Major Reduction in Anti-Malarial Drug Consumption in Senegal after Nation-Wide Introduction of Malaria Rapid Diagnostic Tests

Sylla Thiam1, Moussa Thior1, Babacar Faye2, Médoune Ndiop1, Mamadou Lamine Diouf1, Mame Birame Diouf1, Ibrahima Diallo1, Fatou Ba Fall1, Jean Louis Ndìaye2, Audrey Albertini3, Evan Lee3, Pernille Jorgensen4, Oumar Gaye2, David Bell3*

1 Programme National de lutte contre le Paludisme, Ministère de la Santé, Dakar Fann, Senegal, 2 Faculté de Médecine, Université Cheikh Anta Diop de Dakar, Fann Dakar, Sénégal, 3 Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland, 4 Global Malaria Programme, World Health Organization, Geneva, Switzerland

Abstract

Background: While WHO recently recommended universal parasitological confirmation of suspected malaria prior to treatment, debate has continued as to whether wide-scale use of rapid diagnostic tests (RDTs) can achieve this goal. Adherence of health service personnel to RDT results has been poor in some settings, with little impact on anti-malarial drug consumption. The Senegal national malaria control programme introduced universal parasite-based diagnosis using malaria RDTs from late 2007 in all public health facilities. This paper assesses the impact of this programme on anti-malarial drug consumption and disease reporting.

Methods and Findings: Nationally-collated programme data from 2007 to 2009 including malaria diagnostic outcomes, prescription of artemisinin-based combination therapy (ACT) and consumption of RDTs in public health facilities, were reviewed and compared. Against a marked seasonal variation in all-cause out-patient visits, non-malarial fever and confirmed malaria, parasite-based diagnosis increased nationally from 3.9% of reported malaria-like febrile illness to 86.0% over a 3 year period. The prescription of ACT dropped throughout this period from 72.9% of malaria-like febrile illness to 31.5%, reaching close equivalence to confirmed malaria (29.9% of 584873 suspect fever cases). An estimated 516576 courses of inappropriate ACT prescription were averted.

Conclusions: The data indicate high adherence of anti-malarial prescribing practice to RDT results after an initial run-in period. The large reduction in ACT consumption enabled by the move from symptom-based to parasite-based diagnosis demonstrates that effective roll-out and use of malaria RDTs is achievable on a national scale through well planned and structured implementation. While more detailed information on management of parasite-negative cases is required at point of care level to assess overall cost-benefits to the health sector, considerable cost-savings were achieved in ACT procurement. Programmes need to be allowed flexibility in management of these funds to address increases in other programmatic costs that may accrue from improved diagnosis of febrile disease.

Citation: Thiam S, Thior M, Faye B, Ndiop M, Diouf ML, et al. (2011) Major Reduction in Anti-Malarial Drug Consumption in Senegal after Nation-Wide Introduction of Malaria Rapid Diagnostic Tests. PLoS ONE 6(4): e18419. doi:10.1371/journal.pone.0018419

Editor: Sylviane Pied, Lille 2 University, France

Received November 24, 2010; Accepted March 5, 2011; Published April 6, 2011

Copyright: © 2011 Thiam et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: This study was funded through pre-existing grants to the Senegal Programme National de lutte contre le Paludisme from the Global Fund to fight AIDS, Tuberculosis and Malaria and the United States Presidents’ Malaria Initiative, and by the Foundation for Innovative New Diagnostics (FIND) through a grant from the Bill and Melinda Gates Foundation. The funding agencies had no role in the decision to undertake the study, study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: david.bell@finddiagnostics.org

