RESEARCH

Rapid diagnostic tests compared with malaria microscopy for guiding outpatient treatment of febrile illness in Tanzania: randomised trial

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ABSTRACT

Objective To compare rapid diagnostic tests (RDTs) for malaria with routine microscopy in guiding treatment decisions for febrile patients.

Design Randomised trial.

Setting Outpatient departments in northeast Tanzania at varying levels of malaria transmission.

Participants 2416 patients for whom a malaria test was requested.

Intervention Staff received training on rapid diagnostic tests; patients sent for malaria tests were randomised to rapid diagnostic test or routine microscopy

Main outcome measure Proportion of patients with a negative test prescribed an antimalarial drug.

Results Of 7589 outpatient consultations, 2425 (32%) had a malaria test requested. Of 1204 patients randomised to microscopy, 1030 (86%) tested negative for malaria; 523 (51%) of these were treated with an antimalarial drug. Of 1193 patients randomised to rapid diagnostic test, 1005 (84%) tested negative; 540 (54%) of these were treated for malaria (odds ratio 1.13, 95% confidence interval 0.95 to 1.34; P=0.18). Children aged under 5 with negative rapid diagnostic tests were more likely to be prescribed an antimalarial drug than were those with negative slides (P=0.003). Patients with a negative test by any method were more likely to be prescribed an antibiotic (odds ratio 6.42, 4.72 to 8.75; P<0.001). More than 90% of prescriptions for antimalarial drugs in low-moderate transmission settings were for patients for whom a test requested by a clinician was negative for malaria.

Conclusions Although many cases of malaria are missed outside the formal sector, within it malaria is massively over-diagnosed. This threatens the sustainability of deployment of artemisinin combination treatment, and treatable bacterial diseases are likely to be missed. Use of rapid diagnostic tests, with basic training for clinical staff, did not in itself lead to any reduction in over-treatment for malaria. Interventions to improve clinicians' management of febrile illness are essential but will not be easy.

Trial registration Clinical trials NCT00146796.

INTRODUCTION

Malaria is the most common single diagnosis made in most countries in Africa,[1] but the accuracy of clinical diagnosis is limited by the low specificity of symptoms and signs of malaria.[2-4] Presumptive antimalarial treatment for any fever with no obvious alternative cause is widely practised, and studies suggest that this leads to significant overuse of antimalarial drugs throughout Africa.[5-9] This over-diagnosis of malaria in the formal healthcare sector coexists with under-diagnosis of malaria in the community, with the result that antimalarials are given to people who do not need them and not given to children who do.

With the growth of resistance to older antimalarial drugs, newer but more expensive drugs need to be used, and artemisinin combination treatment is now being introduced in most African countries.[10 11] The cost of these drugs – up to 10 times that of current antimalarial drugs – is their major constraint, and deployment to people who need them is likely to depend on subsidy.[12] This may become unsustainable if most antimalarial drugs continue to be given to patients who do not have malaria. If patients with bacterial disease, an important cause of avoidable death in children in Africa,[13 14] are treated as malaria cases they may not receive appropriate treatment.[8] Improving the diagnosis of acute febrile illness so that antimalarial drugs are targeted to patients who need them and alternative diagnoses sought in others is therefore a public health priority in Africa.

Rapid diagnostic tests have considerable potential as a tool to improve the diagnosis of malaria.[15 16] Several commercially available tests are sensitive, specific, and stable under operational conditions.[17] Although microscopy remains the gold standard for diagnosis of malaria, its accuracy under operational conditions in Africa is often low, and clinicians are aware of this.[4] Results of rapid diagnostic tests are rapidly available, less liable to the theoretical risk of being falsely negative due to parasite sequestration, and visible to both prescriber and patient, and they may result in

greater respect for test results. Initial data indicate that the cost effectiveness of rapid diagnostic tests is reasonable in an era of more expensive drugs such as artemisinin combination treatment, and their use could result in significant savings, especially in areas of low transmission.[18] The national malaria control programmes of several countries, including Tanzania, are therefore considering deploying rapid diagnostic tests in the formal healthcare system as part of the roll out of artemisinin combination treatment. Although studies of the technical performance of rapid diagnostic tests (sensitivity, specificity, and stability) are well advanced, no studies have examined whether their use actually leads to a change in prescribing practice compared with current diagnostic methods, which is fundamental to whether their deployment will be effective and cost effective. We set out to compare rapid diagnostic tests with routine microscopy in guiding treatment decisions for febrile patients in outpatient settings in northeast Tanzania.

