REVIEW ARTICLE

Malaria in South Africa — the past, the present and selected implications for the future

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This paper outlines a brief historical perspective on malaria which is considered essential to an understanding of the gains made in the control of the disease, followed by an emphasis on the fact that control is a dynamic process requiring research back-up, private and public sector and national and international collaboration. Malaria control is based on scientific principles and ongoing success requires continual research input, government commitment to control of the disease and appropriately skilled and trained personnel. This overview cannot do justice to malaria control and research in South Africa in its entirety, but looks at some of the major factors facing malaria control that have motivated the Medical Research Council's research initiative, which includes vector and parasite research, the use of geographical information systems and the epidemiology of the disease, with a view to sustaining control into the future.

Historical perspective

An important reason for reviewing the historical profile of an epidemic vector-borne disease is that it indicates what may happen should there be a resurgence and further outlines the role of operational research in the development of a successful disease intervention programme. As outlined by le Sueur *et al.*,[1] unless total eradication is achieved, vigilance and stringent control measures must be maintained to keep the disease in check. The example of India, among many others, is cited, where the incidence of the disease has done a complete circle and present-day cases number in the millions.

The devastating effects of malaria on communities, tourism and agricultural and industrial development in the provinces of KwaZulu-Natal and Mpumalanga were the major motivations for control of the disease in the first half of this century. Le Sueur *et al.*[1] reviewed the extent of the malaria problem in South Africa prior to its control, and the following excerpts from this work outline its severity.

> Malaria mortality estimates by magistrates in KwaZulu-Natal from November 1931 to June 1932 totalled 22 132 (population at risk = 985 000). During 1932 all the districts

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of Natal, bar one, reported cases of malaria. Huletts representatives had visited hundreds of planters, whose average work force was 80, but typically only three were reporting for work. The Amatikulu mill was receiving only one truck load per day (5 tons of sugar cane) instead of the expected 1 500 tons. The *induna* (headman) in the Umvoti area pointed out a kraal where all five family members had died within 6 weeks. At one kraal visited there was a corpse of an individual who had been dead 2 days but had not been buried because all the local inhabitants were down with malaria.

The severity of the economic impact of these epidemics is summarised by the following resolution adopted by the South African Chamber of Commerce at its annual meeting in Durban in May 1932.

'This convention respectfully urges upon the Government the need for continuous and effective action to eradicate the scourge of malaria which is having a serious effect upon Natal and the Eastern Transvaal, and reacting seriously upon the progress of industry, trade and agriculture in these provinces, and, through them upon the union.'

The advent of early control measures is summarised below.[1,2] Control measures in South Africa started with quinine treatment and prophylaxis, but these measures could not practically be extended to the population at risk as a whole. In 1921 Park Ross, Assistant Secretary for Health of the Union of South Africa, carried out the first malaria survey of the Union, which resulted in the division of the country into five scheduled areas of malaria risk, which were geographically recorded on coloured contour maps. (Fig. 1. The map dating from this period no longer exists; that shown represents the situation in 1938, and is taken from le Sueur *et al.*,[2] redrawn by C. Green.) During 1928, Ingram and De Meillon[3] published the results of a mosquito survey of the Union which covered the types of sites used by the various species and included suggestions for the reductions of such sites, a document that played an important role in future control strategies. Anti-larval measures using oil and Paris green were introduced and continued to be a major means of control until 1946.[3] The first trials using Pyagra (liquid pyrethrum and kerosene) as an indoor spray against adult malaria mosquitoes were carried out in Natal in 1932 by Senior Health Inspector Hamilton under supervision of Park Ross.The results achieved were striking; they formed the basis for the later widespread use of intra-domiciliary spraying with residual insecticides for the control of malaria vector as part of the malaria eradication programme of the WHO. In 1946, the use of Pyagra for indoor mosquito control was discontinued, and it was replaced by DDT.

Experimental work by De Meillon[4] showed that, apart from being more effective, the control of adult mosquitoes cost only about one-third that of larval control. Anti-larval measures were abandoned in 1956 and malaria became a notifiable disease. Total coverage with house spraying of all the malarious areas of South Africa was achieved for the first time in 1958.

