

Between hope and a hard place

Campaigns against malaria are multiplying, but so are malaria deaths. Brian Greenwood asks what can be done to turn the tide.

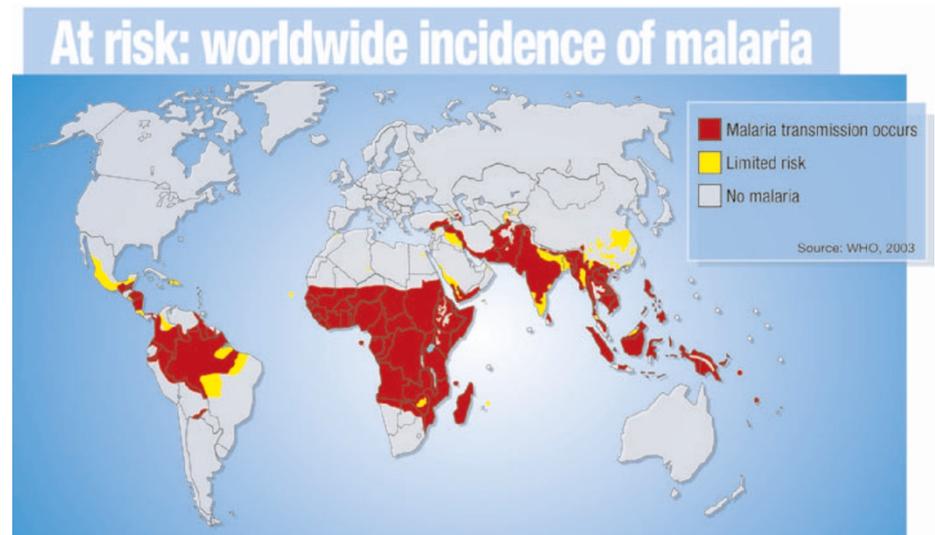
After decades of neglect, the international community is showing renewed interest in malaria. Rich countries are acknowledging that rampant, drug-resistant malaria threatens not only their own citizens when they travel to malaria-endemic areas, but also damages the economies of tropical countries and potential markets for their goods and services¹.

This is a good time to take stock of the situation. How bad is the problem, what is being done to combat the disease, and how is fundraising progressing? There are promising signs on all these fronts, but major obstacles remain. A distinct lack of accurate data on disease burden is hampering the scientific assessment of the impact of control measures. At the same time, a shortage of expertise and infrastructure in the healthcare and research systems of poor countries is threatening their ability to implement international initiatives.

No one knows precisely what the clinical or economic burden is. The official line has long been that 'malaria kills more than 1 million people a year', mostly children, and as a slogan this has been a powerful rallying call in moving malaria up the international agenda.

Whether it is half-a-million child deaths annually or two million, the toll is unacceptable. But to capitalize on the current drive to improve control, getting better statistics on every aspect of malaria is crucial. Estimates of numbers and distribution of malaria deaths have progressed from 'back-of-the-envelope' calculations to sophisticated modelling and geographical information systems that map populations and their levels of risk².

That said, most countries where malaria



is endemic (see map, above) lack a national births and deaths register. In addition, many deaths occur in people's homes without any clinical investigation or diagnosis, making it impossible for demographic surveys to provide precise mortality figures. This in turn hampers accurate assessment of malaria-control programmes (see 'The invisible victims', page 934) — although in many African countries malaria is such an important cause of childhood deaths that overall mortality rates can be used to measure the effectiveness of control measures such as insecticide-treated bednets³. Nonetheless, using various data sources we can make rough estimates of the overall malaria burden by country in Africa⁴.

Front-line attack

Why are so many people still dying from malaria when effective tools are available to control it? One reason is that, despite much noise, the international community and malaria-endemic countries have yet to implement existing tools widely enough (see 'An attack on all fronts', page 930). Experience in Vietnam and a few African countries, such as Eritrea, shows what can be achieved — these nations are running strong and effective national programmes.

In most countries affected by malaria, the lynch-pin of control is readily accessible: effective treatment to prevent deaths. Unfortunately, in much of Africa treatment is anything but accessible and effective. Clinics are few and remote, and resistance has rendered first-line drugs such as chloroquine and sulphadoxine-pyrimethamine ineffect-

ive (see 'Winning the drugs war', page 942).