METHODS

We did the study in three typical government designated public hospitals in northeast Tanzania, one each in areas in which transmission of *Plasmodium falciparum* is very low, low-moderate and high (<1, 1-10, and >100 infected bites/person/year). We phased the study to include the peak malaria transmission season at each site. In low transmission areas malaria is seasonal, peaking in January-March; in high transmission areas it is perennial, peaking in June-August.[19] In common with most hospitals in southern Africa, outpatient care in the study hospitals is largely provided by clinical officers with three years' clinical training.

We invited clinical staff to participate; all agreed and attended training designed to meet or exceed what could be provided by a national malaria control programme. Training included discussion of rapid diagnostic tests and specifically Paracheck (Orchid Pharmaceuticals), a *P falciparum* specific (histidine rich protein-2) test recommended by the national malaria control programme in Tanzania that meets World Health Organization standards for malaria diagnosis and costs approximately $0.7 (£0.4; €0.5) per test in Tanzania.[20 21] The trainers discussed studies showing 94-100% sensitivity and 89-100% specificity for Paracheck and outlined the advantages of visible test results less prone to false negatives caused by parasite sequestration. They reviewed Tanzanian national guidelines for diagnosis and treatment of malaria to emphasise that negative malaria tests should lead to alternative diagnoses being considered.[21]

Malaria tests were free for the duration of the study, irrespective of whether patients consented to the study. Before the trial, we did a baseline observational study to determine the pattern of routine diagnosis of malaria. We inspected the prescriptions of all patients leaving an outpatient consultation and asked them whether a malaria test had been requested. For those sent for testing, we recorded the result and subsequent prescription. A reference slide was taken at the same time as the routine slide.

The entry criterion for the main trial was a clinician's decision to request a malaria test in a patient of any age. The only patients excluded were those for whom the clinician specified microscopy or who were admitted as inpatients for severe disease. Patients with a clinician's request for a malaria test were invited to take part. If they or their guardians gave informed consent, a standardised history was taken, followed by randomisation to rapid diagnostic test or blood slide by computer generated random numbers in blocks of 10; allocations inserted into opaque envelopes were opened in front of the patient on recruitment. All slips had to be accounted for.

Laboratory staff in the clinic did the rapid diagnostic tests, recorded their result, and gave the test strip to the patient for the clinician to interpret independently and record in the review consultation. We used results recorded by clinicians in the primary analysis of prescribing. Patients randomised to microscopy were tested according to routine hospital practice, and clinicians were given results of the test. We obtained a reference slide for later double reading in both arms. Two experienced microscopists blind to allocation stained reference slides with Giemsa and counted parasites against 200 white blood cells; they examined 100 fields before declaring slides negative. We took a third reading of discordant results as final.

Clinic staff with the test result (rapid diagnostic test or hospital slide) reviewed patients in the study and made clinical decisions that they felt were appropriate. As patients left, study staff inspected their prescriptions and recorded them as an objective record of clinicians' decisions.

Sample size calculation

We designed the study to detect a reduction from an estimated 45% over-prescription to 25% over-prescription in the rapid diagnostic test arm. We needed 128 cases with negative test results in each arm to detect this with 95% confidence and 90% power. Estimating that at high, moderate, and low transmission 40%, 70%, and 90% of cases respectively would be slide negative and allowing for a 25% rate of refusal, we needed a total of 800, 457, and 356 cases at the three transmission bands. To avoid the possible bias between sites of a tendency for practice to change over time as health workers became more familiar and better informed about the rapid diagnostic test, we decided to recruit 800 cases at each site.