During the 1970s, the malaria control programme became more structured, with intervention measures aimed at both the mosquito and the malaria parasite. Indoor spraying with

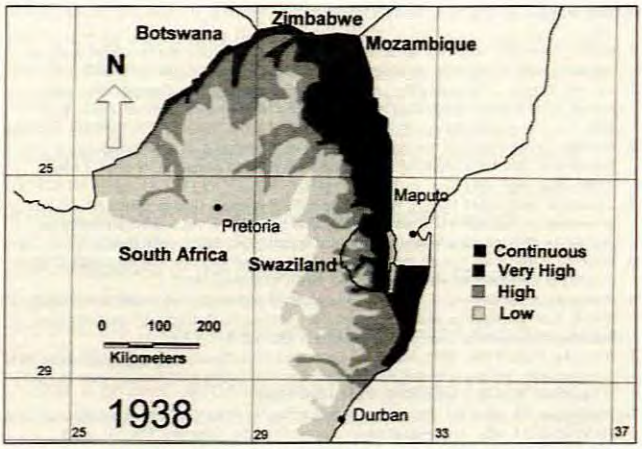

Fig. 1. Malaria distribution in South Africa in 1938 (redrawn by C. Green from le Sueur *et al.*[2])

DDT was carried out on an annual basis in all the malarious areas and treatment of infection was based on definitive microscopic diagnosis and follow-up.[2,5]

The present-day distribution of malaria in South Africa (Fig. 2) follows that in pre-control days but with a dramatically reduced incidence with only three districts having an average annual incidence greater than 3/1 000 over the period 1987-1993. The number of notified deaths is also extremely low, ranging between 12 and 45 per annum for the 6-year period 1989-1994,[6] in contrast to the situation prior to control. The highest risk areas are all border areas, indicating the importance of imported malaria. Imported

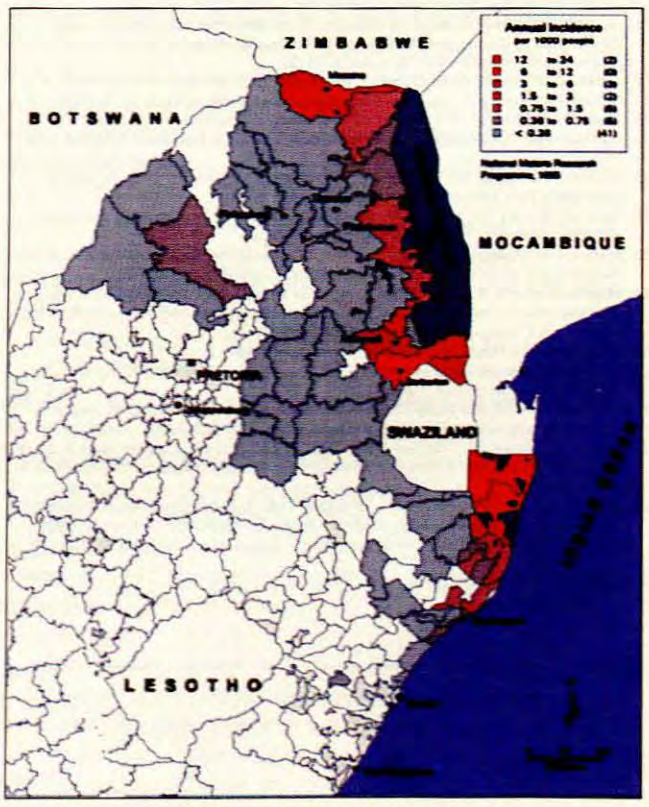

Fig. 2. The distribution of malaria in South Africa, shown as average incidence for the period 1987-1993 (manuscript in preparation, Sharp, le Sueur, Muller and Tscheuschner).

cases have been recorded from all the countries of southern Africa, with the majority being classified as originating in Mozambique. This stresses the importance of viewing malaria as a regional and not just a country-specific problem. Population migration as a result of factors such as family ties, war and famine, and job- and health facility-seeking behaviour facilitates the transmission of disease between countries.