Introduction

The World Health Organization recently strengthened its recommendation for parasite-based diagnosis of malaria, extending it to all cases of suspected malaria prior to treatment with anti-malarial medicines [1]. Accurate diagnosis enables targeting of anti-malarial drugs to those who will benefit, early identification of non-malarial fever requiring alternative management, and accurate and complete surveillance for confirmed malaria cases. Reducing drug wastage, in addition to saving money and conserving stocks of artemisinin-based combination therapies (ACT), may prolong the usefulness of ACTs globally by reducing pressure towards resistance. Clinical (symptom-based) diagnosis of malaria has a very poor specificity [2,3,4], and microscopy is predominantly limited to larger health facilities where the quality of the result can be assured [5]. Provision of universal access to parasite-based diagnosis for populations at risk of malaria will therefore depend on the wide use of malaria rapid diagnostic tests (RDTs); point-of-care tests first introduced in 1993 (with the ParaSight-F test) and with a proliferation of products now coming into wide use [6,7,8,9]. Rapid point-of-care tests are routinely used for several diseases including HIV and syphilis, replacing centralized laboratory testing, as the requirement for a positive diagnostic result has...
The Senegal Programme

Malaria is endemic throughout Senegal. *Plasmodium falciparum* accounts for virtually all reported cases [22]. Approximately 75% of patients access public health facilities for management of fever [23], the vast majority doing so through peripheral health huts (“cases de santé”) rather than hospitals or clinics with established laboratory capacity. Artemisinin-based combination therapy (ACT) was introduced as first-line therapy in 2006 (artesunate-amodiaquine; AS-AQ). Until 2007 malaria diagnosis was predominantly based on clinical assessment, with microscopy-based diagnosis limited to hospitals. Of 1553310 reported fever cases at public health facilities in 2006, only 3.1% (48275) were confirmed malaria cases, as well as data on consumption of antimalarial treatment are notified/reported monthly to the district malaria programme by all levels of the public health system (hospitals, health centres, health posts and health huts) using a standard reporting form. At district level, the reported data is reviewed by NMCP personnel, data received from each district are reviewed by NMCP personnel, secondly, aggregated data reported to the district from the facility; and thirdly, aggregated data reported to the district from the facility; and thirdly, aggregated data reported to the district from the facility. MF malaria surveillance data is assessed regularly at two levels of the country.

The evaluation is based on routinely-collected and collated programme data, retrieved by the national malaria control programme (Programme National de lutte contre le Paludisme) and the Faculté de Médecine, Université Cheikh Anta Diop de Dakar in 2010. The national malaria surveillance system is based on passive case detection. Data on suspected and laboratory confirmed malaria cases, as well as data on consumption of antimalarial treatment are notified/reported monthly to the district malaria programme by all levels of the public health system (hospitals, health centres, health posts and health huts) using a standard reporting form. At district level, the reported data is entered into a database (Epi Info Version 6) and sent to NMCP on a monthly basis. The NMCP stipulates that the quality of malaria surveillance data is assessed regularly at two levels of the system: Firstly, supervisors from the district malaria programme perform quarterly or bi-annual visits to health care facilities within their district area to cross-check patient records at the facility with data reported to the district from the facility; secondly, aggregated data received from each district are reviewed by NMCP personnel, regional and district malaria programme staff at quarterly meetings.

For the purpose of this programme evaluation, the following monthly data were extracted from the national malaria surveill-
lance database for the period January 2007 to December 2009: i) number of malaria-like febrile disease ('suspected malaria') cases, defined as persons with fever (clinically determined or axillary measured temperature $\geq 37.5^\circ$C; ii) number of persons tested for malaria by microscopy or RDT; iii) number of malaria cases confirmed by microscopy or RDT; iv) number of persons treated with ACTs; and, v) total number of all-cause consultations.

We calculated the proportion of persons tested by RDT or microscopy among all persons with suspected malaria and the proportion of persons treated with ACT among all suspected malaria cases in order to assess the impact of universal parasite-based diagnosis using malaria RDTs on anti-malarial drug consumption over a two-year period. The number of ACT courses averted were estimated by subtracting the actual ACT consumption in September 2007–December 2009 from the predicted consumption derived from the proportion of malaria-like fever cases treated with ACTs in January–August 2007 (prior to RDT introduction).