Statistical analysis

We entered data in Microsoft Access and analysed them with Stata version 9. We finalised the analytical plan before analysis. The primary outcome of the study was the proportion of patients in each arm for whom clinicians requested a malaria test, received a negative result, and prescribed an antimalarial drug anyway. We calculated unadjusted odds ratios and then adjusted them in a logistic regression model with the pre-defined potential confounding factors of age,

Table 1 | Baseline characteristics of patients randomised to blood slide or rapid diagnostic test. Values are numbers (percentages) unless stated otherwise

Characteristic	Slide (n=1204)	Rapid test (n=1193)
Median (IQR) age (years)	11.4 (2-30)	7.3 (2-29)
Female	679 (56)	668 (56)
Fever in previous 48 hours	979 (81)	952 (80)
Cough in previous 48 hours	493 (41)	499 (42)
Previous antimalarial drug use in current illness	66 (5.5)	66 (5.5)
Less than eight years' education*	888 (74)	876 (73)
Less than one hour's travel to clinic	698 (58)	685 (57)
Median (IQR) reported days ill	3 (2-4)	3 (2-4)

IQR=interquartile range.
*Patient or patient's mother if patient aged under 15.

Table 2 | Patients with negative test result treated with any antimalarial drug by malaria test method and age group, stratified by transmission intensity of *Plasmodium falciparum*

Age group (years)	Slide negative		Rapid diagnostic test negative		P value*
	No	No (%) given antimalarial	No	No (%) given antimalarial	
Low transmission					
‹5	185	116 (63)	172	129 (75)	0.013
5-15	38	17 (45)	35	18 (51)	0.568
›15	193	94 (49)	194	86 (44)	0.388
Total	416	227 (55)	401	233 (58)	0.308
Low-moderate transmission					
‹5	141	88 (62)	171	110 (64)	0.727
5-15	55	39 (71)	59	44 (75)	0.660
›15	171	103 (60)	156	88 (56)	0.484
Total	367	230 (63)	386	242 (63)	0.995
High transmission					
‹5	88	20 (23)	78	32 (41)	0.012
5-15	29	14 (48)	25	9 (36)	0.364
›15	130	32 (25)	115	24 (21)	0.486
Total	247	66 (27)	218	65 (30)	0.459
All sites					
‹5	414	224 (54)	421	271 (64)	0.003
5-15	122	70 (57)	119	71 (60)	0.719
›15	494	229 (46)	465	198 (43)	0.240
Total	1030	523 (51)	1005	540 (54)	0.182

*Statistical significance of associations in each stratum assessed with fully interacted logistic regression model that included interactions between treatment and indicator variables for each stratum as covariates.
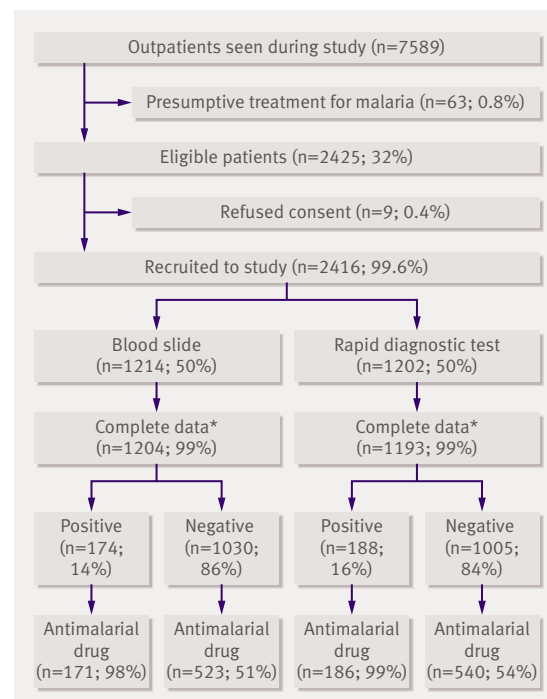

Fig 1 | Total clinic attendances and patients recruited to study by malaria test result and antimalarial treatment prescribed. Data missing from nine patients randomised to rapid diagnostic test (eight missing test result, one missing age) and 10 patients randomised to slide testing (nine missing slide result, one missing age)

request for a malaria slide. For 1813 (90.2%) patients the slide was reported as negative, and 962 (53.1%) of these were treated for malaria.

The intervention ran from January to August 2005. Of 7589 consultations, 63 patients (0.8%) were treated presumptively for malaria and 2425 (32.0%) were sent for a malaria test, of whom 2416 (99.6%) consented to participate and were randomised to rapid diagnostic test or blood slide (fig 1). Data were incomplete in 19 (0.8%) patients, and results are shown for the remaining 2397 cases. Characteristics of patients in each arm were similar (table 1).