During 1993 a total of 13 285 malaria cases were reported from the country as a whole, the highest number recorded going back to the early 1970s. During 1994, 10 286 cases were reported.[6] Prior to 1993 the annual malaria case total for the country rarely exceeded 10 000 per annum (1976-1994) (Fig. 3). The increase in cases over the period 1985-1988 corresponds with the first detection of chloroquine resistance in South Africa[7-9] and is partly due to increased agricultural development in malarious areas.[10]

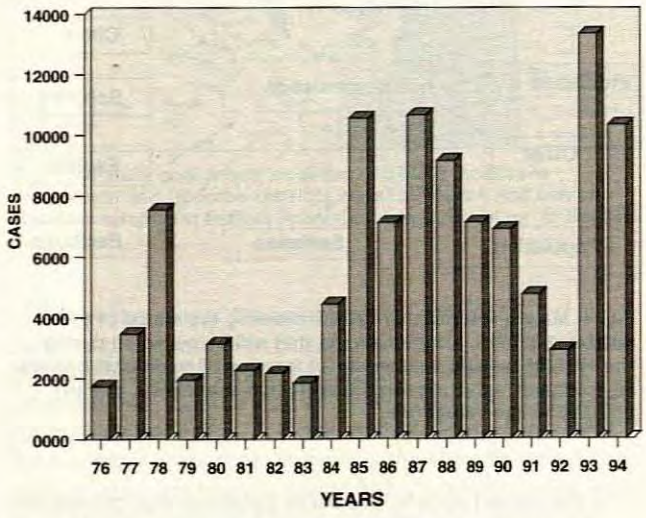

Fig. 3. Annual malaria case totals for South Africa, 1976-1994 (Department of Health notification data).

Constraints

Drug resistance and parasite control

Biological systems are dynamic, and malaria control must, of necessity, be based on sound scientific principles in order to be effective. There are a number of biological developments and research findings that effect a need for changes in control strategies.

Probably the most exacerbating problem associated with malaria control in southern Africa is the resistance *Plasmodium falciparum* develops to antimalarial drugs. Multidrug resistance has been reported from Africa, and this includes reports on resistance to chloroquine, sulfadoxine/pyrimethamine, mefloquine, quinine, pyrimethamine and amodiaquine. Chloroquine chemotherapy has been the most widely used and, until recently, effective measure in malaria control in Africa. Chloroquine resistance in Africa was first reported from both Kenya and Tanzania in 1979, and is now documented as occurring in all the southern African countries. It was first detected in South Africa in 1985 and is now well established in the country.[11-13] Sulfadoxine/pyrimethamine replaced chloroquine as first-line treatment in malaria control in South Africa in 1988. This change had cost implications for the country in that a curative dose of sulfadoxine/pyrimethamine costs four times (commercial sector price) that of a curative dose of chloroquine. Two questions central to sustainable malaria control in South Africa are: (*i*) how long will sulfadoxine/pyrimethamine remain effective? and (*ii*) what do we use next?

Very limited baseline data exist on the sensitivity of *P. falciparum* to sulfadoxine/pyrimethamine in South Africa. Drug sensitivity data are essential for decision-making in respect of prophylaxis and treatment by clinicians, malaria control personnel and health policy-makers. It is therefore essential to monitor the severity and extent of the drug resistance problem in southern Africa. The Medical Research Council has been involved in drug resistance studies since 1984. These have included data collection in KwaZulu, Northern and Eastern Transvaal and Namibia. However, this effort needs to be expanded through collaboration on a national and regional basis.

Insecticides and vector control

There have been a number of developments in recent years relating to vector control and the use of DDT in this regard that necessitate the evaluation of potential alternatives.

