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Economic Evaluation of a Cluster Randomized Trial of Interventions to Improve Health Workers' Practice in Diagnosing and Treating Uncomplicated Malaria in Cameroon

Lindsay Mangham-Jefferies, PhD[1,], Virginia Wiseman, PhD[1], Olivia A. Achonduh, MPhil[2], Thomas L. Drake, MSc[1,3,4], Bonnie Cundill, MSc[5], Obinna Onwujekwe, MD, PhD[6], Wilfred Mbacham[2]*

[1]*Department of Global Health and Development, London School of Hygiene and Tropical Medicine, London, UK;* [2]*Laboratory for Public Health Research Biotechnologies, University of Yaoundé I, The Biotechnology Center, Yaoundé, Cameroon;* [3]*Nuffield Department of Clinical Medicine, University of Oxford, Old Road Campus, Oxford, UK;* [4]*Faculty of Tropical Medicine, Mahidol University, Rajwithi Road, Bangkok, Thailand;* [5]*Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK;* [6]*Department of Health Administration and Management, College of Medicine, University of Nigeria (Enugu Campus), Enugu, Nigeria*

ABSTRACT

Background: Malaria rapid diagnostic tests (RDTs) are a valid alternative to malaria testing with microscopy and are recommended for the testing of febrile patients before prescribing an antimalarial. There is a need for interventions to support the uptake of RDTs by health workers. **Objective:** To evaluate the cost-effectiveness of introducing RDTs with basic or enhanced training in health facilities in which microscopy was available, compared with current practice. **Methods:** A three-arm cluster randomized trial was conducted in 46 facilities in central and northwest Cameroon. Basic training had a practical session on RDTs and lectures on malaria treatment guidelines. Enhanced training included small-group activities designed to change health workers' practice and reduce the consumption of antimalarials among test-negative patients. The primary outcome was the proportion of febrile patients correctly treated: febrile patients should be tested for malaria, artemisinin combination therapy should be prescribed for confirmed cases, and no antimalarial should be prescribed for patients who are test-negative. Individual patient data were obtained from facility records and an exit survey. Costs were estimated from a societal perspective using project reports and patient exit data. The analysis used bivariate multilevel modeling and adjusted for imbalance in baseline covariates. **Results:** Incremental cost per febrile patient correctly treated was $8.40 for the basic arm and $3.71 for the enhanced arm. On scale-up, it was estimated that RDTs with enhanced training would save $0.75 per additional febrile patient correctly treated. **Conclusions:** Introducing RDTs with enhanced training was more cost-effective than RDTs with basic training when each was compared with current practice.

Key words: Cameroon, cluster-randomized trial, cost-effectiveness analysis, health worker training, malaria, practice.

Introduction

In 2010, the World Health Organization updated malaria treatment guidelines to confirm that rapid diagnostic tests (RDTs) are a valid alternative to testing using microscopy and to recommend parasitological testing in all patients before prescribing an antimalarial [1]. Interest in RDTs has intensified, and governments across sub-Saharan Africa are now deciding how to expand access to malaria testing and whether to introduce RDTs in health facilities that already offer malaria testing using microscopy. These policy decisions will require revisions to national malaria treatment guidelines and supporting interventions that ensure that the policy change is accompanied by a change in health workers' practice.

In malaria-endemic areas, cases of uncomplicated malaria are routinely treated in primary health facilities and hospital outpatient departments, and clinical guidelines advise that in high-transmission settings malaria should be suspected in patients who present with a fever or report having a fever in the past 24 hours [1]. Malaria testing is advised because malaria symptoms are nonspecific and the fever may have other causes. Microscopy, however, requires a laboratory and technicians able to prepare and read blood slides and these are often limited in low-income settings. Consequently, it has become common for health workers to make treatment decisions on the basis of symptoms alone and for antimalarials to be presumptively prescribed to febrile patients.

RDTs offer considerable potential to transform malaria diagnosis and treatment because they do not require a laboratory and

* *Address correspondence to:* Lindsay Mangham-Jefferies, Department of Global Health and Development, London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London, UK.

E-mail: lindsay.mangham-jefferies@lshtm.ac.uk.

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can be used with minimal training. This potential, however, will be realized only if health workers prescribe treatment on the basis of test result. Evidence from several countries, including Cameroon, suggests that reliance on a presumptive malaria diagnosis has created a mindset among health workers and patients that febrile illness should be treated with an antimalarial and it is not uncommon for antimalarials to be prescribed to patients who tested negative for malaria [2–6].

The economic argument for introducing RDTs critically depends on health workers' practice [7,8]. This assumption has been emphasized in several studies [7,9,10], and the sensitivity of cost-effectiveness results to health workers' practice has been illustrated using trial data from Tanzania [8]. Results were also sensitive to the prevalence of malaria in febrile patients, specificity and sensitivity of the test, cost of testing and medicines, whether nonmalaria febrile illness was a bacterial or self-resolving viral infection, the efficacy of antimalarials and antibiotics taken, and whether patients take medicines as advised [9]. The literature shows that RDTs tend to be more cost-effective than microscopy when compared with a presumptive diagnosis [7,11,12], while the cost-effectiveness of RDTs compared with microscopy depends on the relative cost of the tests, as well as their specificity and sensitivity in routine use [10,13–15].