Suspected malaria is reported here as recorded by the programme, irrespective of tightening of the definition from late 2007 that was likely associated with re-training on RDT introduction. The 'confirmed malaria rate' is derived from reported confirmed malaria (microscopy-based) up to August 2007, and from the RDT positivity rate after this time, as most microscopy performed after August 2007 involved referred cases previously screened with RDTs. This avoids double-reporting of such cases but will cause a small artefactual decline in late 2007, and possibly a minor underestimation of case numbers thereafter, but as microscopy was performed on only a small subset of patients (5.2% of tested patients through 2009), any underestimation will be small.

Results

In Senegal from 2007 to 2009, 2784532 suspected malaria cases were reported at public health facilities. Case rates followed a clear seasonal trend with an increase in suspected malaria from August to December, accompanied by an increase in both parasite-negative malaria-like febrile disease and in total consultations unrelated to malaria-like fever over the same (wet season) months (Figure 2). As the programme moved from predominantly symptom-based treatment in 2007 to parasite-based treatment in 2009, the frequency of ACT use declined from 67.7% of the malaria-like fever cases (suspected malaria) in 2007 to 31.5% in

Figure 1. Malaria Case Management Algorithm of the Senegal NMCP, introduced from July 2007.

doi:10.1371/journal.pone.0018419.g001

[Diagram of Malaria Case Management Algorithm]
2009. Over the same period, the rate of diagnostic testing of malaria-like fever rose from 4.0% and 6.2% by microscopy and RDT respectively in 2007 (RDTs having been introduced after August), to 5.2% and 86.0% respectively in 2009, rising to 96% in December of that year (Figure 2).

Throughout 2009, ACT consumption closely followed the confirmed malaria rate (test-positive rate), apart from a marked trough in ACT consumption in June corresponding with a temporary stock-out in many clinics (Figure 3). During 2009, 174,990 RDT-positive malaria cases were recorded and 184,170 doses of ACT dispensed.

Table 2 summarizes diagnostic results and the corresponding reduction in ACT courses dispensed and probable courses averted from 2007 to 2009. Taking the period of 2007 prior to RDT introduction (January to August) as a baseline, during which 72.9% of suspected malaria cases were treated with ACTs, the estimated unnecessary ACT courses averted by the programme rose to 249,184 in 2009 (Table 2). An estimated 516,576 courses of ACT were averted over the entire 3 year period.

Discussion

These data demonstrate a significant decrease in reported malaria cases on a national scale after implementation of parasite-based diagnosis for malaria, with a corresponding reduction in ACT consumption. Of similar importance, the introduction of the strategy of universal diagnosis has provided a high degree of certainty on malaria incidence throughout Senegal. This certainty is enabling the national programme to accurately predict antimalarial drug requirements and creating the ability to concentrate resources on areas of higher malaria burden and need, and to assess the impact of future changes in intervention rates with insecticide treated bednets and indoor residual spraying.

Prior to RDT introduction, microscopy was used in only a small proportion of suspected malaria cases. Although the definition of reported ‘malaria’ varied, the vast majority of reported cases were

| Table 1. Key dates in introduction of anti-malaria interventions in Senegal. |
|------------------|------------------|
| Intervention                  | Year of introduction |
| Indoor residual spraying: primary vector control intervention | 1998 |
| Insecticide-treated bednets (more recently long-lasting nets) | 2002 |
| Intermittent prophylactic Therapy for pregnancy (IPTp) | 2004 |
| Artemisinin-based combination therapy | 2006 |
| Rapid diagnostic tests (RDTs) | 2007 (Sept) |
| RDT country 'full coverage' (roll-out to health posts, then health huts) | 2008 (Late) |

Figure 2. Evolution of parasite based diagnosis of malaria in Senegal public health services 2007–2009. A: Introduction of new case definition for suspected malaria. B: Partial stock-out of ACT due to late replacement of expired stock in some clinics. doi:10.1371/journal.pone.0018419.g002
based on non-specific symptoms and were treated with ACTs. These figures for assumed malaria were the basis on which the programme had forecast ACT consumption and base procurement. With the introduction of RDTs, subsequent utilization of ACTs was well below the predicted rate, and large stocks of ACTs expired in mid-2009 (delays in replacement resulting in the reported stock-out in some clinics, which accounts for the drop in ACT consumption below the confirmed malaria rate at that time). While the reported malaria-like fever rate remained high despite a tightening of the clinical definition, the near-universal use of RDTs in these cases has provided the national malaria control programme with a solid basis for predicting drug consumption. Senegal can now procure an appropriate quantity of ACTs - a small proportion of the volume previously required. In 2009, the Global Fund retained 1201764 Euros (~US$1.57) in unused funds allocated for ACT procurement within the grant previously agreed for the Senegal programme.