In all, 523/1030 (50.8%) patients with a negative hospital slide and 540/1005 (53.7%) patients with a negative rapid diagnostic test were prescribed an antimalarial drug (odds ratio 1.13, 95% confidence interval 0.95 to 1.34; P=0.18). Rapid diagnostic tests showed no advantage in any of the transmission settings (fig 2); the odds ratio was 1.16 (0.88 to 1.52) at the low transmission site, 1.00 (0.76 to 1.35) at low-moderate transmission, and 1.17 (0.78 to 1.75) at high transmission. We found a trend towards an age effect, in that children aged under 5 were more likely to be treated with an antimalarial drug if they tested negative by rapid diagnostic test than if they tested negative by routine slide (table 2). The proportion of test negative patients treated with an antimalarial drug did not vary with the duration of the trial, whether tested by blood slide (odds ratio 0.99 (0.95 to 1.05) per week of trial duration) or by rapid diagnostic test (1.02 (0.97 to 1.07) per week).
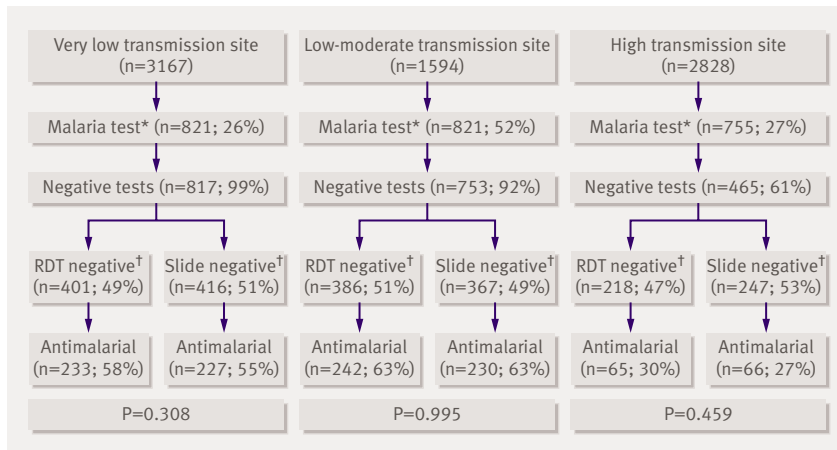
hospital site, a history of fever, a history of cough (used as an indicator of a possible non-malarial cause of illness), and clustering in study sites. We did further analyses by study site and age group. Secondary outcomes were the proportion of febrile patients given an antibiotic by test outcome and the proportions of patients for whom antimalarial drugs were correctly prescribed, defined as antimalarial drugs given to patients with malaria parasites seen and not given to those with no parasites seen on the research slide. We also used the double read research slide as a gold standard to calculate the sensitivity and specificity of the rapid diagnostic test and hospital slide for each site.

RESULTS
In the one month baseline study, 4081 consultations took place; 70 (1.7%) of these resulted in presumptive treatment for malaria, and 2011 (49.3%) resulted in a

Fig 2 | Clinic attendances, malaria test results, and antimalarial treatment prescribed at each of the study sites. *Data are shown for cases with complete data; 3, 3, and 13 cases had incomplete data in the low, low-moderate, and high transmission sites. †Positive test results at low, low-moderate, and high transmission hospitals were: rapid diagnostic test 3, 15, and 168; blood slide 1, 53, and 168. All but five patients with positive tests results were treated with an antimalarial drug; reason for omission of treatment in these five not known

Table 3 | Crude and adjusted odds of prescribing antimalarial drug in presence of negative test result for malaria

	Crude		Adjusted*	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Diagnostic test				
Blood slide	1		1	
Rapid test	1.13 (0.95 to 1.34)	0.182	1.11 (0.97 to 1.26)	0.128
Age group (years)				
<5	1		1	
5-15	0.97 (0.72 to 1.30)	0.829	1.01 (0.44 to 2.33)	0.978
>15	0.55 (0.46 to 0.67)	<0.001	0.60 (0.38 to 0.94)	0.025
Transmission intensity				
Low	1		1	
Low-moderate	1.30 (1.07 to 1.60)	0.010	1.26 (1.20 to 1.31)	<0.001
High	0.30 (0.24 to 0.39)	<0.001	0.28 (0.28 to 0.29)	<0.001
Fever in previous 48 hours				
No	1		1	
Yes	1.37 (1.11 to 1.69)	0.004	1.56 (1.48 to 1.64)	<0.001
Cough in previous 48 hours				
No	1		1	
Yes	1.07 (0.90 to 1.28)	0.430	0.86 (0.72 to 1.05)	0.133

*Logistic regression model in which dependent variable was prescription of antimalarial drug with a negative malaria test result (1) compared with no antimalarial drug (0); independent variables as specified in table. Standard errors for adjusted odds account for clustering within study sites.

