

APPENDIX 1
Meeting Session Summaries

DAY 1

MORNING SESSION 1

Session Chair: Professor David Schellenberg

1. Welcome and objectives for the consultation—Professor Rifat Atun and Dr Hiro Nakatani
2. Rationale for universal access to parasite-based malaria diagnosis—Robert Newman
3. Economics and financing of expansion from status quo to universal access: fundamental concepts, questions and tools—Dean Jamison

The speakers introduced the partners in the consultation and oriented the attendees to the issues.

1. Welcome and objectives for the consultation—Professor Rifat Atun and Dr Hiro Nakatani

Professor Atun, Director of the Strategy, Performance and Evaluation Cluster at the Global Fund and Dr Nakatani, WHO Assistant Director-General opened the meeting. They stressed the importance of malaria diagnosis to both WHO and the Global Fund, recognizing that economics—and in particular relative pricing—was a key factor in ensuring the best use of both rapid diagnostic tests (RDTs) for diagnosis and artemisinin-combination therapies (ACTs) for malaria treatment.

2. Rationale for universal access to parasite-based malaria diagnosis—Robert Newman

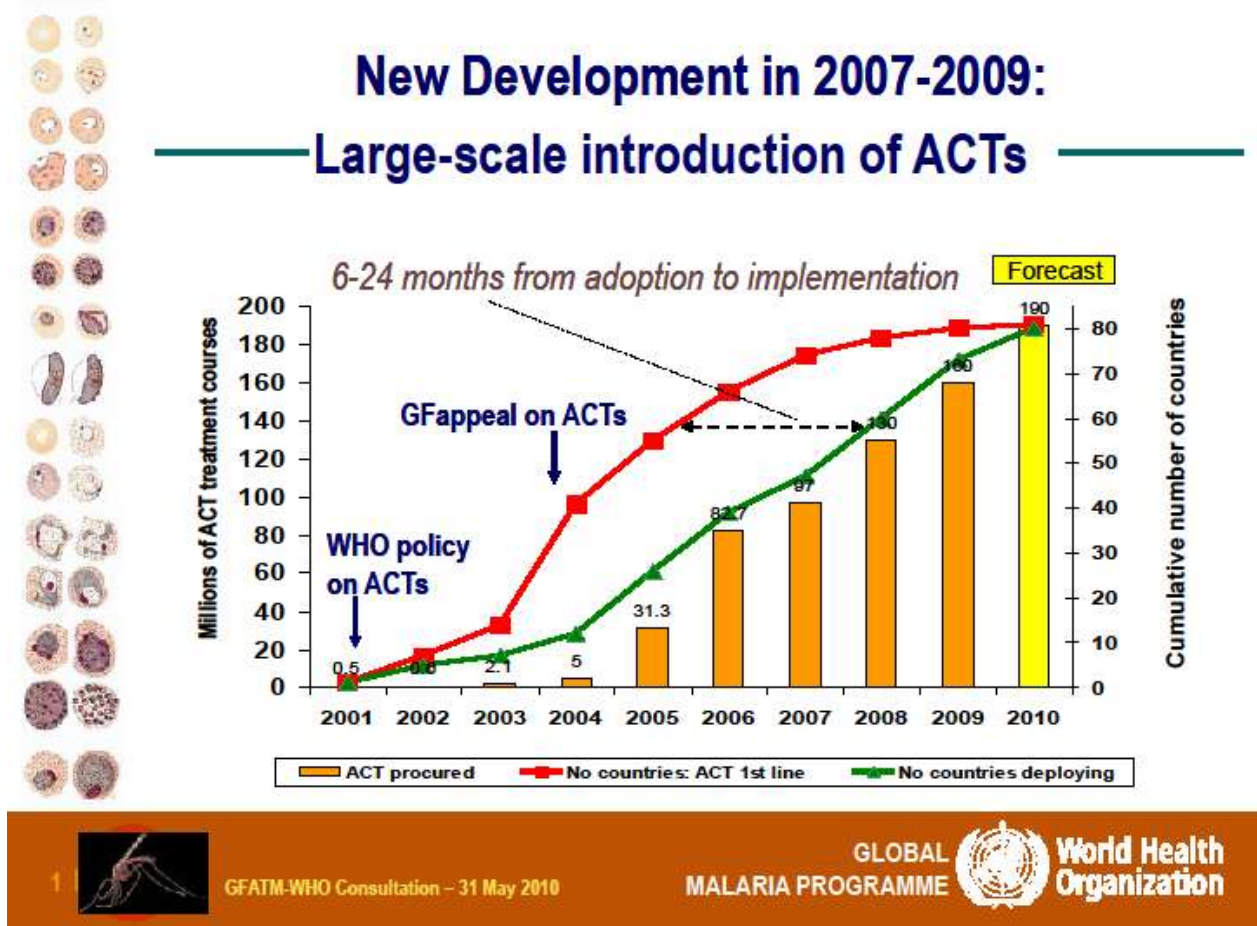
Dr. Robert Newman, Director of WHO’s Global Malaria Programme (GMP), reviewed the history behind the changing WHO recommendation and grounds for moving forward.

As recently as the 1980s, presumptive treatment with chloroquine was recommended as the most appropriate course when malaria was suspected in view of the limited availability of microscopy to provide parasitological confirmation of a malaria diagnosis. It was 2006 when WHO, in its official treatment guidelines, recommended that parasitologic confirmation by microscopy or RDT become the norm for all except “children under 5 years of age living in areas of high transmission where treatment is based on clinical diagnosis” and any case of “suspected severe malaria where parasitological confirmation is not immediately possible.” In 2010, the 2nd edition of the guidelines broadened the recommendation to include children under 5, leaving only an exception for cases where parasitologic confirmation is not accessible, defined as “results not available within 2 hours of patient presenting to health facility.”

Progress has been made rapidly in recent years. The Integrated Management of Childhood Illness (IMCI) has been systematically rolled out in developing countries around the world. Since 2007, the WHO Malaria RDT Evaluation Programme, jointly coordinated by WHO, TDR, FIND and US CDC, completed Rounds 1 and 2 product testing in 2009 and 2010, providing a tool for countries to use in choosing an appropriate RDT. Quality assurance guidelines for microscopy also have been developed by WHO.

Since 2001, ACTs have been adopted by nearly all malaria-endemic countries and sales went from less than one million to a projected 190 million courses in 2010 (Figure 1).