1. It is generally accepted that agricultural pesticide use associated with large-scale agricultural irrigation projects exacerbates the development of insecticide resistance in mosquitoes. A large-scale irrigation project has been initiated in the malaria area of northern KwaZulu-Natal[14] and a further one is planned for Mpumalanga province.
2. Social attitudes against the use of DDT have increased to the degree that certain international research funding agencies will no longer fund research in any way associated with DDT.[15]
3. Research on DDT levels in men and women in the endemic malaria area of KwaZulu-Natal showed 20 times the acceptable daily intake overall in the study and 31 times the acceptable daily intake in primiparous mothers.[16]
4. Sharp *et al.*[14] showed that *Anopheles arabiensis* exhibited 'hut-leaving behaviour' in the presence of DDT and that alternative insecticides should be investigated for more effective control.
5. DDT resistance in bedbugs has resulted in large numbers in the sprayed area, and social resistance by homestead owners to DDT has resulted in the need to control these with an additional insecticide at increased cost.
6. Homeowners have become reluctant to have their houses sprayed with DDT because of discoloration of their walls.
7. The cost of residual spraying is such that the budget for insecticides to control malaria vectors in the southern African area runs into millions of US dollars.
8. Multidrug-resistant *P. falciparum* compromises parasite control and places a greater emphasis on effective vector control.
9. The need exists to assess the efficacy of the new-generation insecticides, e.g. synthetic pyrethroids; these are biodegradable and the most environmentally friendly of the insecticides.

As a result the MRC, in collaboration with the private sector and the Department of Health, has been involved in the evaluation of alternative insecticides for just over 5 years. Current research is centred on the evaluation of the biodegradable synthetic pyrethroids as alternatives to DDT for vector control.[17,18] Laboratory evaluations have now been completed on five formulations with encouraging results from three (le Sueur *et al.* — manuscript in preparation). The most promising candidate showed an effective residual life of 57 weeks on a daub substrate, far in excess of the 6-month transmission period. The first large-scale field trial of this insecticide by the Department of Health in KwaZulu-Natal is ongoing. The laboratory studies have shown synthetic pyrethroids to be effective in controlling DDT-resistant bedbugs, alleviating the need for an additional insecticide to be used in their control. Changing to a synthetic pyrethroid has cost implications for malaria control. Table I clearly shows that all the potential alternatives cost more and, in most cases, double the cost per square metre sprayed with DDT. Should they prove more effective in vector control, they may well also prove to be more cost-effective.

Table I. The cost of insecticides used for adult mosquito control (reproduced with permission from R. Maharaj, Ph.D. thesis in preparation, University of Natal)

Insecticide (wettable powders)	Concentration (g AI/l)	Application rate (AI/m²)	Cost/kg (R)	Cost/m² (c)
DDT	750	2	20.07	5.35
Bendiocarb	800	0.4	394.40	19.7
Cyfluthrin	100	0.02	577.20	11.5
Deltamethrin	50	0.02	178.12	7.12
Lambda-cyhalothrin	100	0.031	324.00	10.04
Fenitrothion	400	1	42.52	10.6

AI = active ingredient.

The future

Increased expenditure on drugs and insecticides would appear to be unavoidable in the future if we are to maintain malaria transmission at the current low levels. There are, however, a number of research developments and collaborative options that can facilitate the sustainability of this effective dual-focus intervention programme by reducing overall costs in other ways. These include the cost-effective focusing of control operations facilitated by the use of a geographic information system (GIS), decentralisation of diagnosis as part of offering a better service at the PHC level, thereby reducing the need for the current level of active surveillance, and regional co-operation with regard to malaria control.

GIS in malaria

The implementation of malaria control has led to each magisterial district in KwaZulu-Natal being divided into approximately 20 malaria areas, which are again sub-divided into 10 sections. One team of 8 - 12 personnel is responsible for malaria control activities in two areas. Each house within a section is numbered by means of a malaria 'green card' stored under the eaves of the roof. This card also records visits by surveillance personnel who take thick blood smears for parasite detection, as well as the annual application of residual insecticide.

Thus, each house is visited annually and it was during these routine visits that a database was established for every house. The current status of the malaria information system (MIS) is shown in Fig. 4.[19,20] The database is printed every year and updated by control programme staff during their annual spraying; changes recorded are subsequently made to the existing database. With each update, additional information is added.