We used a logistic model to explore associations between presenting features and prescription of an antimalarial drug for a patient with a negative test result. Adults and patients with a history of fever in the previous 48 hours were more likely to be prescribed an antimalarial drug despite a negative test; we found no significant association with the type of test used (table 3). In 203/1063 (19.1%) of cases in which treatment for malaria was given with a negative test result, the patient did not report a history of fever.

Antibiotics were prescribed to 51/362 (14.1%) patients who tested positive for malaria and to 1044/2035 (51.3%) with a negative test (odds ratio 6.42, 4.72 to 8.75; P<0.001); the difference was especially marked in children aged under 5 (16.8, 11.3 to 25.1; P<0.001) (table 4). Prescription of an antibiotic was not influenced by test method: 525/1030 (51.0%) slide negative patients and 519/1005 (51.6%) rapid diagnostic test negative patients were prescribed an antibiotic (P=0.76), and 308/414 (74.4%) slide negative and 310/421 (73.6%) rapid diagnostic test negative children aged under 5 were prescribed an antibiotic (P=0.80).

When we used double read research slide results as a gold standard, 269/1420 (18.9%) patients prescribed an antimalarial drug had *P falciparum* parasitaemia, and in the low and low-moderate transmission sites this proportion fell to 20/1004 (2.0%). Among children aged under 5, 3/99 (3.0%) tested by rapid diagnostic test had >2000 asexual *P falciparum* parasites/μl on the research slide and did not receive an antimalarial drug, compared with 4/72 (5.6%) in the hospital slide group (P=0.41). If we define a correct prescription of an antimalarial drug as one that is prescribed when parasites are present on research slides and not prescribed when they are not, 616/1193 (51.6%) of patients randomised to the rapid diagnostic test and 606/1204 (50.3%) randomised to a slide test had a correct

prescription of an antimalarial drug (odds ratio 1.05, 0.90 to 1.12; P=0.524).

We compared hospital slide and rapid diagnostic test results with the double read research slide (table 5). Rapid diagnostic tests generally performed well (both sensitive and specific) under field conditions. However, in seven cases the rapid diagnostic test result was negative according to both the prescribing health worker and the laboratory assistant but the research slide was positive; in five of these the parasite density was >5000 *P falciparum* parasites/l. In two cases, non-falciparum species were detected. Hospital laboratory slide results were less sensitive than rapid diagnostic tests (71.3% v 95.4%), and 39 reference slide positive cases were reported as slide negative by the hospital laboratory; in 13 of these the parasite density was >5000/l. The agreement between the health worker and the laboratory assistant in interpreting the rapid diagnostic test result was high (κ=0.913); 4/996 (0.4%) of rapid diagnostic tests were reported as negative by the health worker and positive by the laboratory assistant, and 22/1014 (2.2%) were reported as positive by the health worker and negative by the laboratory assistant.

DISCUSSION

Malaria is the single most common diagnosis in most hospitals in Africa and consumes a considerable proportion of available resources. During an era of cheap

and virtually limitless antimalarial drugs, the policy for treating malaria has assumed that it is safer to treat several cases of non-malarial febrile illness with an antimalarial drug than to miss one true case. Our study shows that this policy is associated with high levels of overuse of antimalarial drugs, especially in low-moderate transmission settings where a significant proportion of people in malaria endemic countries of Africa live.[22] Clinicians frequently requested tests, but they paid limited attention to negative results, irrespective of intensity of transmission. At the low transmission site, less than 1% of patients treated with an antimalarial drug had malaria parasites in their blood.