'Home treatment' options are being explored to provide quicker access to therapies. These include training mothers and community volunteers to treat malaria, improving the therapeutic skills of the local shopkeepers from whom most people in Africa obtain their antimalarial drugs, and evaluating suppositories for the front-line treatment of severe malaria in places where there are no staff trained to give injections.

Artemisinin-based combination therapies (ACTs), derived from the herb *Artemisia annua*, provide a rapid cure and are an immediate solution to the problem of drug resistance. But ACTs cost several times as much as existing drugs, so some aid donors have been reluctant to support their widespread introduction.

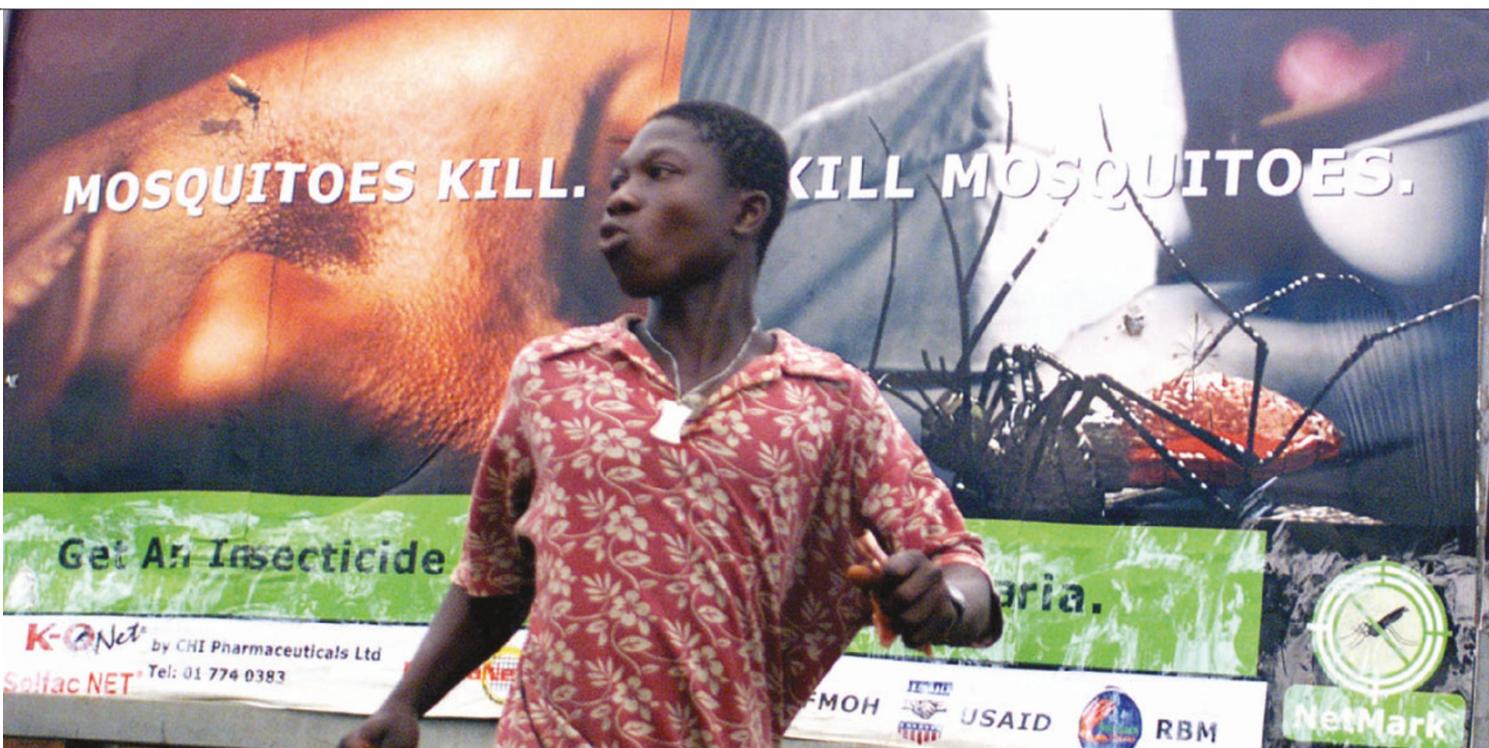
The recent decision by the Global Fund to Fight AIDS, Tuberculosis and Malaria to switch its malaria grants for all African countries to support the use of artemisinins is good news. But relying on treatment as the mainstay of control is an admission of defeat: the

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failure to prevent infection in the first place. Better prevention strategies must be the goal.