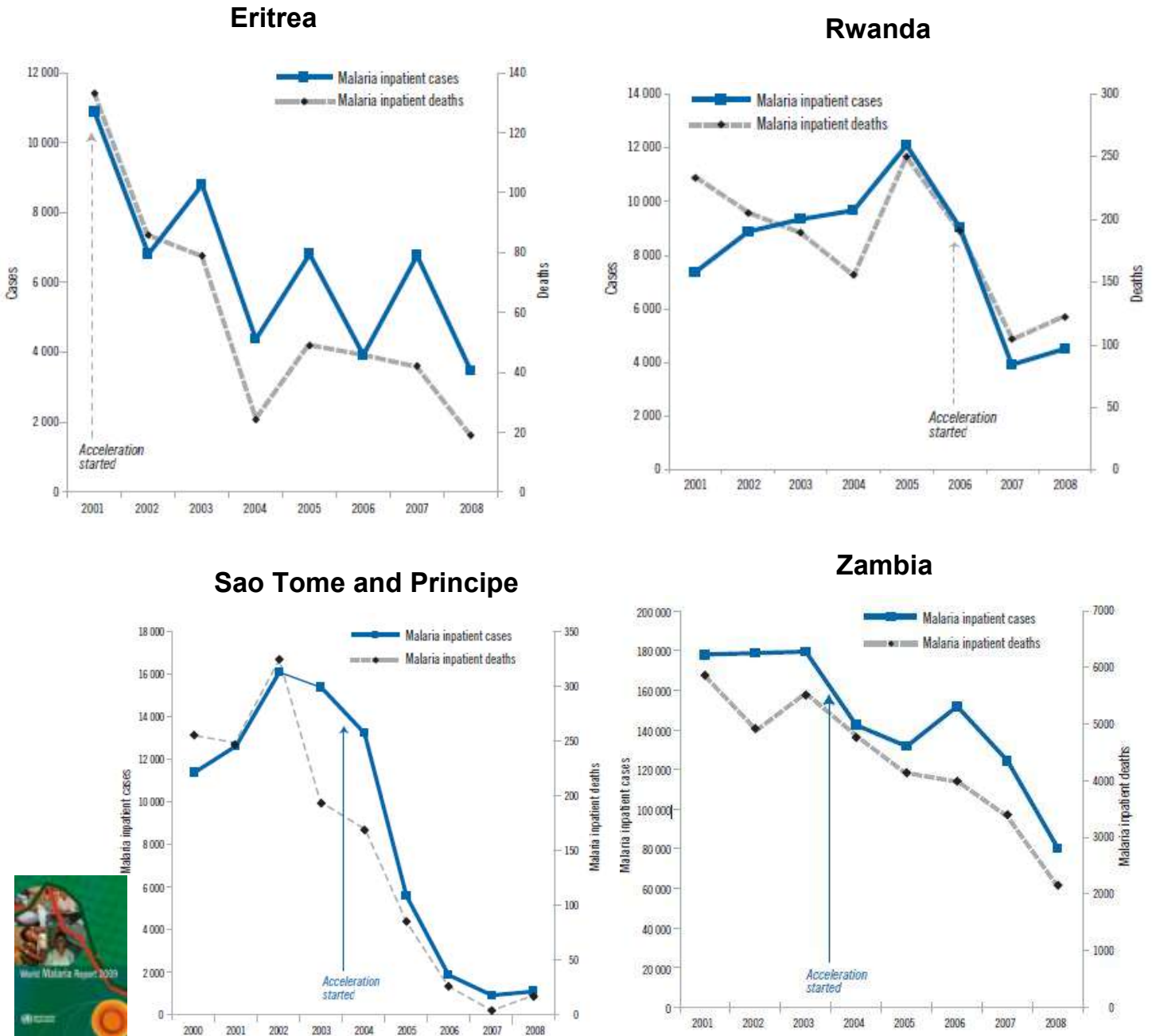
Figure 1



At the same time, malaria control has been successful—remarkably so in some countries—reducing the proportion of fever patients who have malaria (Figure 2). A systematic review of 24 studies between 1989 and 2005 found that a median of 26 percent of patients suspected of having malaria actually had parasites present, and the median *Plasmodium falciparum* parasite prevalence rate at ages 2-10 fell from 37 percent in 1985-1999 to 17 percent in 2000-2007.

Figure 2

**Reduction of > 50% in cases:
9 African countries and 29 outside of Africa**



Malaria is not the only pathogen making people sick. Focusing only on malaria means that people are not treated effectively for the other possible cause of illness. Evidence confirms that patients initially wrongly diagnosed as having severe malaria and managed as such do worse than patients correctly diagnosed sooner. The dangers of presumptive treatment for malaria are:

1. Misdiagnosis of (potentially fatal) non-malarial febrile illness
2. High ACT wastage (most fevers are not malaria in most settings)
3. May accelerate development of antimalarial drug resistance
(especially long acting partner drugs in high transmission settings)
 1. No idea of true number of malaria cases
(difficult to assess impact, identify residual transmission foci, promptly identify resurgences, assess progress toward elimination)
 1. Lose credibility of health workers and health service

The successful expansion of access to parasitological confirmation of malaria diagnosis will require the collaboration of many groups within both the public and the private sectors.

3. Economics and financing of expansion from status quo to universal access: fundamental concepts, questions and tools—Dean Jamison

Professor Jamison, University of Washington, laid the economic and financing groundwork for the consultation and explained terms to the largely non-economist attendees.

Five assumptions underlie the near-term malaria outlook:

1. There is likely to be continued growth in public sector funding (domestic and external) for malaria control.
2. Recent favorable trends in malaria incidence and mortality will continue.
3. Operational and health system constraints to expanding use of RDTs will become less important as time goes on (even though it is true that some of these constraints can't be addressed by money alone in the short term.)
4. Increased availability of and experience with treatment options for RDT negative cases will lead to increased provider/patient compliance with RDT results.
5. Technological progress will continue to offer better and easier-to-use RDT options.

Assuming that access to diagnosis, mainly in the form of RDTs, is going to be expanded from the current 15 percent to approach the WHO target of 100 percent, decisions about expansion paths will be informed by some cost considerations very broadly and some other realities that are discussed by other speakers. The elements of cost that are relevant are:

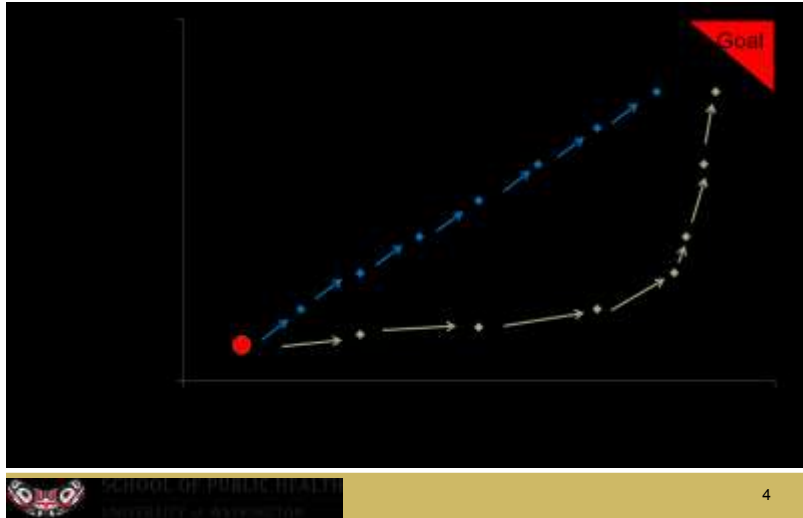
- Financial – the things that money can buy
- System capacity – things money can't buy (in the short run)
- Drug Resistance

With those elements in mind, expansion path choices can be looked at in many ways, including the following four that are of clear importance:

1. Children and adults (Figure 3)

Figure 3

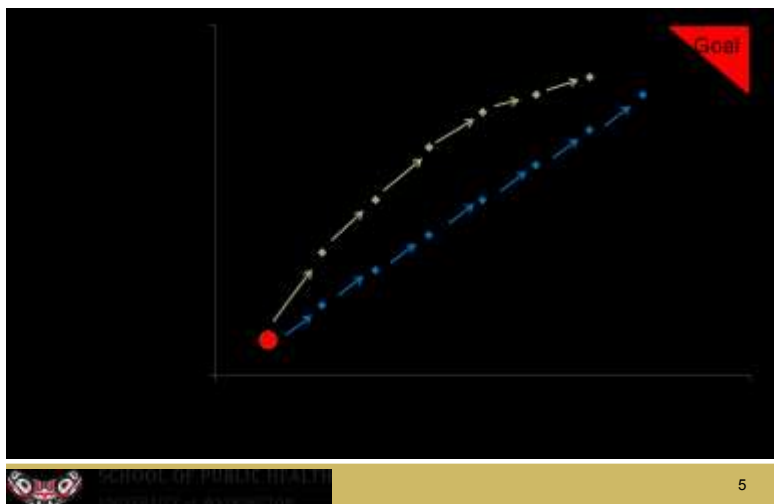
Alternative Expansion Paths



2. Low entomologic inoculation rate (EIR) and High EIR environments (Figure 4)

Figure 4

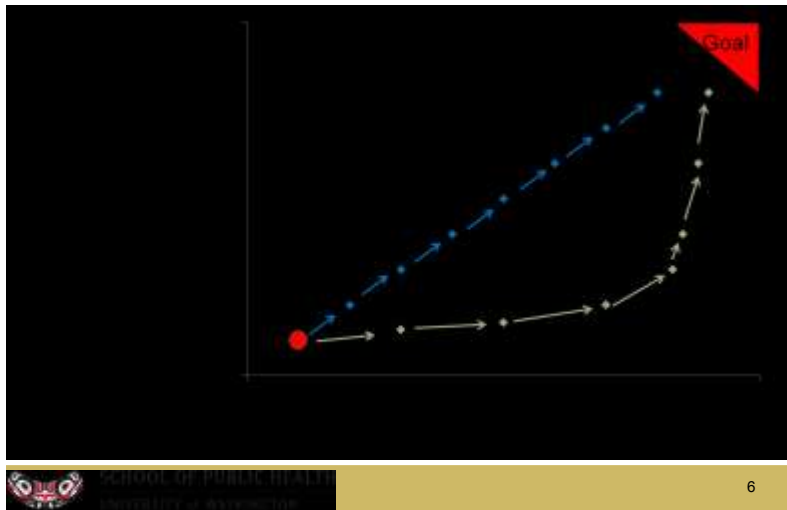
Alternative Expansion Paths



3. Informal private sector and formal public and private sector healthcare facilities (Figure 5)

Figure 5

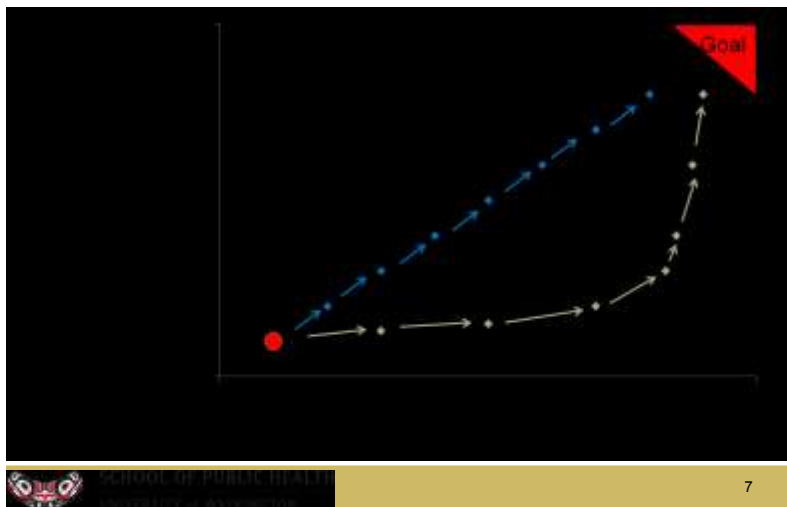
Alternative Expansion Paths



4. High and low availability of treatment for nonmalarial fevers (Figure 6)

Figure 6

Alternative Expansion Paths



To some extent, these schematic representations of possible expansion paths for parasitological diagnosis of malaria can help us think about how easy or difficult it will be to reach the goal along each dimension. The decisions, however, are always about emphasis, and not about

exclusivity. Early attempts can always inform attempts about how to operate under more difficult circumstances. Making good decisions about how to proceed is inextricably linked to getting the financial incentives right.

MORNING SESSION 2

Session Chair: Professor David Schellenberg

1. Malaria diagnostics in endemic countries - David Schellenberg
2. Current costs of RDTs and probable future evolution of malaria diagnostics – Mark Perkins
3. Impact of the use of guidelines for the management of malaria and non-malaria fevers - Valerie d'Acrémont
4. Requirements and challenges for correct management of febrile illness at health facility and community level, including the private sector
 - Panelists: Barry Bloom, Mary Ann Lansang & Franco Pagnoni

This session addressed the current status of parasitological confirmation of malaria diagnosis and of RDTs. Speakers also introduced the main challenges and requirements for large-scale implementation of access to malaria diagnosis, including the need to address non-malaria febrile illnesses.

1. Malaria diagnostics in endemic countries - David Schellenberg

Professor Schellenberg, London School of Tropical Medicine and Hygiene, gave an overview of the main topics. (See the background document prepared for the meeting by Professor Schellenberg and colleagues; Appendix 2).

Access to parasitological diagnosis of malaria provides multiple benefits: to the patients, as it avoids expense and adverse effects due to unnecessary malaria treatment, and allows better identification and treatment non-malarial illnesses; to the prescribers, as it increases confidence in diagnosing febrile illnesses; to the health system, as it strengthens malaria surveillance and capacity for estimating drug requirements, the cost effectiveness and sustainability of ACT policies. By better targeting antimalarial treatment it limits the supply requirements for *Artemisia annua* and, by improving identification and investigation of treatment failures, it contributes to reducing the risk of drug resistance. All benefits related to better targeting of antimalarial treatment with malaria diagnostics increase with the progressive reduction of malaria.

The greatest need is to increase access to malaria diagnostics in the private sector, where most patients acquire drugs for malaria, often through unlicensed, unregulated drug outlets. More operational research is required, especially in low-income settings with weak regulatory capacity, to identify incentives for patients and caretakers to seek parasitological confirmation of malaria and to dispense appropriate treatment on the basis of the results. The proportion of RDT negative patients who are given antimalarials is highly variable, and affected by seniority of staff (good compliance by VHWs), prior use of diagnostics (poor compliance if previous experience with microscopy), and the common practice of treating all fevers as malaria.

Implementation of RDT programmes requires funding of all the operational components: in addition to the cost of goods, funding should cover transport/storage, community education, training and supervision, quality assurance, lot-testing and test accuracy monitoring in the field, gloves, sterile sharps and disposal containers, as well as medicines for the management of non-malaria fevers. There is a need to better understand the full economic requirements of universal access to malaria diagnostics, as well as the cost-effectiveness of alternative expansion pathways in different settings. More operational research is needed, especially to increase access to RDTs in the private sector.

2. Current costs of RDTs and probable future evolution of malaria diagnostics – Mark Perkins

Dr Perkins, Chief Scientific Officer of FIND, provided an overview of the expected technological improvements in malaria diagnostics in the near future.

Since the introduction in 1993 of the first malaria RDT in the market, *ParaSight F* test (Becton Dickinson Advanced Diagnostics), the use of malaria RDTs has progressively increased, especially in recent years. According to the WHO World Malaria Report, a total of 86 million RDTs were procured in 2008, and 142 million blood films examined for malaria by microscopy (missing data from the Eastern Mediterranean and the Western Pacific Region). The current FCA prices to WHO are on average USD 0.63/test for Pf-detecting RDTs and USD 0.99/test for combo RDTs. It is expected that the quality of RDTs based on current technology (lateral flow immuno-chromatography) will improve in sensitivity, specificity, species identification, reproducibility, thermostability, shelf-life and standardization, as these parameters are already assessed by the ongoing WHO/FIND/CDC malaria RDT product testing programme.

In the future, pending major technological investments and progress, the same technologies could be used to analyse alternative samples, additional pathogens and may also include disease severity indicators. Alternative approaches using molecular markers can be developed into field reference standards for specific investigations of malaria cases or for clinical trials, against which other methods (including RDTs) may be evaluated (loop mediated isothermal DNA amplification [LAMP]). Systems in the development pipeline could provide operator-independent optical detection of malaria parasites with automatic readers, even with "cell phone" technologies using the mobile phone built-in camera. New methods have the potential of reagent-free sampling, such as multidimensional spectroscopy analysis and magneto-optical detection methods based on the refractivity of haemozoin, which could be the basis for non-invasive diagnostic methods. New diagnostic tools are also required to support malaria elimination efforts, especially new antibody detection assays, field tests for G6PD deficiency, and high-throughput molecular testing for malaria surveillance.