Impact of over-diagnosis on cost effectiveness

The potential impact of this level of over-prescription is considerable. Substantial numbers of cases of potentially fatal febrile illness treatable with affordable antibiotics are almost certainly being missed.[23] Over-diagnosis of malaria on this scale also threatens the sustainability of deployment of artemisinin combination treatment. These highly effective drugs are essential in east Africa, where alternative treatments are failing, but they are considerably more expensive than current monotherapy and depend on subsidy from the Global Fund and others if they are to reach the poorest groups who are most vulnerable to malaria.[24] Sustaining the subsidy for artemisinin combination treatment, which is essential for malaria in Africa, will be possible only if this regimen is seen to be cost effective. These drugs are cost effective if used for malaria in areas where other drugs have failed, but this depends on the drug being used for children with true malaria, as cost effectiveness rapidly falls away at high levels of misdiagnosis.[25] Recognising the increasing importance of accurate diagnosis in an era of more costly artemisinin combination treatment, governments, encouraged by expert opinion, have been placing substantial orders for rapid diagnostic tests to guide treatment of febrile illness. Although rapid diagnostic tests are significantly more costly than microscopy in a hospital setting, they are potentially cost effective, but only if clinicians using the test act on the result.[26]

Finding realistic ways to improve the quality of health care in hospitals in Africa is a priority.[27] Although the literature on improving prescribing in developed countries is extensive, a recent WHO review identified only 36 trials of strategies to improve prescribing behaviour in developing countries, of which six included antimalarial prescribing as a major outcome.[28] Improving diagnosis of febrile illness is essential but will not be easy. It depends first on improvements in diagnostic facilities so that clinicians can rely on diagnostic tests, but then on changes in longstanding diagnostic behaviour by clinicians. Both of these are difficult with limited resources, but experience from Europe in changing antibiotic prescribing behaviour suggests that encouraging changes in clinicians' behaviour will be the harder of the two.

The challenges for diagnostic laboratories in Africa, which include defective microscopes, intermittent power, poor consumables, and limited time to examine slides, are well known.[29] Improving hospital laboratories to the point where their results are as accurate as a rapid diagnostic test is neither simple nor easy to sustain.[30] Rapid diagnostic tests are the only new tool on offer for improving diagnosis of malaria both within the formal sector and where diagnosis is currently

Table 4 | Prescription of any antibiotic for patients with positive or negative malaria tests by age group

Age group (years)	Positive test		Negative test			
			Antimalarial drug		No antimalarial drug	
	No	No (%) given antibiotic	No	No (%) given antibiotic	No	No (%) given antibiotic
‹5	228	33 (14)	495	365 (74)	340	253 (74)
5-15	50	7 (14)	141	49 (35)	100	55 (55)
›15	84	11 (13)	427	143 (33)	532	179 (34)
Total	362	51 (14)	1063	557 (52)	972	487 (50)

Table 5 | Sensitivity, specificity, and predictive values of rapid diagnostic test or routine blood slide as judged against research slide results

	Research slide*		Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Negative predictive value (%)	Positive predictive value (%)
	Positive	Negative				
Rapid diagnostic test†						
Positive	146	42	95.4 (94.2 to 96.6)	95.9 (94.8 to 97.0)	99.3	77.7
Negative	7‡	985				
Hospital slide						
Positive	97	77	71.3 (68.8 to 73.9)	92.8 (91.3 to 94.3)	96.2	55.8
Negative	39§	991				

*Slide results are positive or negative for any *Plasmodium falciparum* asexual parasites; in addition, two slides were positive for *P malariae* asexual parasites.
†Positive by either laboratory technician or prescribing health worker.
‡Parasite densities/l were ‹1000, 0; 1000-4999, 2; 5000-100 000, 2; ›100 000, 3.
§Parasite densities/l were ‹1000, 15; 1000-4999, 11; 5000-100 000, 8; ›100 000, 5.

syndromic, and they have considerable potential to improve diagnosis. In this study, rapid diagnostic tests were more accurate than routine slide testing, and both patients and clinicians reported liking them. Introducing them into routine care, free of charge and after delivering targeted training had, however, no impact on the overuse of antimalarial drugs. Incurring the cost of a test and then prescribing antimalarial drugs for patients with a negative result represents the worst possible outcome economically. Deployment of rapid diagnostic tests or any other diagnostic test to promote the sustainability of artemisinin combination treatment in Africa is likely to fail unless ways can be found to bring about a major change in current prescribing behaviour.