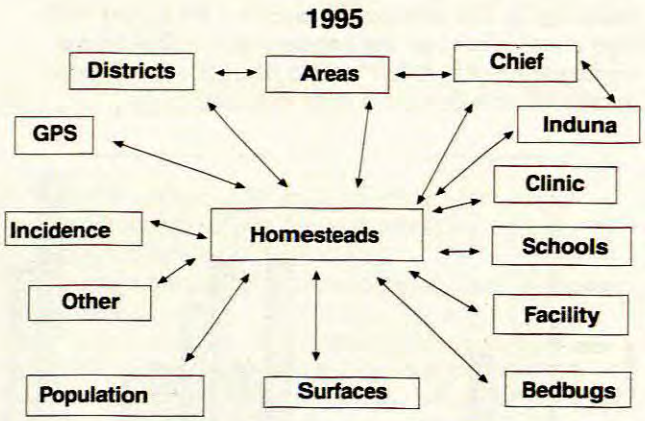

Fig. 4. Malaria information system showing the status of the database in 1995. Additional data that will be collected during the 1995/96 malaria season are: (*i*) location of traditional healers; (*ii*) source of water supply; (*iii*) sanitation availability; and (*iv*) population age categories.

In the current update, the entire database was printed and the sheets for each malaria control area were bound into a folder and given to the spray team leader for updating. Information on school and clinic attendance was also obtained. Collaboration was established with the Department of Agriculture and a total of 23 global positioning systems (GPSs) were deployed in the field. This enabled many of the teams equipped with a GPS to obtain the longitude and latitude of individual family units. It is important to note that people in the area do not live in villages but in scattered patriarchal homesteads. A malaria information system has therefore been established which is able to facilitate other areas of development. Exact school and clinic catchments can be defined, the position of all facilities can be plotted and the entire data set can be referenced to tribal boundaries.

In Fig. 5 the GPS location of 34 943 families is shown and buffers have been thrown around the fixed clinics to assess the distance that people have to travel to access health care. The importance of such geo-referenced population data is highlighted by the fact that our data are being used by the Electricity Supply Commission to plan electrification, as well as for water provision as part of the Reconstruction and Development Programme activities in the region. This has all been made possible through the integrated activities of the Medical Research Council and the Department of Health (Malaria Control Programme).

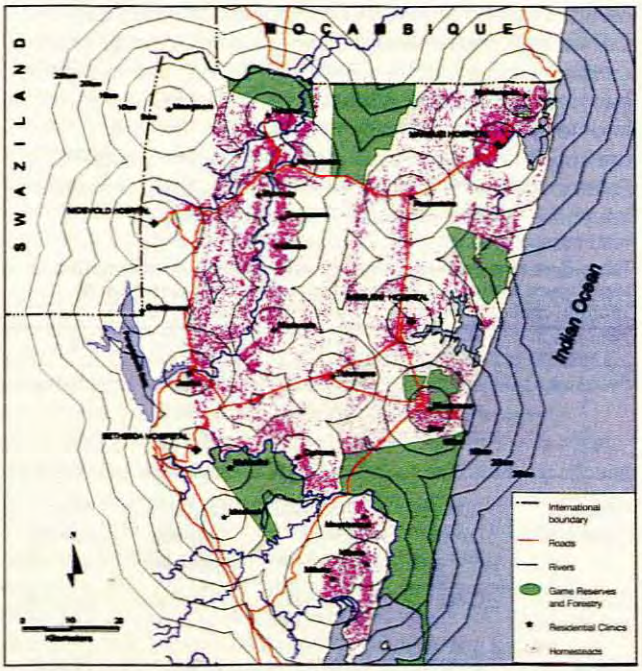

Fig. 5. Globally positioned localities of 34 943 families in Ingwavuma and Ubombo districts, KwaZulu-Natal, and clinics showing catchment buffers (manuscript in preparation, le Sueur).