3. Impact of the use of guidelines for the management of malaria and non-malaria fevers - Valérie d'Acremont

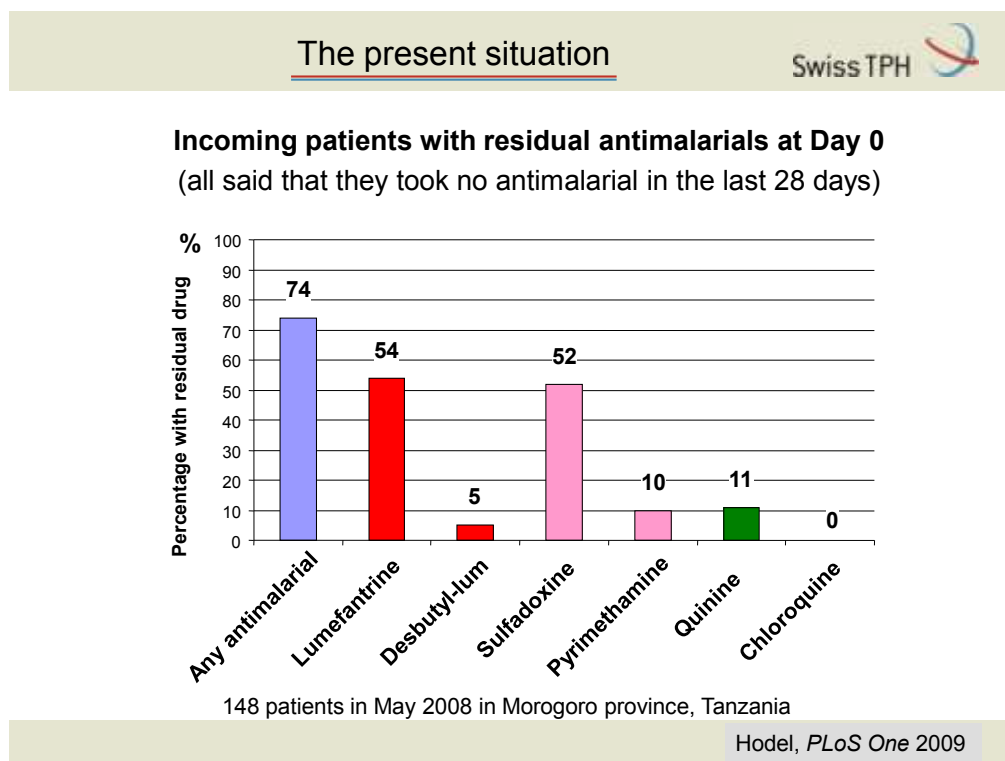
Dr d'Acremont, Swiss Tropical and Public Health Institute, presented an overview of current WHO guidelines for the management of people who test negative for malaria, and the results of studies completed recently in Tanzania.

Different guidelines are available for the management of febrile patients at different levels of care. The WHO guidelines for the management of common illnesses with limited resources at district hospital level recommend the use of malaria diagnostics if the child has a fever for less than 7 days duration. Malaria is considered in the differential diagnosis if there are no localized signs of fever and no rash. In the past, the Integrated Management of Childhood Illness (IMCI) guidelines for peripheral health facilities were mainly for areas without laboratory facilities and based on clinical diagnosis. More recently malaria testing has been added to the IMCI guidelines to assess all children presenting without danger signs with fever of less than 7 days duration. In areas of low transmission malaria testing is done only in the absence of other obvious causes of fever. The guidelines for the Integrated Management of Adolescent and Adult Illnesses (IMAI) are very similar and currently being updated. The guidelines for integrated Community Case Management deal with the management of fever, cough and diarrhea, in a very similar way to IMCI, i.e., RDTs are recommended to assess children without danger signs presenting with fever of less than 7 days duration.

The current practice in many endemic countries, however, is to treat all cases, regardless of high/low endemicity levels, age or even history of fever or not, with Artemisinin-based Combination Therapies (ACTs). If the patients also have diarrhea or vomiting, they are often given both ACTs and antibiotics. If the patient has cough, or there is suspicion of typhoid fever or urinary tract infection, then antibiotics are most often administered. As a result of this large over-treatment with antimalarials, many people in the community have sub-therapeutic blood levels of antimalarials, contributing to the development and spread of drug resistance. A recent study (Hodel et al., 2009)¹ reports that among patients presenting to a health center in Tanzania, all reporting no antimalarial treatment over the previous 28 days, a total of 74% had residual concentration of antimalarials in their blood, the highest proportion with lumefantrine (54%), and sulfadoxine (52%) (Figure 7).

¹ Hodel EM, Kabanywanyi AM, Malila A, Zanolari B, Mercier T, Beck HP, Buclin T, Olliaro P, Decosterd LA, Genton B. Residual antimalarials in malaria patients from Tanzania--implications on drug efficacy assessment and spread of parasite resistance. *PLoS One* 2009;4(12):e8184.

Figure 7



A study of the etiologies of fever in Tanzania has documented that malaria is responsible for 10% of cases of fever, the rest being mainly acute respiratory infections (50%), followed by fevers of unknown etiology (20%), gastroenteritis (9%), urinary tract infections (5%) and typhoid (3%).

In Tanzania the introduction of malaria RDTs resulted in a significant reduction of the consumption of ACTs and of iv quinine in all health facilities in both urban and rural areas. After the introduction of RDTs, the proportion of febrile patients treated for malaria in spite of negative results decreased considerably, but the consumption of antibiotics increased.

The current situation in which ACTs are deployed without RDTs and no IMCI implementation is not acceptable. The introduction of RDTs alone did not help to rationalize the prescription of antibiotics. The way forward is large-scale deployment of malaria RDTs combined with IMCI and IMAI implementation.

4. Requirements and challenges for correct management of febrile illness at health facility and community level, including the private sector

- Panelists: Barry Bloom, Mary Ann Lansang and Franco Pagnoni

The panel session focused on the requirements of handling non-malaria febrile illness based on a series of projects of community management of fever, using simplified IMCI guidelines.

A cluster-randomized trial of community case management of febrile children was implemented in Zambia, using RDT positivity to confirm malaria (treated with ACT) and high respiratory rate as a sign of pneumonia (treated with antibiotics). This approach resulted in a 4-fold reduction in the use of ACTs, a 5-fold increase in the management of non-severe pneumonia at community level, and a 56% reduction in treatment failures for pneumonia. Implementation of this approach demands financial support and subsidies for all components, i.e. ACTs, RDTs and antibiotics, and review of regulations to allow CHWs to use RDTs and dispense ACTs and antibiotics. More investment is needed in education, training, incentives and oversight of public and private sector pharmacies and shopkeepers to promote the integrated management of fevers at the community level.

More efforts should be made to investigate fever etiologies, not only among febrile patients with a negative RDT result, but also among the febrile patients with a positive RDT result, as other causes of fever may be present concurrently with a malaria infection. The IMCI approach aims at improving case management skills of health providers, family and community practitioners and health systems, and should be promoted more. Also larger investments should be made in implementation research, especially to identify the determinants of persistent/durable behavioral changes.

TDR is coordinating studies in 6 African countries to compare community-based presumptive treatment of fever with community case management using RDT positivity to confirm malaria (to be treated with ACT) and high respiratory rate as sign of pneumonia (to be treated with antibiotics). Preliminary results from Nigeria, Uganda and Ghana show that the CHWs can accurately perform RDTs, assess respiratory rate and correctly prescribe ACTs or antibiotics. In Burkina Faso, there were problems with apparently low specificity with RDTs used by CHWs. In Ghana the use of RDTs and measurement of respiratory rate resulted in a decrease in the consumption of both ACTs and antibiotics.

Key points of discussion

- ▶ For the evaluation of non-malaria treatable febrile illnesses, test detecting C - reactive protein (CRP), including semi-quantitative assays, are being developed and considered with interest by malaria RDT developers. There is also interest in the identification of biomarkers for pneumonia and typhoid, but there is no international forum for setting priorities, i.e. to identify the 4-5 priority causes of non-malaria febrile illnesses, on which to invest for test development over the next 5+ years.
- ▶ There are no major incentives for the manufacturing companies to invest in the development of new malaria tests. A systematic market analysis of malaria diagnostics and its increasing role in control, as it was done in the past by TDR-FIND for TB diagnostics, may play a positive role. This analysis should also include the evaluation of ongoing and potential funding to support research in malaria diagnostics.