The reduction of ACT use to near-equivalence with the confirmed malaria rate took some time. Obviously, the gradual introduction of RDTs across the public health sector, necessitated by the requirement to train health workers in RDT use, partly explains this [19]. Eighteen months elapsed before ACT consumption closely tracked the RDT-positive rate, by which time RDT consumption had risen above 80% of the reported malaria-like fever rate. Experience of poor compliance elsewhere suggests that non-adherence to RDT results may also have been responsible for the lag [15,16]. However, by mid-2008, high adherence with diagnostic results was achieved and continues to be sustained on a national scale.

The high adherence rate to RDT results is likely due to a combination of factors. The Senegal programme, somewhat unusually, charged patients diagnosed with malaria for first-line anti-malarial drugs. While the cost to the consumer was small, this is likely to have contributed to adherence to diagnostic results.

### Table 2. Malaria case management in Senegal, January 2007 to December 2009.

|                        | Reported suspected malaria cases | Suspected malaria cases testeda (%) | Suspected malaria cases confirmeda (%) | Cases of suspected malaria treated with ACTsb (%) | Estimated ACT courses avertedc |
|------------------------|----------------------------------|------------------------------------|----------------------------------------|---------------------------------------------------|-------------------------------|
| Before introduction of RDTs | Jan–Aug 2007                     | 857179                             | 33263 (3.9)                            | 12468 (1.5)                                       | 624601 (72.9)                | N/A                           |
| After introduction of RDTs | Sept–Dec 2007                    | 605066                             | 90313 (14.9)                           | 40178 (6.6)                                       | 365740 (60.5)               | 75353                         |
| 2008                   | 737414                           | 487188 (66.1)                      | 217096 (29.4)                          | 338335 (45.9)                                     | 199239                       |
| 2009                   | 584873                           | 502739 (86.0)                      | 174890 (29.9)                          | 184170 (31.5)                                     | 241984                       |

aTested by microscopy up to August 2007, and RDT only from September 2007. After August 2007, only RDTs became the first-line diagnostic test and microscopy was confined to referral centres and results were likely to involve re-testing of a case. In 2009, 30414 cases were tested by microscopy.

bArtemisinin-based combination therapy.

cBased on treatment rate of malaria-like febrile disease (suspected malaria) in 2007 prior to rapid diagnostic test introduction.

doi:10.1371/journal.pone.0018419.t002
(non-treatment of RDT-negative cases). The cost of antibiotics was higher than anti-malarial drugs, but only certain RDT-negative patients were prescribed these (NMCP). Other major contributors to adherence are likely to include: (1) a history of prioritizing malaria diagnosis at a central and academic level in Senegal which may have eased acceptance among planners and senior physicians, despite the limited reach of microscopy [28]; (2) strong Ministry of Health support for the programme, backed by policy change and combined with a strong public sector (which is the first point of access for most febrile patients) [23]; (3) tested training materials and job-aids specifically adapted by the NMCP for use at the district and community level [19]; a comprehensive supervisory programme that maintains contact with peripheral health workers; (4) an aggressive roll-out schedule sufficient to achieve near-blanket national public-sector coverage in a relatively short time, with RDT use thereby becoming the norm rather than confined to certain clinics or regions; and (5) a quality assurance system based on lot-testing of RDTs, capable of demonstrating that the particular product used was working prior to deployment and thereby at least partly allaying fears of false-negative results. The University of Cheikh Anta Diop also actively collated and disseminated data to community organizations and NGOs to build public awareness of the change in national malaria policy and guidelines, and engaged key opinion leaders to advocate for RDT use.