Spraying the interior of houses with insecticides that leave a lasting residue, insecticide-treated bednets and

intermittent treatment in pregnancy with sulphadoxine-pyrimethamine can all reduce the incidence of new infections. But such measures are not being used widely enough. Few children sleep under bednets⁵, because of their costs, difficulties in getting them to remote areas and ignorance about their benefits. We need to find ways to increase the



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use of bednets, for example by distributing them through antenatal and infant immunization clinics.

Existing control measures must be supplemented or replaced with new tools. It takes more than a decade to develop new drugs, so we should be priming the pipeline now with molecules that have new mechanisms of action and are less susceptible to resistance. Here, prospects are much more promising than five years ago, thanks to organizations such as the Medicines for Malaria Venture, a Geneva-based body set up to discover and develop new drugs.

Work in progress

New insecticides are also on the horizon. Current bednets use one of the pyrethroid group of insecticides, but the main mosquito vectors *Anopheles gambiae* and *A. funestus* are already developing resistance to these (see 'Taking aim at mosquitoes', page 936).

Substantial progress is being made in the development of malaria vaccines, and in the creation of genetically modified mosquitoes that are resistant to malaria⁵. But both are still far from being ready for widespread use (see 'Save the children', page 940).

In parallel, work on the parasite and vector genomes will ultimately provide a better

understanding of the biology of the *Plasmodium* parasite and aid the discovery of weaknesses in its armour. This will spur the rational design of a new generation of drugs and vaccines. But it is going to be a long, hard battle before we see the fruits of genomics and proteomics turned into products that save lives (see 'Know thine enemy', page 944).

Despite a lack of progress on some fronts, prospects for rolling back malaria look more encouraging in 2004 than at any time since the global malaria eradication campaigns of the 1950s and 1960s. Poor countries have access to increasingly large sums of money for control from international organizations such as the Global Fund. Malaria research is now better funded than ever, thanks to new donors such as the Bill & Melinda Gates Foundation, which has injected several hundred million dollars into the field. Some established donors have doubled or even trebled their funding.

Meanwhile, an essential component of control risks being forgotten: the human resources needed for researching and implementing control measures. The benefits of increased funding will not be fully realized if control efforts continue to rely on poorly trained and paid staff (see 'Power to the people', page 928).

Trained staff are in woefully short supply in all malaria-endemic countries, at every level, from community workers and public-health specialists to researchers. And those health personnel that do exist are being asked to do more and more as additional funds become available for the

Bitten by the bug: posters promote insecticide-treated bednets, but cost and poor distribution mean nets are rarely used in remote areas.

control and treatment of other major infections such as HIV. Many aspects of research can only be tackled in endemic areas, but there is a drastic shortage of support for either research institutions or staff to achieve this.

Organizations such as the World Health Organization's Roll Back Malaria initiative, the Gates Malaria Partnership and the Multilateral Initiative on Malaria are attempting to address the situation, but their efforts are fragmented and insufficient. A major push is needed to tackle the problem coherently across Africa and elsewhere, but it is not clear who will be up to the job (see 'Where did it all go wrong?', page 932). The World Health Organization lacks the funds, and some major donors are nervous about investing in what may seem like a bottomless pit. But if this challenge is not taken up, new tools and the increasing sums of money that are being made available risk being wasted and put into the field with insufficient thought.

A new international impetus is now needed to prevent this happening. Otherwise, the present period of hope for malaria research and control may turn out to have been an illusion. ■

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2. Korenromp, E. L., Williams, B. G., Gouws, E., Dye, C. & Snow, R. W. *Lancet Infect. Dis.* **3**, 349–358 (2003).
3. Phillips-Howard, P. A. et al. *Am. J. Trop. Med. Hyg.* **68** (Suppl.), 23–29 (2003).
4. *Africa Malaria Report 2003* (WHO/UNICEF, Geneva, 2003); available at www.rbm.who.int/amr2003/amr2003/amr_toc.htm
5. Coleman, P. G. & Alphey, L. *Trop. Med. Int. Health* **9**, 433–437 (2004).

Malaria is estimated to cause each year:

- More than 1 million deaths
- Up to 500 million attacks of acute illness
- Up to 50,000 cases of neurological damage
- Up to 400,000 episodes of severe anaemia in pregnancy
- Up to 300,000 low-birthweight babies