- ▶ More efforts are needed to expand diagnosis and treatment at community level. RDTs should be deployed as part of comprehensive programmes for community-based management of fever, in both public and private sectors. It is not clear how the IMCI algorithm could be implemented by shopkeepers, and this may need intensified training, behavior change and communication and regulatory oversight.
- ▶ Quality assurance needs to be strongly implemented in both the public and the private sectors, but innovative methods need to be developed to address the specific requirements of the private sector. This is even more critical as the regulatory capacity for diagnostics is particularly weak in malaria endemic countries.
- ▶ It is important to address the management of RDT negative cases, investing in the identification of patients who do not need antibiotics. Promoting the measurement of respiratory rate may lead to better targeting of the prescription of antibiotics. For the evaluation of the non-malarial treatable febrile illness, it is important to develop algorithms to identify the site of infection and the possible causes of illnesses. In adults it is important the evaluation of bacterial septicaemia and tuberculosis, which are common among febrile patients.
- ▶ Most of the studies have considered the requirements for *P. falciparum*-detecting RDTs, but more studies are needed to also consider the requirements for *P. vivax* diagnosis.
- ▶ In countries in which HIV RDTs and syphilis RDTs are being deployed, the implementation of malaria RDTs should be combined with these programmes, to share resources in term of training, supervision, supply management and external quality assurance.

AFTERNOON SESSION 1

Session Chair: Professor David Schellenberg

1. Tools and experience with RDTs + ACTs deployment at community level - David Bell
2. Operational costs of large scale implementation of RDTs in Senegal - Moussa Thior
3. Experience in Cambodia with private sector deployment of RDTs and ACTs - Duong Socheat
4. Malaria mortality in India—Prabhat Jha

The first session in the afternoon focused on a sharing of experiences with the deployment of RDTs and ACTs, starting with an overview of deployment at the community level and followed by presentations from Senegal (public sector deployment) and Cambodia (private sector deployment), and a new analysis of malaria mortality in India.

1. Tools and experience with RDT + ACT deployment at community level - David Bell

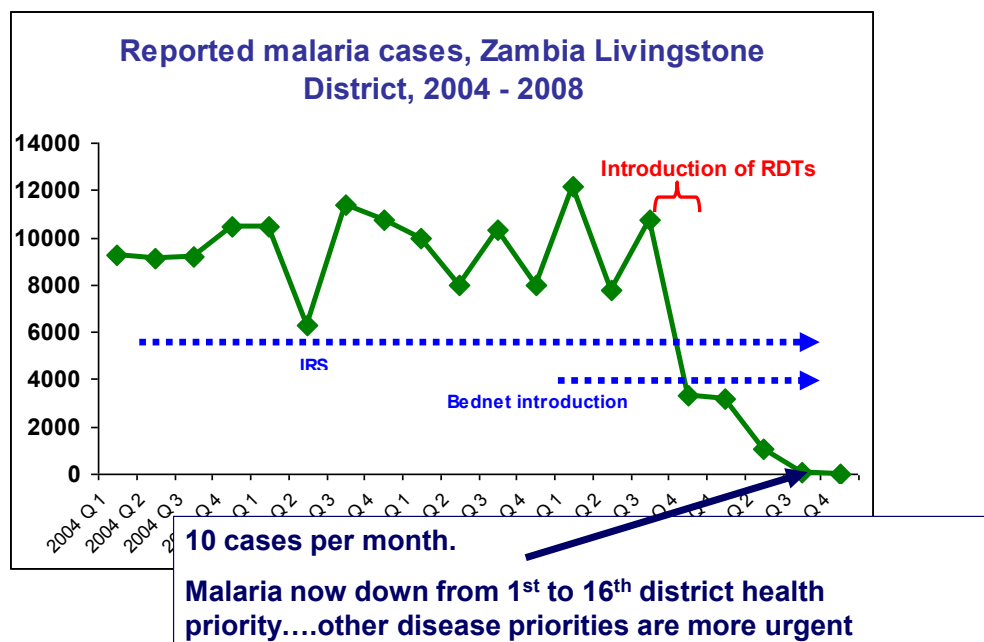
Dr David Bell, from the WHO Global Malaria Programme, provided an overview of the steps and processes required to ensure accurate malaria diagnosis at the community level and discussed implementation experiences in countries such as Zambia, Uganda, Tanzania and Cambodia. The key determinants for ensuring effectiveness of RDTs in communities are: manufacturing quality, procurement and product testing; lot testing of procured RDTs; maintaining quality in the field; user proficiency through job aids and training; and use of RDT results to guide appropriate case management and reporting. The stability of RDTs in the WHO/FIND product testing programme is assessed at two months at 35 and 45°C. However, continuous monitoring of RDT quality through lot-testing is important because of lot-to-lot variation that could affect the accuracy of RDTs. FIND, TDR, WHO and other partners are conducting field implementation trials on the use of positive control wells, which would facilitate community-level evaluation of RDT performance.

One of the notable examples featured was the experience of Zambia, where job aids and training improved the proficiency of community health workers in the short term (3 – 6 months post-training) and long term (12 months). Figure 8 below shows the rapid drop in the number of reported malaria cases in 2007 – 2008 after introduction of RDTs. The use of short message services (SMS) by mobile phones in Uganda and Tanzania were shown to improve reporting of parasitologically confirmed malaria cases and stock levels of RDTs and ACTs. In Uganda “Rapid SMS” project, it was noted that stock-outs of RDTs were associated with dramatic increases in ACT consumption.

Figure 8

12 month CHW follow-up Zambia 2007-8

Zambia NMCC, Mal Consortium, WHO, FIND, URC



The minimum standard for funding and building a diagnostic program should cover not only the procurement of RDTs but the full package, including: transport and storage; training and supplies for management of non-malarial fever; community education; training on RDTs and supervision; monitoring of accuracy in the field; lot-testing and laboratory monitoring; and procurement of gloves, sharps containers and other supplies. The following points summarize much of the discussion:

- Microscopy is unlikely to be sustainable at sufficient quality, particularly at the community level;
- Good quality RDTs are available for community-level malaria case management, with good levels of sensitivity, specificity and thermal stability;
- Good procurement and monitoring of quality of RDTs will be critical issues to address in scaling up RDT use;
- Experience shows that RDTs can be used safely at clinic level, with health workers adhering to results, but this requires good resourcing and planning;
- Innovative ways to monitor resource use and adherence to results are likely to be necessary;
- Most febrile patients, who would receive an ACT if treated presumptively, do not have malaria. Without parasitological confirmation, patients with non-malarial febrile illness will continue to be incorrectly managed;

- Lack of parasitological confirmation cannot delay ACT access, but RDT deployment needs to catch up with efforts to scale up access to antimalarial treatment.

2. Operational costs of large scale implementation of RDTs in Senegal - Moussa Thior

Dr Moussa Thior, Coordinator of the National Malaria Control Program (NMCP) in Senegal, presented the experience of the Senegal Ministry of Health and the NMCP in scaling up RDT deployment. Based on a 2006 pilot study that demonstrated the feasibility of RDT introduction in Senegal, RDTs were deployed in 2007 in 65 districts where 2,607 health care workers (HCWs) were trained. In 2008, RDTs were also introduced in hospitals and military centers, and 2,187 HCWs were re-trained. In 2009, RDTs were deployed at the community level (covering 94% of health huts) and 3,716 community health workers were trained. Also in 2008 – 2009, home-based case management was implemented, enabling ACT and RDT access in remote villages.

Figure 9 below shows the dramatic drop in malaria-confirmed cases from 2006 to 2009, coinciding with the implementation of the national malaria strategy calling for scaling up of WHO-recommended malaria interventions (introduction of RDTs, microscopy strengthening, prompt and effective treatment with ACTs, and data quality assurance).