While considerable cost savings have been achieved by the Senegalese NMCP by reducing unnecessary ACT procurement, overall financial costs to the health service are unclear. Senegal's procurement costs per course of ACT (AS-AQ) averaged US$1.12 per course. As patients paid US$0.60 and US$0.30 for adult and paediatric courses of treatment respectively, the overall cost to the programme, ignoring logistical costs, is approximately US$0.70. Cost savings through reductions in ACT use will have been offset by costs in RDTs (similar to the adult ACT course cost-to-programme). Costs of antibiotics that can be provided to RDT-negative patients are higher; full courses of amoxicillin and cotrimoxazole cost the programme about US$2.00 and paracetamol US$1.00, while US$0.60 and US$0.20 is recouped from patients. Figures on antibiotic dispensing prior to and after RDT use were not available, but anecdotal evidence indicates that many RDT-negative patients, probably appropriately, do not receive them. While a limited evaluation in central Senegal indicated that overall cost savings are likely to accrue [26], a full cost-benefit analysis would need to take into account the likely benefit of earlier appropriate management of non-malarial febrile illness where this occurs, and the wider benefits of improved targeting of health interventions enabled through the availability of more accurate incidence data.

Modelling elsewhere suggests that an overall cost-benefit may be expected when RDTs replace presumptive therapy; but these rely on ACT costs higher than those of Senegal, and improved management of non-malarial febrile illness is important to achieving these benefits [13,29,30]. Other modelling and field experience also suggests that overall cost implications will be relatively neutral [14,31]. Through partial recoupment of antibiotic costs from the consumer, the Senegal programme will have limited the impact on less-well funded areas of the health system that fund antibiotic prescription. However, funds saved on ACT conservation could also be spent in future on support for non-malarial fever management if more flexibility was allowed by external agencies in the use of allocated funds.

Irrespective of financial loss or gain, the public health imperative of not mis-leading patients or their carers into reliance on an inappropriate three-day course of anti-malarial medication, ineffective for their illness, is clear. Resultant delays in achieving a correct diagnosis and appropriate management may increase mortality from other potentially fatal or debilitating infections. Mortality due to non-malarial febrile disease is twice that of malaria globally, with malaria-endemic countries accounting for a large proportion of this burden [32]. Thus, a basic public health good is at issue, not just a possible benefit in terms of financial cost. As malaria declines through much of sub-Saharan Africa [22], the need to differentiate malaria from non-malarial fever becomes more pressing. It is too early to confirm from the Senegal data whether an overall decline in malaria is occurring, or whether the apparent decline seen in Figure 2 reflects only better discrimination of malarial from non-malarial febrile illness, initially through a tightening of clinical criteria and now by demonstration of parasitaemia. Interestingly, the introduction of RDTs imposed an additional burden on health workers on diagnosing ‘malaria-like fever’; they now must perform a finger-prick and RDT prior to further management and this may result in at least a subconscious reduction in readiness to assign this diagnosis to febrile patients. A decline in reported annual malaria deaths during this period from 1935 to 722 indicates that any increased reluctance to test for malaria was not resulting in poorer outcomes [22]. Alternatively, the downward trend in both non-malarial fever and confirmed malaria could be real, due to environmental changes over this period affecting multiple pathogens or, speculatively, due to reduced rates of malaria parasite carriage resulting in improved health and resistance to other pathogens. RDT consumption remains below the reported malaria-like fever rate, largely accounted for by the incremental roll-out of RDTs to clinics, this gap reducing toward the end of 2009 as RDT use reached 96% of malaria-like fever cases (Figure 2). As ACT consumption ends 2009 marginally above the RDT-positive rate, these undiagnosed cases are likely to account for much of the remaining over-prescribing of ACT at this time.

