctance and scepticism to change behaviour based on a single interaction with a new technology, the RDT, and a simple SMS reminder. Previous analysis of care-seeking behaviour in this study population showed that caregivers of sick children were more likely to obtain a prescription prior to attending a drug retailer, wait less time before seeking care, to have been asked about symptoms by the retailer, to have their child be given an examination, and to have purchased an ACT compared with sick adults seeking care for themselves (Liu *et al.* 2015). Elsewhere in North Central Nigeria, caregivers of sick children who are brought to drug shops are also more likely to have a discussion about the illness with the retailer, have an exam conducted on the child, and spend more money on drug purchases than adults seeking care for themselves (Prach *et al.* 2015).

Second, the overall greater concern for sick children, coupled with caregivers' prior beliefs about the necessity and urgency to treat malaria in children, directly contradict the RDT information on malaria status for children testing negative. Reinforcing negative results and directions to not treat the child with a short text message may not have been enough to overcome default behavioural impulses. Further, the expanded SMS message, while intended to be neutral and informative, may have instead heightened caregivers' caution towards treating malaria in children, for which formal clinical care is recommended.

Third, the reverse effect on treatment adherence for children may be related to the absence of directions for alternative treatment options for children who were RDT-negative. Caregivers may feel it necessary to give a sick child some treatment, even if it may be the incorrect treatment, over no treatment at all. Although the SMS message recommended caregivers to seek care at referral hospitals, it did not specify a different treatment course for non-malaria cases. The importance of having alternative treatments is highlighted by the current focus on implemented integrated community case management of childhood illnesses (iCCM) that specifies a more complete decision tree for diagnosing febrile illnesses, including treatment for malaria, diarrhoea, and pneumonia (WHO and UNICEF 2012). Thus, while we show positive effects of the SMS interventions for adults, such simple interventions may not be as effective for sick children for whom diagnosis and treatment may be more complex and have greater associated risks for incorrect treatment.

A priori we expected that the direct experience with and the demonstration of the ease and simplicity of RDTs would make participants more likely to accept RDTs in drug retail shops (Outcome 4). However, we found no effect of the basic SMS on changes in the acceptability of either chemists or pharmacists in administering RDTs. The targeted, but neutral message in the expanded SMS informing participants of the potential expansion of RDT availability

had the opposite effect of what we expected: the effect of the expanded message actually lowered the likelihood of acceptance for chemists and pharmacists to administer RDTs. These results suggest that small differences in message language and content may trigger different perceptions and result in unintended consequences for associated behaviours, and that greater attention to message content is needed.

The reverse effect associated with the expanded message may be related to obtaining conflicting advice between the pharmacist/chemist and the RDT results given by the study surveyor. Rather than providing information on potential expanded health services offered by drug retailers to perform malaria diagnosis, the message may have instead served as an indictment of the relatively poorer quality of malaria care provided by retailers (Beyeler *et al.* 2015). Our recruitment strategy enrolled people who had just purchased an anti-malarial drug, among which most of these adults (83%) tested negative for malaria. Therefore, the text message may have reminded participants that the drug retailer had given them the wrong diagnosis and treatment advice in the first place.

These results should be interpreted in light of several caveats. Adherence to treatment advice is a self-reported measure; some social desirability reporting bias may be present if the SMS message also prompted individuals to self-report 'better' outcomes. This may be particularly the case for estimates of the treatment effect on the treated, which additionally relies on participants' reports of reading the text message. To the extent that the SMS message increased reporting bias, the intervention effect size could be overestimated. However, because results for malaria drugs and non-malaria drugs showed differential drug-taking behaviour, we suspect that such self-reporting bias may be minimal. Care-seeking and treatment behaviour among populations in North Central Nigeria may also not necessarily be representative of health behaviours in other parts of the country, even though results of the basic SMS intervention were able to be replicated for adults. Further examination of the replicability of the intervention for caregivers of children is warranted with a larger sample size. Due to the smaller overall effect size detected, and the differential effects among children, this study was underpowered for the primary outcome; where there was weak statistical evidence for a significant effect, the differences could have arisen by chance. However, finding that the directionality of the basic SMS intervention was consistent with our previous, sufficiently powered study lends some confidence that an effect exists under a unidirectional alternative hypothesis. Lastly, while we suggest plausible explanations for the observed intervention effects of the expanded SMS, more in-depth data on participants' perceptions of the drug retailers, the contradictions resulting from the RDT diagnosis, and the content of the SMS is needed to disentangle the intervening pathways and inform the design of mass messaging that may accompany any policy change in RDT availability at retail drug shops.

In light of the growing body of evidence of their effectiveness, researchers are trying to use simple nudge devices to change a broad set of health and healthcare goals, including health-seeking behaviour. While the design of this intervention may not necessarily mimic how RDTs and accompanying text message reminders may be implemented in reality—regulations in Nigeria currently prohibit drug retailers from selling and performing RDTs themselves—our results (1) support the large body of evidence showing that increasing access to malaria diagnosis at drug retailers is necessary to improve the quality of malaria treatment (Mbonye *et al.* 2015; Visser *et al.* 2015), and (2) suggest that, automated text message reminders can be effective for improving treatment adherence. In fact, many public health initiatives targeted towards behaviour change now incorporate mHealth components as standard practice, ranging from HIV adherence to contraception, some of which are being delivered by frontline community-based health workers (WHO and UNICEF 2012; Källander *et al.* 2013).

Together, the results of this study and our previous pilot in Oyo State (Modrek *et al.* 2014) also indicate that the timing, content and frequency of messages should be carefully crafted and tested on different populations before being deployed, especially for messages that may contain more than one type of communiqué. Differential effects among children also indicate that more consideration of how messages are perceived by caregivers is needed—whether separate messages are needed or whether overall messages need to be adjusted to resonate with this population. When drug retailers in Nigeria are allowed to sell and administer RDTs, then additional consideration may be given to instituting an automated text message reminder system for individuals purchasing a RDT and/or antimalarials, whether through user self-subscription or provider-assisted enrolment. The feasibility of such a subscription-based opt-in message reminder system has been demonstrated elsewhere (Raifman *et al.* 2014). Regardless, future messaging interventions should show consistent positive results across populations before initiating a broader campaign.

Note

1. About 97% of respondents who self-reported taking any of the anti-malarial drug reported that they had or were nearly finished with the complete course; 2.7% reported that they had stopped taking the drug because they were feeling better.

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