Figure 9

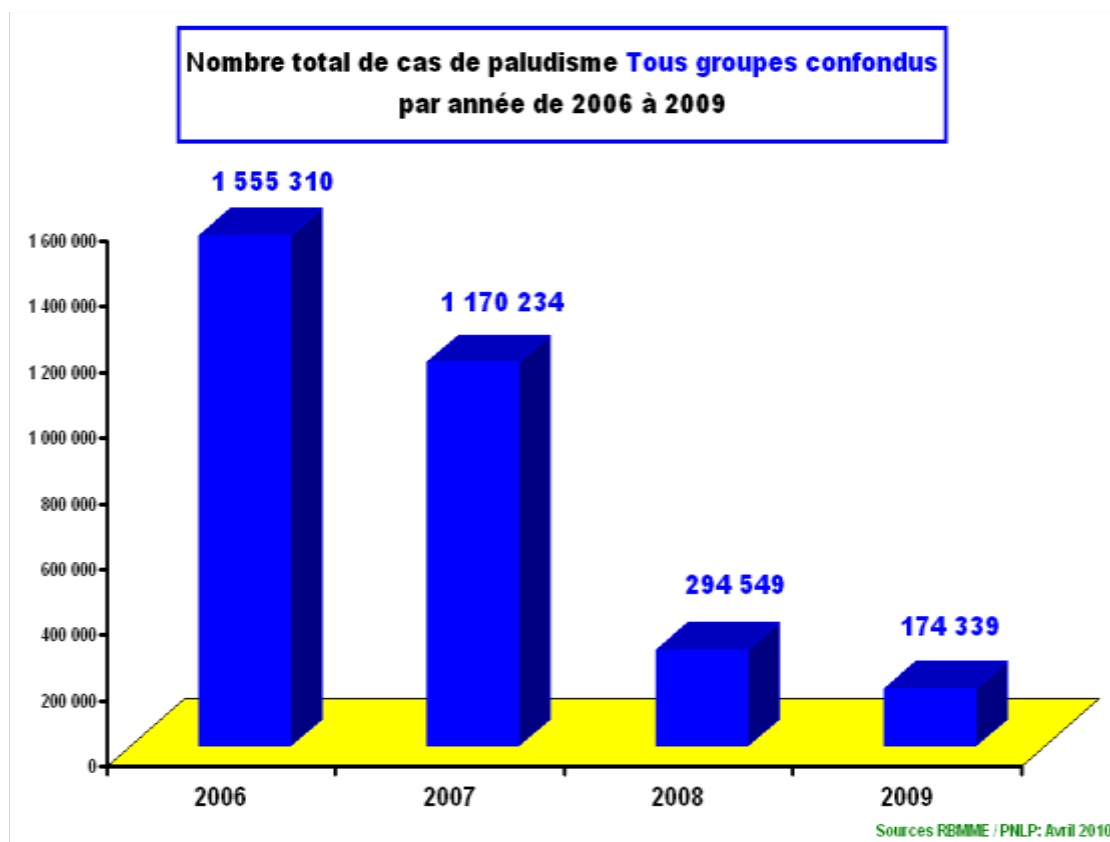
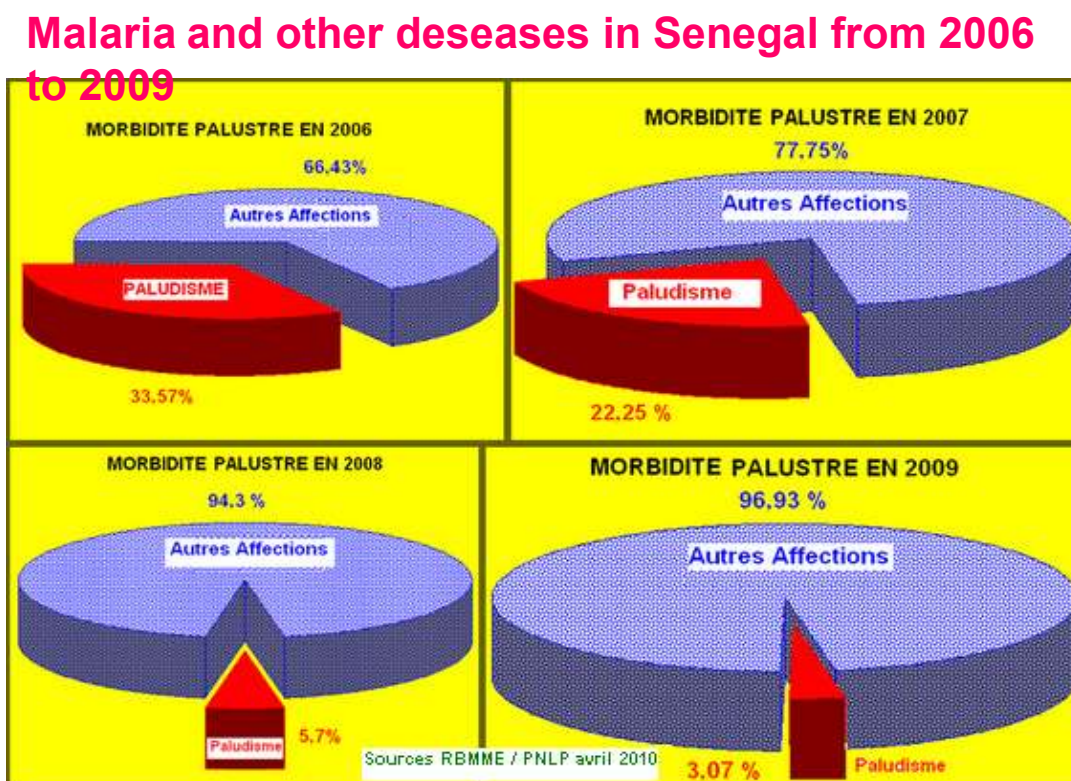


Figure 10 below illustrates the significant drop in cases attributable to malaria from 33.6% in 2006 to 3.1% in 2009. As a result, ACT consumption decreased from 1,555,310 in 2006 to 184,170 in 2009, equivalent to total savings of ~ US\$ 3.2 million for the period 2007 – 2009 (assuming US\$ 1.00 per ACT treatment). On the other hand, it was estimated that the cost to train one HCW was only 62 Euros and another 42 Euros to train one CHW.

Figure 10



Key factors in the success of the national malaria strategy and RDT implementation in Senegal are: the political commitment of the Ministry of Health and the NMCP; a well-organized health system; training of healthcare providers with appropriate tools; regular supervision of the healthcare providers; technical assistance provided by local partners such as the University of Dakar; and sustained communications with community-based organizations and NGOs.

3. Experience in Cambodia with private sector deployment of RDTs and ACTs - Duong Socheat

Dr Socheat, Director of the Cambodian National Centre for Parasitology, Entomology and Malaria Control, shared the experience of Cambodia in using an innovative strategy for the deployment of RDTs and ACTs using a community-based public-private mix approach to early diagnosis and appropriate treatment. This was developed as a response to the growing problem of multidrug resistance in Cambodia, inappropriate prescription practices in the private sector,

the proliferation of fake antimalarial drugs (up to 70 – 80% in drug retailer shops in 1999), and inappropriate treatment-seeking behavior and drug use.

In 2000, the government instituted a policy to make available co-packaged artesunate and mefloquine and RDTs both at highly subsidized prices. The RDTs were most heavily subsidized, making them very inexpensive at retail stores. Quality assurance of the commodities and training of village malaria workers (VMWs) was also part of the program. Figure 11 shows an increase in the number of RDTs in the public sector, including those deployed through VMWs, from 2004 to 2010.

Figure 11

Evolution (quantity used) of RDT to detected malaria in Cambodia

Year	Public		VMWs	
	Quantity	Total price	Quantity	Total price
2004	86,000	66,220 \$	18,771	14,454 \$
2005	79,875	61,504 \$	50,855	39,181 \$
2006	31,250	16,707 \$	84,917	45,400 \$
2007	65,000	34,802 \$	60,304	32,263 \$
2008	164,200	125,449 \$	57,882	44,222 \$
2009	432,200	330,201 \$	123,157	94,092 \$
2010	574,844 *	439,181 \$		

In the private sector, the Malarine® social marketing project implemented by PSI since 2003 resulted in the deployment of the same co-packaged ACTs (Malarine® - \$0.63/blister pack for adults and \$0.30/blister for children) in 17 endemic provinces in Cambodia. In 2009, RDTs (Malacheck® - \$0.25/test) were also distributed widely. In addition to the deployment of 20 sales representatives who each visited 300-350 outlets per month and 10 medical representatives who visited more than 600 health providers, the project carried out multi-level training of 1,800 qualified, semi-qualified and non-qualified providers.