The experience in Senegal demonstrates that parasite-based diagnosis reliant on the use of malaria RDTs can be successfully introduced on a national scale and dramatically reduce ACT consumption. In the presence of a strong public health sector, and possibly influenced by some financial incentive to the consumer, RDTs have been used to transform the accuracy of malaria case reporting and open new possibilities for addressing non-malarial febrile illness and manage other causes of morbidity and mortality. The ability to track the identify cases and track the impact of anti-malarial interventions in this way through the widespread use of parasite-based diagnosis will enable malaria elimination to be seriously contemplated, but more flexibility is required in management of funds saved from ACT procurement that will be required to address increased programmatic costs in other areas.

Acknowledgments

The authors wish to acknowledge the many dedicated personnel of the Senegal national malaria control programme and Ministry of Health who collected and collated the data reported in this study. We thank Anne Guilloux of WHO for assistance with graphics.

Author Contributions

Conceived and designed the experiments: BF JLN OG MT ST LD MBD ID FBF. Performed the experiments: BF JLN OG MT ST LD MBD ID FBF MN MLD. Analyzed the data: MT ST BF AA EL DB PJ. Wrote the paper: MT ST BF AA EL DB PJ.
References

1. WHO (2009) Malaria Case Management Operations Manual. Geneva: World Health Organization.
2. Armstrong-Schellenberg JRM, Smith T, Alonso PL, Hayes RJ (1994) What is clinical malaria? Finding case definitions for field research in highly endemic areas. Parasitology Today 10: 439–442.
3. Chandramohan D, Jaffar S, Greenwood B (2002) Use of clinical algorithms for diagnosing malaria. Trop Med Int Health 7: 45–52.
4. Reyburn H, Mbatai R, Drakeney C, Carneiro I, Mwakasungula E, et al. (2004) Overdiagnosis of malaria in patients with severe febrile illness in Tanzania: a prospective study. Brmj 329: 1212.
5. WHO (2009) Malaria microscopy quality assurance manual - Version I. Manila: World Health Organization - Regional Office for the Western Pacific.
6. Shiff CJ, Premji Z, Minja JN (1993) The rapid manual ParaSight-F test. A new diagnostic tool for Plasmodium falciparum infection. Trans R Soc Trop Med Hyg 87: 646–649.
7. Moody A (2002) Rapid diagnostic tests for malaria parasites. Clin Microbiol Rev 15: 66–78.
8. Bell D, Wongrichanalai C, Barnwell JW (2006) Ensuring quality and access for malaria diagnostic: how can it be achieved? Nat Rev Microbiol 4: 682–695.
9. WHO-FIND-CDC-TDR (2010) Malaria Rapid Diagnostic Test Performance: Results of WHO product testing of malaria RDTs: Round 2 (2009). Geneva: World Health Organization.
10. WHO-TDR-FIND (2010) Methods Manual for Laboratory Quality Control Testing of Malaria Rapid Diagnostic Tests, Version Six. Geneva: World Health Organization.
11. Faucher JF, Makoutode P, Abiou G, Beheton T, Houze P, et al. (2010) Can treatment of malaria be restricted to paraclinically confirmed malaria? A school-based study in Benin in children with and without fever. Malar J 9: 104.
12. D’Accremont V, Malila A, Swai N, Tillya R, Kahama-Marco J, et al. (2010) Withholding antimalarials in febrile children who have a negative result for a rapid diagnostic test. Clin Infect Dis 51: 506–511.
13. Shilkcutt S, Moore G, Goodman G, Coleman P, Bell D, et al. (2008) Cost-effectiveness of malaria diagnostic methods in sub-Saharan Africa in an era of combination therapy. Bull World Health Organ 86: 101–110.
14. Mielheim MI, Martinsson A, Roillau G, Bhattachar A, Stromberg J, et al. (2009) Influence of rapid malaria diagnostic tests on treatment and health outcome in fever patients, Zanzibar: a crossover validation study. PLoS Med 6: e1000070.