The central aim of the establishment of the MIS, consisting of a relational database linked to a GIS, was the production of digital maps of malaria prevalence at a localised level. Such a map of malaria distribution for South Africa is shown in Fig. 2. A map of this nature is important for a number of reasons: (*i*) to allow travellers to assess the need to take prophylactic precautions in specific areas; and (*ii*) to enable control authorities to direct both human and material control resources to the areas most in need of them.

Mapping malaria at this level (i.e. magisterial district) is, however, inadequate as the disease is more focal than this (le Sueur *et al.*, 'Using a geographic information system to investigate the macro-epidemiology of malaria in South Africa' — manuscript in preparation). This is clearly illustrated in Fig. 6, where malaria incidence is shown at malaria sector level for the two districts of Ingwavuma and Ubombo, for 1987 - 1991. It is important to note that the 'background incidence' of 0 - 18/1 000 is comparable to that for the entire district (Fig. 2). Thus plotting of the data at district level results in a 'diluting out' of the high-risk areas evident in Fig. 6. There are two high-risk areas in the region, one in the north-west, close to the Mozambican border, and the other further south near the inland town of Jozini. The former is associated primarily with the influx of infected migrants from Mozambique as well as the Pongola floodplain. The latter is associated with the Makhatini irrigation scheme, where the spillage of excess irrigation water has resulted in the year-round breeding of *A. arabiensis*.[14,21-23] Detailed maps allow control authorities to focus their activities in the areas where they are most needed, thus facilitating cost-effective control.

With disease mapping (more so with tabular data) there is a tendency to focus on high-risk areas and to ignore a more detailed study of low-risk areas. Plotted data in Fig. 7 show that from 1980 to 1991, the low annual case incidence of 0.2% or less was concentrated along the coast, with the figure increasing closer to the high-risk areas in the north-west. This is a marked change from 1938 (Fig. 1) when this same coastal area between Lake St Lucia and Kosi Bay was the only area of all-year-round transmission. This reduction is due to the efforts of the malaria control programme, which have resulted in the eradication of one of the mosquito vectors, *A. funestus*. The breeding sites in this area are those favoured by *A. funestus* (which was recorded to have occurred in the region in 1931 and been sporozoite-positive, i.e. infected with malaria). The remaining vector, *A. arabiensis*, does not favour these sites and is therefore largely absent from the area. Extensive entomological surveys have been carried out in the entire region and were published in 1988.[24] The implications for control are that surveillance activities can be minimised in this area, but residual spraying must be continued to prevent reinvasion of the area by *A. funestus*. This information is also important to tourists visiting the region, a fast-developing eco-tourism area.

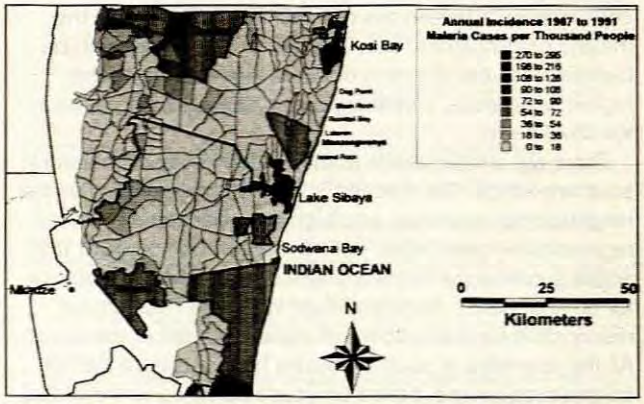

Fig. 6. Malaria distribution for the period 1987-1991 at the sector level in Ingwavuma and Ubombo district (manuscript in preparation, le Sueur *et al.*).