There continue to be challenges such as: timely procurement of RDTs and ACTs, supply chain management, quality assurance, and interpretation of and adherence to RDT results. Proposed recommendations include the following:

- Ensure availability and access to both ACTs and RDTs in all public health facilities and invest efforts to increase motivation of staff at all levels

- Encourage social marketing of ACTs and RDTs, which can reduce the presence and use of counterfeit drugs and monotherapies in the market;
- Establish monitoring and supervision of ACTs and RDTs sold under the social marketing project, particularly in terms of pricing;
- Strengthen the community-based approach in remote malaria-endemic areas; and
- Encourage close collaboration between the public and private sectors to achieve universal access to ACTs and RDTs.

4. Malaria Mortality in India—Prabhat Jha

Professor Jha, Director of the Centre for Global Health Research at the University of Toronto, briefly presented the results of the Million Deaths Study (MDS), a survey of 1.1 million homes in India to investigate the causes of death for 0.13 million deaths in 2001 – 2003 through verbal autopsy. There were around 200,000 deaths coded as malaria (65% agreement between two trained research staff), mostly in the states of Orissa and Chhattisgarh. Most notably, the MDS showed a U-shaped distribution of malaria deaths, with peaks at 0 – 4 years and 60 – 69 years of age. This is in contrast to WHO malaria mortality statistics, which indicate a slight preponderance of deaths at the 0-4 year age group. In relation to 1.7 million fever-associated deaths in 2005 among people less than 70 years old, malaria was the fourth leading cause of death.

These observations are relevant to an expansion of parasitological confirmation of malaria: (1) there are more adult malaria deaths in India than previously estimated; (2) greater access to ACTs remains a top priority, particularly in highly endemic areas of India; and (3) separate guidelines for RDT and treatment are needed for those with access to health facilities and those without access.

AFTERNOON SESSION 2

Session Chair: Professor Dean Jamison

1. Cost-effectiveness analysis of malaria diagnostics as a basis to evaluate the effectiveness of alternative pathways to reach universal access to parasitological confirmation of malaria – Yoel Lubell
2. Prices, incentives, demand for malaria diagnosis and treatment – Jessica Cohen
3. Affordable Medicines Facility-malaria (AMFm): lessons from conception, design and preparatory phase - Olusoji Adeyi

This session focused on some of the economic aspects more in detail, from general considerations based on cost-effectiveness analysis to consideration of consumer behaviour related to the use of subsidized RDTs and ACTs from drug shops in rural Kenya. It also drew some lessons from the setup of AMFm Phase I.

1. Cost-effectiveness analysis of malaria diagnostics as a basis to evaluate the effectiveness of alternative pathways to reach universal access to parasitological confirmation of malaria – Yoel Lubell

Dr Lubell, from the Mahidol-Oxford Research Tropical Medicine Unit in Bangkok, reviewed existing approaches to and general conclusions from different cost-effectiveness analysis models for malaria diagnostics, highlighting some limitations and the need for local adaptation.

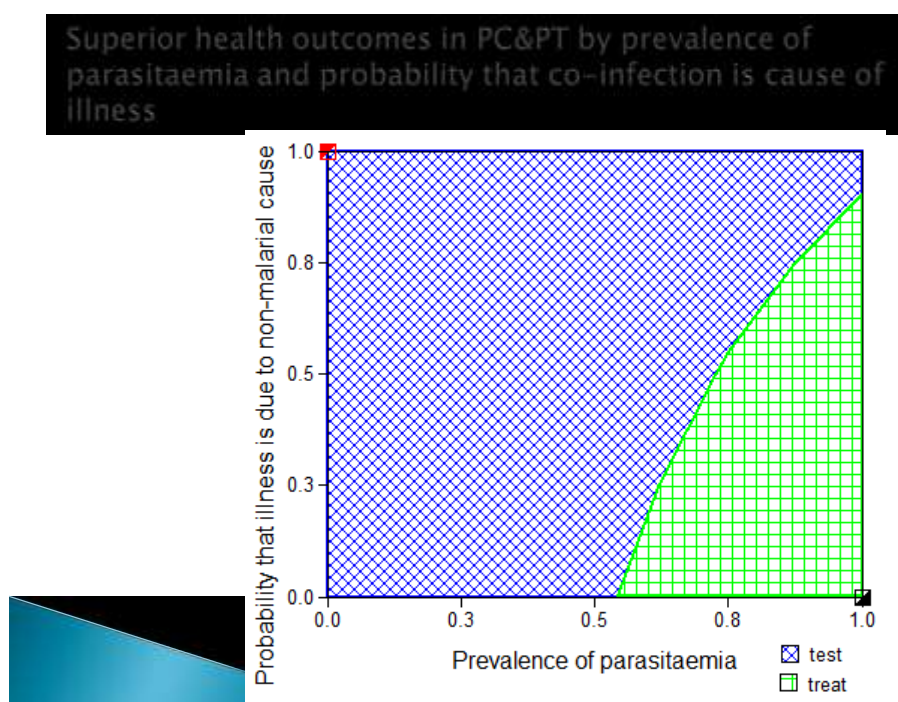
The cost-effectiveness of malaria RDTs is dependent on multiple factors, including: 1) accuracy, costs, durability and target antigens of the RDTs; 2) costs and effectiveness of the antimalarial treatment, 3) adherence to test results and treatment practices for non-malaria illnesses; 4) malaria epidemiology and access to health facilities; and 5) perspective/scope of the analysis/evaluation itself.

The various types economic studies of RDTs vary in scope. At the least detailed level are the studies focusing on direct expenditures, calculating the cost of presumptive treatment as opposed to parasitological confirmation based on costs of RDTs and ACTs, prevalence, sensitivity, specificity, and, in some cases, costs of alternative treatment and severe illness. All studies demonstrate a reduction in over-treatment with antimalarials with increasing use of RDTs, and most studies find targeted treatment less costly, assuming high, pre-subsidy ACT prices. If a decision on the universal use of RDTs has been reached, cost studies for immediate expenditure provide simple but essential tools to determine target prices.

In studies evaluating health outcomes, a number of modeling and trial based evaluations have found RDTs to be cost-effective in both high and low transmission settings, taking into account the health outcomes of non-malaria febrile illnesses. The main limitation of these models is that they mostly assume perfect adherence, and uncertainties are not always explored, especially the risk of untreated severe malaria progressing to death by age-group and transmission levels (for which there is wide heterogeneity of expert opinions).

The probability that RDTs are cost-effective exceeds 50% in all areas where the prevalence of parasitaemia among febrile individuals is below 80% - probably everywhere. The parasitological confirmation of malaria generates superior health outcomes in almost all settings except in areas where the prevalence of parasitaemia is very high, and where the probability that illness is due to non-malaria cause is relatively low. Results, however, vary by setting, perspective and assumptions and there is a need for locally relevant decision making rather than a global recommendation.

Figure 12



2. Prices, incentives, demand for malaria diagnosis and treatment – Jessica Cohen

Professor Cohen, from the Harvard School of Public Health in Boston, presented the results of a voucher scheme project recently completed in Kenya, to analyse the impact of different levels of subsidies on the use of RDTs and ACTs sold by drug vendors.

RDTs in drug shops present an opportunity, but also pose many challenges, including: 1) treatment of RDT-negative cases, 2) cold chain/sharp disposal, 3) incentives/subsidy and training at full scale, 4) affordable price to consumers and 5) consumer demand for RDTs.

