Access to antimalarial therapy: accurate diagnosis is essential to achieving long term goals

Increased attention to and funding for malaria promises to improve access to effective treatment, but Heidi Hopkins, Caroline Asiimwe, and David Bell argue that without diagnostic testing much of this effort will be wasted.

Health care in malaria endemic areas of Africa is at a crucial tipping point. On the positive side, increased commitment to and funding for malaria control is leading to improved access to effective antimalarial drugs, with over the counter availability and extensive subsidies. However, current efforts do not yet adequately address the need for tools to diagnose malaria accurately and track its incidence. Since prescriptive case management leads to dramatic overuse of antimalarial drugs, programmes to improve access will also inevitably lead to further inappropriate treatment for individual patients, increased risk of parasite resistance to antimalarial compounds, and the potential diversion of hundreds of millions of dollars worth of antimalarial drugs to patients who do not actually have malaria. It is vital to make effective antimalarial treatment widely available, but doing so without equally intensive efforts to improve access to parasite based diagnosis is likely to be counterproductive. Thoughtful implementation of malaria diagnostics has the potential to improve care and resource allocation, with broad public health significance.

Improving early access to artemisinin based treatment means, in effect, making the drugs available at a cost that every family can afford and close enough for any sick person to obtain promptly. Various models are currently proposed to achieve this, from scaling up public sector provision of health care at no cost to the patient, to schemes to heavily subsidise drugs provided through the private sector. For example, the Affordable Medicines Facility for malaria aims to reduce market prices through a copayment at the factory gate, allowing buyers to purchase artemisinin based combination therapies at prices comparable to those of older, ineffective drugs such as chloroquine. Several international agencies and public health advocates have expressed support for this model, and details of the proposed design are being discussed.

A major challenge in case management is that malaria typically presents with non-specific symptoms that are indistinguishable from those of several other febrile illnesses common in the same areas. Even in sub-Saharan Africa, which has the greatest burden of malarial disease, the prevalence of parasitaemia among febrile patients varies widely, with most reports well under 50%. Most fevers are not due to malaria, and a significant proportion of mortality is from other causes.

In addition, there is evidence that the incidence of malaria is falling in many parts of Africa, as long lasting insecticide treated nets and artemisinin based treatments are made more widely available. This makes distinguishing malaria from non-malarial febrile illness before starting treatment even more important. The World Health Organization estimates that in most African countries, fewer than 20% of people with suspected malaria in public health facilities are given a diagnostic test, and it seems likely that the proportion in private facilities is even lower.

People who receive treatment for non-malarial disease have poor outcomes. Illnesses that cannot be reliably distinguished from malaria on clinical grounds alone in their early stages include meningitis, acute respiratory infection, and sepsis. These diseases have high mortalities in Africa; mortality is increased significantly by delays in early diagnosis and appropriate management. Unrestricted availability of artemisinin based treatment may divert people from established clinics with diagnostic facilities and therefore delay diagnosis of other potentially severe disease. By the same token, such programmes may be expected to undermine community education initiatives on the importance of correct diagnosis for improved management of febrile illness.

Secondly, improved targeting will preserve drug supplies. This is vital while uncertainty persists in global artemisinin supply and while programmes encounter delays in procurement. Thirdly, improved targeting is likely to preserve drug efficacy through reduction in exposure of malaria parasites to low levels of artemisinin derivatives circulating in
communities. It may also improve adherence to therapy by providing patients with clear evidence of current infection. Unmonitored access to artemisinin based treatment may contribute to poor adherence, with patients taking only enough to reduce symptoms, increasing the likelihood of resistance. At present, there are few affordable new drugs to replace artemisinin derivatives if resistance develops to this class of drugs. WHO recognises the possibility of artemisinin resistance as a “global emergency” that may seriously threaten efforts to control and eliminate malaria.

Fourthly, parasite based diagnosis is essential to monitor trends in malaria prevalence; falls in the incidence of malaria are not likely to be reflected in the rates of febrile illness because most fevers have other causes. Reporting parasitaemia is invaluable in monitoring the impact of interventions, targeting malaria control resources, and sustaining enthusiasm and financing for malaria control programmes.

A final consideration is economic. Misdiagnosis and overdiagnosis of malaria drain resources at the household level, affecting the poorest families most; improving the accuracy of diagnosis is expected to reduce unnecessary expenses incurred by patients. In addition, as artemisinin based treatment is relatively expensive, irrespective of the level of the supply chain at which the costs are covered, better targeting should have economic and public health benefits in allowing more efficient use of healthcare resources. Studies and models indicate an economic advantage to parasite based diagnosis across a range of parasite prevalences when test results are adhered to, partly because of potential reductions in morbidity and mortality from non-malarial fever as a result of prompt management. Cost effectiveness of case management strategies is, however, complex, and the picture is likely to change over time with shifts in price, funding mechanisms, and malaria epidemiology.