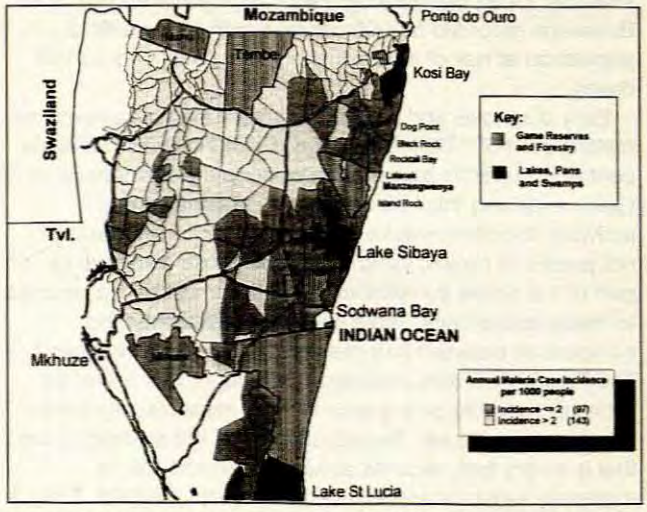

Fig. 7. Malaria sectors in Ingwavuma and Ubombo districts with malaria incidence less than and greater than 0.2% (manuscript in preparation, le Sueur *et al.*).

Increased service at the primary health care level and active surveillance

In excess of 50% of all malaria cases in South Africa during the period 1987 - 1990 were detected by active surveillance. This high detection of malaria cases by active surveillance outlines its importance in the reduction of the parasite reservoir and of transmission. These actively detected cases are infected people who did not report to hospitals or clinics but were detected by malaria control personnel primarily during house-to-house surveys and mass blood examinations. In the KwaZulu areas, 30% of cases were detected by hospitals and clinics and only 12% of these by clinics.[5] From Fig. 5 it is evident that the high-risk malaria area of KwaZulu-Natal is not necessarily under-served in terms of clinics. We hypothesise that the relatively minor role of clinics in malaria case detection in South Africa can be addressed in a cost-effective manner by community involvement and enhanced service at the clinic level, effectively reducing the need for active surveillance and reducing cost. Any change to the system should, however, be closely monitored to ensure that it is effective and that we do not lose the gains we have made in malaria control. A study in this regard is under way, a project reliant on close collaboration between the community, research and the malaria control authorities. The use of GIS would also be beneficial for the directing of active surveillance to the highest-risk areas, a strategy that is already being used in KwaZulu-Natal.

There are similar trends in the epidemiology of malaria in southern Africa. The disease is distinctly seasonal in all our neighbouring countries, and high-risk years tend to be a regional phenomenon as well. There can be no doubt that active surveillance of malaria which, as outlined, accounts for 50% of cases detected, must in a large measure be responsible for the success of malaria control in the country. All the countries of southern Africa have a malaria vector control programme, based on house spraying with residual insecticides, but only South Africa uses active surveillance to detect and treat infection; the annual malaria case rate is the lowest in the region. A comparison of the malaria case rates for Botswana and South Africa in 1993 serves as an example. Of a population at risk of approximately 667 000, Botswana recorded 53 000 cases. South Africa, with a population at risk of approximately 12 million, had 13 285 cases.

Early diagnosis and prompt treatment are fundamental to malaria control.[25] Definitive diagnosis of infection in malaria control is currently based on microscopic examinations of Giemsa-stained thick blood smears. Malaria control activities therefore require laboratories which are generally not placed at clinics; clinic slides and those collected as part of the active surveillance operation must be transported to these laboratories. Table II includes a summarised comparison between four malaria diagnostic techniques.[26] The Para*Sight* F test, a dipstick technique, was found by Tscheuschner[26] to be superior in most respects, relative to the other techniques. The advantages of this technique are that it is very fast, requires almost no experience, is extremely sensitive and can be carried into the field. This, we believe, is the malaria diagnostic tool of the future. It would do away with the need for slides, their transport to centralised laboratories and the required infrastructure and trained staff, thus enabling diagnosis at the primary health care level and by active surveillance agents. The technique has further revolutionised malaria self-diagnosis for residents in or long-term travellers to malaria areas. The only drawback to the technique is that it is currently specific to *P. falciparum*. This species accounts for > 95% of malaria infections in South Africa and southern Africa.