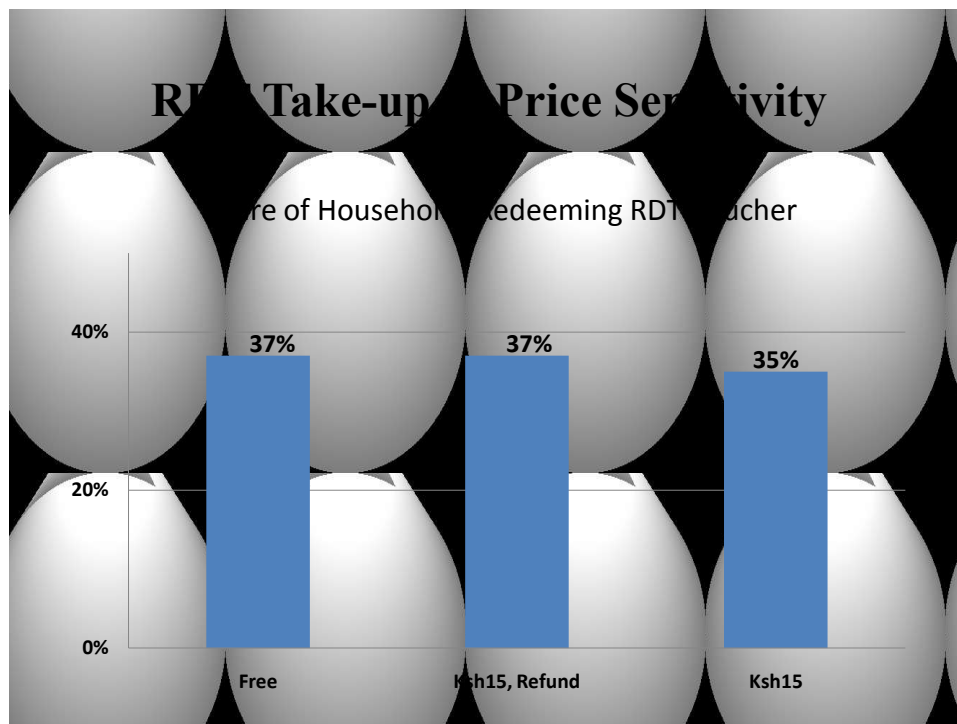
Pilot studies with ACTs and RDTs made available to drug vendors have been implemented in Kenya and Uganda to explore the impact of RDT pricing/subsidies on demand for parasitological confirmation of malaria versus presumptive treatment. The study in Kenya involved randomized distribution at the household level of vouchers for ACTs and RDTs redeemable at local drug

shops. Three values of vouchers were distributed to the ACT price treatment group (40, 60, 100Ksh per adult treatment course) and three values of vouchers assigned for RDTs (0, 15 with refund if positive, 15 Ksh). A control group also received a high priced voucher for ACTs (500Ksh) and another group was randomly assigned to receive no RDTs. A total of 2928 households participated in the study and no IEC/BCC interventions were implemented.

Most ACT buyers (78-84%) wanted to be tested, regardless of RDT price. However, there was no price sensitivity with RDT vouchers (Figure 13). In addition, availability of vouchers (or not) for RDTs had no influence on ACT use.

Contrary to what one might expect, households were less likely to use RDTs at higher ACT prices. RDT were used most for young children (3 months - 3 years) and for teenagers and adults (14+ years). RDTs did not increase treatment seeking, and it moderately increases the adherence to treatment with ACTs once the test results are positive.

Figure 13



Behavioral patterns related to RDTs are hard to understand, and messages of BCC campaigns should be guided by local perceptions about malaria diagnosis and treatment.

3. Affordable Medicines Facility-malaria (AMFm): lessons from conception, design and preparatory phase - Olusoji Adeyi

Dr Adeyi, Director of the Affordable Medicine Facility-malaria (AMFm) provided an overview of this project, its objectives, timelines and expected results.

The AMFm is a new initiative providing a supranational ACT subsidy at the top of the supply chain, plus measures to support its implementation, working with public and private sectors and NGOs. The AMFm is a new architecture of financing, and a new approach to development assistance in which market forces will play a dominant role to provide public health benefits. The objectives are to increase the affordability, availability, use of ACTs and crowd out oral artemisinin-based monotherapies, chloroquine and sulfadoxine-pyrimethamine for falciparum malaria. The overall goal of this initiative is to reduce malaria mortality and to delay the spread of resistance to artemisinin.

Phase 1 of AMFm is a short-term exercise to demonstrate how this approach works in practice over a 24-month period in 8 countries (Cambodia, Ghana, Kenya, Madagascar, Niger, Nigeria, Tanzania and Uganda) to derive lessons that can guide its possible extension to other countries. Based on principles laid out in the 2004 IOM report *Saving Lives, Buying Time*, it was developed under the auspices of RBM and approved by the Global Fund Board in November 2008. The first ACT deliveries are expected to reach the pilot countries in September 2010.

The work of AMFm includes: 1) negotiations with manufacturers to reduce the ACT sales price; 2) co-payment to manufacturers to further reduce the price of ACTs to first-line buyers to a target price of USD 0.05; 3) supporting interventions to ensure safe and effective scale-up, including: public education and awareness campaigns; training/monitoring/supervision of ACT providers; planning for national policy and regulatory preparedness; interventions to reach poor and vulnerable groups; expanded diagnostic use in the public sector and learning scalable approaches in the private sector; monitoring drug quality, safety and therapeutic efficacy.

In small-scale demonstration projects at district level in Tanzania and Uganda, subsidized (co-paid) ACTs were chosen 44-54% of the time in private sector outlets over a 6-month period, at an average price to consumers of USD 0.58 per treatment course. During the country-wide implementation in Phase 1, an important element to monitor is how the benefits of the subsidy are distributed in the private sector: are they transferred to consumers or captured by distributors and retailers (middlemen)?

This initiative has a budget of approximately USD 216 million for ACT co-payment, funded by UNITAID, Gates Foundation and UK, and USD 126.7 million for supporting interventions, mainly funded through host grant ACT budget savings made possible through the lower price of co-paid ACTs under AMFm. The AMFm is hosted and managed by the Global Fund Secretariat.

Additional points of discussion

- ▶ Cost-effectiveness analyses of RDTs will benefit from broadening to include resistance and transmission, taking into account the variability in suitability of RDTs.
- ▶ Adherence to results of malaria testing must improve for any RDT subsidy scheme to be cost-effective. BCC campaigns should target both patients and providers. Price alone is not the primary factor in changing consumer and provider behavior to request parasitological confirmation of malaria diagnosis and to prescribe/adhere to treatment on the basis of the test results. Field studies on cost-effectiveness of RDT subsidies

should also monitor impact on ACT and antibiotic consumption (especially for the management of negative cases).

- ▶ The rational use of diagnostics and ACTs by frontline health workers (in both the public and private sectors) is one of the areas of operational research included in the AMFm country-specific grants, but only 3 countries have included this component in their grant applications. In particular, the evaluation of economic incentives for frontline workers, particularly in the private sector, to correctly sell and use diagnostic tests, and incentives to dispense treatment on the basis of the findings should be given high priority. Efficiency of different models for in-country distribution of malaria commodities should be assessed, including distribution from the central medical stores, to serve not only the public sector, but also the NGO and private-for-profit sector.

DAY 2

MORNING SESSION 1 (planned as afternoon session 3, day 1)

Panel discussion: What do we know and what do we need to find out about the economics and financing of expansion from the status quo to universal access to diagnostics?

Panelists: Fred Binka and Phil Musgrove

Professor Binka, a malaria and public health specialist, now at the University of Ghana, led off with the reminder that we have to make a start at expansion, even though all the blocks are not in place, and even though RDTs themselves are not perfect. The main thing is getting the relative prices right. RDTs should be available in both the public and the private sectors, but are likely to pose more challenges in the private than the public sector. Effective, simple and cheap treatment for non-malaria febrile illnesses should be made available in parallel with the large-scale deployment of RDTs.

Dr. Musgrove, an economist from the journal *Health Affairs*, agreed, especially on prices. He reminded the group that patients, healthcare providers and people who sell drugs have different priorities and goals, and would respond to different incentives, all of which must be considered, but all of which include large unknowns. He identified as a huge void knowing what to do if a test at a shop is negative. Then what? A related research question is whether an incentive package can be designed so that the shopkeeper makes the same profits no matter what the outcome of the test results and treatment dispensed.

A discussion took off from this introduction covering many areas, including:

- Better definition of the differences between access and practices in urban and periurban areas versus rural areas
- Continued research on new diagnostic technologies
- Unknowns in the RDT supply chain
- The need to include resistance in modeling and other analyses
- The need to develop a tool for accountability related to RDTs
- General improvement in the understanding of incentives
- Trials of various intervention bundles

A need for prioritization was identified, through an analytic process. This would include a time factor—what do we need to know and when. The question of who is responsible for commissioning and funding research and who can carry it out was asked.