



Antimalarial treatment with artemisinin combination therapy in Africa

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levels of research funding are increased. The recommendation by the Commission on Health Research for Development that at least 2% of national health budgets and at least 5% of development aid should be invested in health research and on building research capacity must be heeded without further delay.¹⁴

Research with, rather than in or about, Africa is the goal. This will demand joint working to set agendas for research and mutual respect for countries' priorities, values, and choices. Partnerships should be transparent, clearly showing what each side brings and what each stands to gain. Furthermore, there must be clear mechanisms to ensure that some funds for research are directed to strengthening the capacity to conduct research, manage research (by establishing processes to handle grant funding and to review the ethics of proposed research), and develop skills in scientific writing. Finally, Africa's researchers, policy makers, and partners will have to give special attention to ensuring that knowledge generated from research is acted on to improve health for all.

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Desirable, achievable, but not easy

The steady increase of drug resistant malaria across Africa is a crisis for which there are achievable solutions, but no easy ones. The scale of the problem is not in doubt. In Africa malaria remains one of the commonest causes of death and serious morbidity, especially for children and pregnant women.¹ Despite a decision in principle by many countries in Africa to use artemisinin based combination therapies (ACTs), most cases of malaria are still treated with monotherapy and in many areas most of these treatments will fail.^{2,3}

Drug combinations, rather than monotherapy, are now seen to be the best solution for treating malaria, and artemisinin based drug combinations are highly effective, with cure rates similar to that of chloroquine 30 years ago. They seem to be a good long term choice for most African countries, being safe and well tolerated (with the caveat that their safety in early pregnancy is not yet clear). Compared with other antimalarials, ACTs can reduce gametocyte carriage and thereby lower the risk of infectiousness in those who take treatment. In areas of relatively low malaria transmission in South East Asia and South Africa, widespread use of ACTs has reduced significantly the burden of malaria.⁴ This benefit is likely be less marked

in areas of very high transmission in Africa, where much of the reservoir of malaria infection is in asymptomatic people who never seek treatment.

The primary problem with using ACTs in Africa is cost. The least expensive treatment courses currently cost more than \$1, roughly 10 times that of current monotherapy. In much of the continent people have malaria several times a year, and this cost could be prohibitive both for governments and households. In response to this problem policy makers have made strenuous efforts—led by the Global Fund for HIV/AIDS, Tuberculosis and Malaria—both to increase the supply of artemisinins (alleviating a current global shortage) and to provide drugs to governments at well below their market price.

This has prompted two parallel debates which have not yet been fully resolved. One is among donor agencies on how to achieve a sustainable subsidy. Nobody who understands this issue believes that subsidy can be avoided if ACTs are to reach those who need them most.⁵ What form that subsidy should take is, however, a complex technical matter on which there is no current consensus. Using these drugs will depend on a sustainable stream of funding; ministries of health in Africa are understandably wary of the

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fickleness of the donor community and are reluctant to commit to a policy which depends on a subsidy which could dry up.

In Africa there is an equally difficult technical debate about how to deploy ACTs to maximise their effectiveness and cost effectiveness. In this issue (p 734) a paper from Zambia, one of the earliest adopters of ACTs, illustrates some of the many formidable barriers to effective deployment.⁶ Even where the drugs were freely available and clinic staff knew they were being observed, only 22% of patients eligible for ACTs actually received them. This is only one of several issues which need to be addressed, and the scale of the change in approach to malaria treatment that will be needed if ACTs are to achieve their potential to reduce the burden of malaria is often underestimated. Three things in particular require careful thought.

For 40 years we have been treating malaria with monotherapies, essentially in limitless supply, which are cheap enough for individual households to buy. Healthcare workers have treated almost all febrile illness as malaria on the rational grounds that it is better to treat several viral illness with an antimalarial than to miss one potentially fatal infection which could be treated with chloroquine or sulfadoxine-pyrimethamine. Most people treated for malaria, even in the formal healthcare sector, do not actually have the disease.^{7,8} To continue this approach will lead to substantial unnecessary use of ACTs and will undoubtedly threaten the affordability and sustainability of any subsidised programme. The magnitude of the shift in mindset and practice which will be required for ACTs to be used only in proved cases of malaria will not be easy to achieve, however, and attempting it increases the risk that some true cases will be missed.

Another concern is how to involve the private sector. In many countries, most treatment for malaria is provided outside the formal healthcare sector, often by shopkeepers.⁹ Providing subsidised drugs to the formal public sector but not to the private or informal sectors may make affordable ACT treatment unavailable to people who rely on the informal sector, suddenly and substantially increase the workload for the formal sector, increase the potential for fake drugs entering the market, and encourage some patients to sell on unfinished courses of subsidised drugs in the marketplace when they start to feel better.

There is also a clear tension between the need to restrict the use of more expensive drugs to reduce costs and slow the development of malarial resistance, and the need to expand access into the community so that treatment is near home and therefore accessed early. Ministries are wary of complex tiered policies for malaria treatment that differ between rural and peri-urban areas, or that target drugs at certain vulnerable groups, but they may have to consider these options.

These technical problems can be solved, but at present few data are available to inform evidence based policy decisions regarding the most effective and cost effective deployment strategies, and ministries and researchers urgently need to work in partnership to fill this evidence void. It is unhelpful to ignore these major practical questions or to assume that, when ministries express caution about deploying ACT immediately, they are doing so out of negligence or ignorance. In

some countries in Africa the high level of drug resistance means ACTs are now the only effective option, and existing resources should be concentrated on these countries. For countries with good evidence of low levels of resistance to at least two monotherapies, an interim policy using cheaper non-artemisinin combinations, at least for some, may be sensible while evidence of the best deployment strategies for ACTs is being built up.¹⁰ ACT has the potential to be one of the greatest public health interventions for Africa this decade. We must get it right.

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