Table II. A summarised comparison between four diagnostic techniques evaluated (reproduced with permission from M. Tscheuschner, M.Sc. thesis, University of Natal, 1995)

	GTS	AOTS	QBC	PS
Sensitivity	Least sensitive of these four	Second highest	Third highest	Highest
Specificity	100%	Very high	Very high	Very high
Parasite quantification	Accurate Direct estimate	Accurate Direct estimate	Good Indirect measure	Poor Indirect indication
Species identification	Clear	Unreliable	Unreliable	Species-specific
Speed	Slowest	Third fastest	Second fastest	Fastest
Experience required	Moderate to a lot	Very little	A lot	Almost none
Methodology	Relatively simple Fairly robust	Relatively simple Sensitive to variations	Relatively simple Fairly robust	Simple Robust
Facilities required	Laboratory Electricity Microscope	Laboratory Electricity Microscope AO filters Halogen lamp	Laboratory Electricity Microscope Fluorescent objective Centrifuge	None
Materials (per test)	Cheap (10c)	Cheap (10c)	Expensive (R5.80)	Expensive (R5.90)

GTS = Giemsa-stained thick smear; AOTS = acridine orange-stained thick smear; QBC = quantitative buffy coat analysis; PS = Para*Sight* dipstick.

Regional co-operation

The health status of communities in the southern African region is considered to be among the poorest in the world, a situation exacerbated by war, famine, drought, dislocation, economic recession and political instability.[27] Historically, health has been viewed from a country-specific, and not a regional, perspective. This is underlined by the WHO activity in the region which has been primarily country-based and the fact that the Southern African Development Co-ordination Conference (SADCC) did not have a commission devoted to health.[27]

During 1993 workers in malaria research and control were invited to this country by the MRC with a view to developing a regional initiative, and in 1994 collaborative research talks were held with 6 countries, viz. Namibia, Botswana, Zimbabwe, Zambia, Mozambique and Swaziland.

We believe that it is only through appropriate research, training and information exchange that malaria control will be sustainable in South Africa and southern Africa. As

outlined, a high percentage of our malaria cases are classified as imported into the country. However, irrespective of where drug resistance develops, it spreads, and we are not an island, but part of the southern African malaria problem. Our highest-risk malaria transmission areas are international border districts (Fig. 2). Malaria is not a country-specific problem and we believe that collaboration, information and expertise exchange are vital to the future control of the disease in the region. In collaboration with the public and research health sector, industry and international funding agencies, we are developing a regional approach to capacity development, research and control. As a direct result of this philosophy a collaborative protocol is under development between the MRC, the Department of Health and the Ministry of Health (Mozambique) with a view to extending the effective malaria control in South Africa to the communities in neighbouring Mozambique. This will augment economic development and provide a platform for general health care in southern Mozambique. The areas of highest risk in South Africa are border areas (Fig. 2); for example, within 1 km of the border in northeast KwaZulu-Natal the annual parasite incidence is about 500 per 1 000, dropping to < 2 per 1 000 over 10 km from the border. Malaria control in southern Mozambique would reduce the burden of disease for approximately 1 million people and contribute to the elimination of the high-risk areas in South Africa. Investment in malaria control in southern Mozambique by South Africa would have cost-benefit implications for South Africa, as a result of reduced incidence and a reduction in the control requirements in our country.

Tourism is a major earner of foreign exchange for all southern African countries and, in many instances, travellers visit more than one country. There is a need for good maps outlining the malarious areas of southern Africa to facilitate informed advice to tourists and businessmen. The need did not exist before, as chloroquine was a cheap, readily available, effective and relatively well-tolerated antimalarial. The arrival and spread of *P. falciparum* drug resistance has changed this. The MRC is currently negotiating with the relevant authorities in these countries towards collaboration on the production of malaria distribution maps for the region as a whole.

Malaria research in South Africa played a major role in the early developments of malaria control strategies. We are now entering a period when we can again take up our rightful place in Africa and South African malaria research can again play a major role in research and training.

Much of the work presented here would not have been possible without close collaboration with the Department of Health staff, specifically those in malaria control, and the National Malaria Research Programme. The Medical Research Council, Health Systems Trust, Roche and Agroevo are thanked for financial support in respect of quoted work.

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