To improve malaria diagnosis and treatment using RDTs in Cameroon, interventions were designed following formative research with patients and health workers in two regions of Cameroon [3,6,16]. The formative research showed that microscopy was available in most of the public and mission facilities but was underused and less than 50% of the febrile patients were tested for malaria [6]. Malaria was overdiagnosed: 73% of the febrile patients received an antimalarial, yet malaria was present in only 30% of the febrile patients tested by the study team [6]. Moreover, patients often received an antimalarial regardless of the test result: 82% of the patients who reported that they tested negative for malaria were prescribed an antimalarial [6]. Qualitative research also provided an insight into health workers' practice and highlighted both a mistrust of malaria test results and challenges in managing patient expectations [3].

In collaboration with the National Malaria Control Programme (NMCP) of Cameroon, training modules were developed to support the introduction of RDTs in public and mission facilities. The basic training was intended to equip health workers with the knowledge and practical skills needed to diagnose and treat uncomplicated malaria, including how to conduct an RDT. Because improving health workers' adherence to the malaria treatment guidelines was a key objective, additional training was designed that used interactive methods and sought to address the gap between health workers' knowledge and practice, and change prescribing behavior.

This article reports the incremental cost per febrile patient correctly treated (according to the malaria treatment guidelines) of each intervention compared with current practice. Cost-effectiveness was assessed from both a provider perspective and a societal perspective. The analysis uses statistical methods suitable for individual patient data on costs and effects obtained from a cluster randomized trial [17,18].

Methods

Trial Design and Intervention

A cluster randomized trial was designed to evaluate the effectiveness and cost-effectiveness of introducing RDTs with basic or enhanced training in facilities in which microscopy was available compared with current practice. The three-arm cluster randomized trial was conducted at 46 public and mission health facilities that offered malaria microscopy testing and were located in central and northwest regions of Cameroon where malaria is endemic. The trial design and interventions are summarized here, and further details are available elsewhere [19,20]. The trial was registered (clinicaltrials.gov: NCT01350752), the study protocol is available [19], and the main trial article has been published [20]. The effect of the interventions on the proportion of febrile patients correctly treated according to the malaria treatment guidelines was measured by surveying febrile patients exiting health facilities.

Facilities were stratified by site, randomly selected, and allocated to one of three arms: control, basic, and enhanced. There was no intervention at facilities in the control arm. Each facility in the two intervention arms was supplied 100 RDTs (SD Bioline Malaria Ag Pf/Pan, Standard Diagnostics, Yongin, South Korea) per month without charge. The brand and number of RDTs supplied was selected on the basis of advice from the NMCP, and the test is reported to have a minimum detection rate of 97.5% for *Plasmodium falciparum* malaria, even at low levels of parasitemia (200 parasites/μl) [21]. Each facility in the basic arm was invited to send three health workers to a 1-day training course that was organized by the study team. The 1-day training had three lectures on the revised malaria clinical guidelines and a practical session on how to use RDTs. The enhanced intervention replicated not only the basic intervention but also contained an additional 2 days of training. The additional training used participatory methods to reinforce material covered in the basic training, while also encouraging health workers to adapt to change, communicate effectively, and support each other. For instance, trainers facilitated small-group work and used problem-solving exercises, a treatment algorithm game, self-developed participatory drama, and role-playing. The training courses were delivered by representatives from the NMCP and members of the study team. Health workers who attended basic and enhanced training courses were encouraged to hold training sessions at their facility (hereafter referred to as in-facility training) and inform their colleagues about RDTs and the revised malaria treatment guidelines. The trial was designed to approximate "real-world" rather than controlled conditions, and it was possible, for example, that a facility encountered stock-outs of RDTs and artemisinin combination therapies (ACTs) during the evaluation.

Effectiveness of Interventions

The effect of the interventions was measured by the proportion of febrile patients attending facilities who were correctly treated according to the revised malaria treatment guidelines. This was a composite measure that required all febrile patients to be tested for malaria using microscopy or RDT, patients to receive an ACT if they have a positive malaria test result, and patients not to receive an antimalarial if they have a negative malaria test result. Patients were invited to participate in an exit survey if they sought treatment for a fever at one of the facilities participating in the trial, were more than 6 months old, were not pregnant, and did not have symptoms of severe malaria. With informed consent, the exit survey was administered by trained fieldworkers to the patient or his or her caregiver. A copy of the malaria test register in each facility was also obtained. Data collection took place between October and December 2011 and commenced 3 months after interventions were implemented. The effectiveness results have been submitted for peer-reviewed publication in an academic journal [20].

Cost Measurement and Valuation

Health care cost for each patient in the exit survey was estimated taking into account direct and indirect costs incurred by the