Policy on parasite based diagnosis

WHO currently recommends that parasite based diagnosis, with either microscopy or rapid diagnostic tests be used for all cases in malaria endemic areas, except in certain circumstances including young children in high transmission areas and severe outbreaks of proved malaria in resource poor areas. However, the term “high transmission” in this context is not clearly defined, and in the light of the growing availability of rapid diagnostic tests, the question of how to manage young febrile children in areas of high transmission is an area of active debate. For older children and adults, the WHO policy is clear that treatment with antimalarial medicines should be based on parasite based diagnosis.

Light microscopy for malaria diagnosis remains unavailable to most patients in Africa, although efforts to boost access and expertise may lead to improvements in some circumstances. Guidelines to improve field microscopy are available from WHO, but microscopy is likely to remain essentially confined to hospitals and large clinic settings. Rapid diagnostic tests, which do not require the laboratory infrastructure or expertise of microscopy, are increasingly seen as a reliable alternative for case management in virtually all endemic settings. The variable quality of commercially produced rapid diagnostic tests has been an obstacle to widespread use, but the product testing programme set up by WHO and the Foundation for Innovative New Diagnostics (FIN Diagnostics) in collaboration with the US Centers for Disease Control and Prevention and a network of other laboratories is helping to overcome this problem. In addition, the programme now facilitates lot testing of rapid diagnostic tests procured by national malaria control programmes through a network of regional laboratories.

Many malaria control programmes in Africa are working to institute national policies of parasite based diagnosis and to expand availability to more remote areas through the use of rapid diagnostic tests. For example, the Uganda Ministry of Health is finalising a national policy on malaria diagnosis and developing a comprehensive work plan for national roll-out of rapid diagnostic tests. Ethiopia plans to procure over 10 million tests in 2009 (personal communication, Worku Bekele, WHO/AFRO, Ethiopia country office). In Madagascar in 2007-8, rapid diagnostic tests were used in 93% of suspected malaria cases at sentinel sites; malaria was confirmed in 10% of cases, leading to a reduction in use of antimalarial drugs (personal communication, Luciano Tuseo, WHO/AFRO, Madagascar country office).

The potential benefits of parasite based diagnosis depend on accurate results and use of these results in patient management, which requires good programme planning, training, quality assurance, and capacity to deal effectively with non-malarial illness. Some studies have shown that distribution of rapid diagnostic tests does not by itself lead to improved case management because health workers continue to prescribe antimalarials to large numbers of patients with negative results. More recent evaluations—for example, incorporating specific training and efforts to modify long taught and long held beliefs that “fever equals malaria,” show promise for better adherence to test results (Zambia National Malaria Control Programme, unpublished data; H Hopkins, unpublished data). In addition, a structured quality assurance system must be in place to sustain health worker and community confidence in results of diagnostic tests. Community education programmes will be useful to promote awareness and acceptance.

A challenge for effective introduction of malaria diagnostics is the need to engage not just public health agencies but also the private sector; sale of antimalarial drugs can be an important source of income in this sector and better diagnosis is likely to reduce sales. Models need to be developed for maintaining diagnostic accuracy in the private sector, which is less regulated than the public sector, and for ensuring appropriate case management based on results. A subsidy on diagnostics as well as drugs, for instance, may make more sense both for public health and in terms of targeting of resources to maximise cost benefits. Current work with the private sector in other areas of malaria control—for example, in improving access to bed nets and antimalarial drugs—may inform policies for wider implementation of diagnostics.

For every billion dollars in subsidy for antimalarial drugs, around $500m to $960m will be spent on treatment for people who do not have malaria

Conclusion

Malaria incidence is likely to continue to fall in many parts of Africa over the next few years as preventive measures are implemented and sustained. Against this backdrop, improved diagnostic capacity will provide major advantages for individual clinical outcomes, monitoring of trends in malaria epidemiology, and efficient use of public health funds. Although symptom based treatment to improve immediate access makes sense in some countries as an interim measure, funding development of improved diagnostic capacity must be a priority. Investment in the infrastructure and training to achieve this will not only avoid wasting antimalarial drugs, but will provide a basis for tackling other febrile illness. Care must be taken in directing funding not only to avoid waste, but to build structures that will provide long term health benefits.

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Accepted: 30 May 2009
Competing interests: HH has conducted clinical studies related to malaria case management and diagnosis in Uganda since 2003. CA has 10 years of laboratory field research, and implementation experience with malaria diagnostics and malaria control programmes in East Africa. DB has a PhD in malaria epidemiology and research experience in malaria diagnosis and policy development. BB had the idea for this article; all authors contributed to researching, writing, and revising, and all authors have reviewed and approved the final draft. HH is guarantor.

Contributors and sources: None declared.

Provenance and peer review: Not commissioned; externally peer reviewed.


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