Although rapid diagnostic test and slide results were equally disappointing in guiding antimalarial treatment, the fact that they both seemed to influence the decision to prescribe antibiotics is potentially encouraging given the increasing realisation of the importance of bacterial disease as a cause of infant and childhood mortality.[23] Clinicians with a positive test for malaria were, however, highly unlikely to prescribe anything except an antimalarial drug; this is not always appropriate, as dual infection occurs in all ages.

Potential limitations of rapid diagnostic tests and this study

Current rapid diagnostic tests have limitations. This study showed false negative results in patients with high parasite counts, but we cannot determine whether this was because the test was done incorrectly or because of technical limitations of the test. Possible technical problems include deletion of HRP-2 genes in certain parasites,[31] "flooding" of the antigen capture sites, and defects in the device membrane (Anthony Moody, personal communication, 2006). This supports the legitimate concern that in areas of very high malaria transmission, withholding antimalarial drugs from children under 5 with febrile illness is potentially hazardous even in the face of negative test results, although where clinicians intend to treat for malaria anyway it makes little sense to request a test. In other epidemiological settings and age groups, the negative predictive value of tests will be excellent and the risks of withholding antimalarial drugs from patients with negative tests will be minimal.

Three reasons exist why this trial might not reflect reality in the rest of Africa and may wrongly lead to an impression that deploying rapid diagnostic tests without major additional interventions will have a limited impact. Firstly, prescribers might have altered their normal practice as a result of the study (Hawthorne effect); however, if anything, this is more likely to have encouraged them to follow national policy and take test results into account. Secondly, the levels of over-diagnosis were atypical, but all the available evidence indicates that the findings of over-diagnosis are wholly typical of hospitals throughout the continent[5-9]; these are well run, government designated hospitals in a stable area, with staff who have received training typical for healthcare providers in Africa. Thirdly, the training provided in the trial was not adequate, but as it was considerably more intensive and

tailored to individual settings than would be possible in a national roll out, this seems unlikely to have led to bias against rapid diagnostic tests. The fact that rapid diagnostic tests were a newly introduced technology might have affected their use either positively or negatively, but we found that the tendency to respect negative rapid diagnostic tests did not vary with the duration of the trial.

Deploying more expensive antimalarial drugs may lead to behavioural change, so theoretically the results of this trial will not reflect what will happen if clinicians are prescribing artemisinin combination treatment. The cost of centrally subsidised artemisinin combination treatment to both clinicians and patients will, however, be the same as existing drugs, so it seems unlikely the cost will in itself lead to marked behavioural change. The study reflects behaviour in a hospital setting, and a substantial proportion of febrile illness (often the great majority) is treated outside hospital or not treated at all; a paradox of malaria treatment throughout Africa is that simultaneously with a high proportion of patients given antimalarial drugs not having malaria, a significant proportion (and often the majority) of those who have malaria are not given an antimalarial drug.[32]

Can behaviour be changed?

Rapid diagnostic tests could, if they guided results, have a major impact on the management of malaria in Africa.[33] This trial shows that providing quick and reliable diagnostic tools with basic training may, in itself, have little impact on overuse of antimalarial drugs. The combination of artemisinin combination treatment and rapid diagnostic tests creates an important opportunity to both reduce the burden of mortality from malaria in Africa and improve the treatment of bacterial disease. Understanding the reasons for, and then changing, the habit of over-prescribing antimalarial drugs will need to be a priority if the potential benefits of artemisinin combination treatment are to be realised; simple technical fixes are unlikely. Our findings indicate an urgent need to identify and implement more effective ways to improve the use of antimalarial and antibiotic treatment in Africa.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Cases of malaria in the community are often missed, but at the same time over-diagnosis of malaria is widespread in Africa

Rapid diagnostic tests are sensitive and specific for falciparum malaria, and could be cost effective if their use guided practice

WHAT THIS STUDY ADDS

In areas of low or moderate malaria transmission, malaria is massively over-diagnosed in hospital outpatients and microscopy results are often ignored

Deploying rapid diagnostic tests for malaria, with standard training, made no difference to the over-diagnosis of malaria in febrile patients

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