15. Reyburn H, Mbakilwa H, Mwangi R, Mwerinde O, Olomi R, et al. (2007) Rapid diagnostic tests compared with malaria microscopy for guiding outpatient treatment of febrile illness in Tanzania: randomised trial. BMJ 334: 406–407.
16. Biotlii Z, Sirima BS, Anguelben A, Lodesani C, Cobbi F, et al. (2009) Rapid malaria diagnostic tests vs. clinical management of malaria in rural Burkina Faso: safety and effect on clinical decisions. A randomized trial. Trop Med Int Health 14: 491–498.
17. Amah EK, Narh-Bana S, Epoko M, Akankpiah S, Quartey AA, et al. (2010) Rapid testing for malaria in settings where microscopy is available and peripheral clinics where only presumptive treatment is available: a randomized controlled trial in Ghana. Brmj 340 p.
18. Williams HA, Causer L, Metta E, Malila A, O’Reilly T, et al. (2008) Dispensary level pilot implementation of rapid diagnostic tests: an evaluation of RDT acceptance and usage by providers and patients-Tanzania, 2005. Malar J 7: 93.
19. Harvey SA, Jennings L, Chinyama M, Masaninga F, Mulholland K, et al. (2008) Improving community health worker use of malaria rapid diagnostic tests in Zambia: package interventions, job aid and job aid-plus-training. Malar J 7: 160.
20. English M, Reyburn H, Goodman C, Snow RW (2009) Abandoning presumptive amnarial treatment for febrile children aged less than five years: a case of running before we can walk? PLoS Med 6: e1000015.
21. D’Accremont V, Lengeler C, Mshinda H, Musaiva D, Tanner M, et al. (2009) Time to move from presumptive malaria treatment to laboratory-confirmed diagnosis and treatment in African children with fever. PLoS Med 6: e252.
22. WHO (2009) World Malaria Report 2009. Geneva: World Health Organization.
23. Oliver Sabour SY, Franco Pagnoni, Megumi Gordon, Nora Petty, Kristin Schmits, Ambrose Talisuna (2009) Distribution of Artemisinin-Based Combination Therapies through Private-Sector Channels - Lessons from Four Country Case Studies. Prepared for the Consultative Forum on AMFm—the Affordable Medicines Facility-malaria, September 27–28, 2008 Washington, DC: Resources for the Future.
24. Senegal NMCP (2006) Directives nationales pour le traitement du paludisme au Sénégal. Dakar: Programme National de Lutte contre le Paludisme, Senegal Ministry of Health.
25. WHO-WPRO (2010) Malaria RDT Job-Aids and Training Manuals. Manila: WHO Regional Office for the Western Pacific.
26. Ly AB, Tall A, Perry R, Baril L, Badane A, et al. (2010) Use of HRP-2-based rapid diagnostic test for Plasmodium falciparum malaria: assessing accuracy and cost-effectiveness in the villages of DieHLo and NDLop, Senegal. Malar J 9: 153.
27. WHO (2008) Methods Manual for Laboratory Quality Control ‘‘Testing of Malaria Rapid Diagnostic Tests. Version 5a: WHO - Regional Office for the Western Pacific.
28. Senegal NMCP (2008) Manuel de procédures pour le contrôle de qualité du diagnostic biologique. Dakar: Programme National de Lutte contre le Paludisme, Senegal Ministry of Health.
29. Lubell Y, Belham L, Mbakilwa H, Mwangi R, Chonya K, et al. (2007) The cost-effectiveness of parasitologic diagnosis for malaria-suspected patients in an era of combination therapy. Am J Trop Med Hyg 77: 126–132.
30. Lubell Y, Hopkins H, Whitby CJ, Stardek SG, Mills A (2008) An interactive model for the assessment of the economic costs and benefits of different rapid diagnostic tests for malaria. Malar J 7: 21.
31. Yakubu J, D’Accremont V, Kahama J, Swai N, Lengeler C (2010) Cost Savings with Rapid Diagnostic Tests for Malaria in Low-Transmission Areas: Evidence from Dar es Salaam, Tanzania. Am J Trop Med Hyg 83: 61–68.
32. Black RE, Cousins S, Johnson HL, Law J, Rudan I, et al. (2010) Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet. 11 p.