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Malaria research, 1980–2004, and the burden of disease

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Abstract

Malaria is estimated to cause about 1.6% of the 57 million deaths occurring annually and 2.3% of the disease burden. However, it accounts for only about 0.4% of world biomedical research, and this percentage is barely changing. Most of the research takes place in Europe and North America, which are little affected directly by the disease, 90% of whose burden occurs in sub-Saharan Africa. Research includes both pharmaceutical and non-pharmaceutical approaches; the fastest growing ones involve the artemisinins and genetics. Leading countries in malaria research (including India, Thailand, Kenya and Nigeria) differ greatly in the subjects that they favour.

Keywords: Malaria; Disease burden; Bibliometrics; Research outputs; Sub-Saharan Africa; Pharmaceuticals

1. Introduction

Malaria has been one of the most potent scourges of mankind from time immemorial, and it remains, with AIDS and tuberculosis, one of the three major communicable diseases. Previously it was widespread, with many deaths in Europe, but it is now mainly confined to Africa, Asia and Latin America. Most of the estimated 900,000 deaths each year occur among children in sub-Saharan Africa, and malaria is responsible for over 10% of the disease burden in 15 African countries, and for between 5% and 10% in a further 19[1]. The problems of malaria control in tropical countries are aggravated by inadequate health infrastructures and poor socio-economic conditions. Moreover, in the last few decades the disease has shown resistance to the drugs normally used to combat the protozoan parasite (*Plasmodium*) that causes it, and the vector (the mosquito, *Anopheles*) has become resistant to some of the insecticides used to control it. The spread of malaria has been facilitated by population movements, some water development projects and the effects of climate change, and between 300 million and 500 million people now suffer episodes of the disease.

Although the bitter-tasting component of the bark of *Cinchona ledgeriana* was known as an effective anti-malarial since the 15th century in Peru, and an infusion of qinghao (*Artemesia annua*) has been used for more than 2000 years in China, the active ingredients were only isolated by pharmacists in the early 19th and late 20th centuries, respectively. Systematic control of malaria really began with the discovery of the malaria parasite by Laveran in 1880, and the demonstration by Ross that the mosquito was the carrier (vector) in 1897 – both discoveries leading to the award of Nobel prizes for medicine or physiology (in 1907 and 1902, respectively). One of the most effective means of control was through the removal of surface water in which the mosquitoes could breed: this was applied with great effect to the region around Rome in the 1930s. The second world war stimulated the search for new methods, and DDT was developed as an insecticide to kill the mosquitoes, and the chloroquine group of drugs were synthesised as an effective treatment.

Because malaria depends solely on human hosts for its onward transmission, if all the members of a population are free of the disease, then it will not be spread to any newcomers. Thus, the possibility that malaria could be eliminated from the planet took hold in the post-war period, and major campaigns were carried out in many countries to kill the mosquitoes and distribute drugs. There was also a major effort by USAID, unfortunately badly managed, to produce a malaria vaccine (Desowitz, 1993).

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[1] Based on disability adjusted life years (DALYs), as reported on the WHO website (2002 estimates). The percentage burden of disease from malaria is higher in 39 African countries than in any Asian one.

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The consequence was a big reduction in the death toll from the disease in many countries (Spielman et al., 1993), but over-confidence led to a reduction in the research effort. Data for India are fairly typical: the annual number of recorded deaths from malaria was about 800,000 at Independence, and then fell rapidly in the 1960s and 1970s to a low of fewer than 100, only to rise again to 200–300 at the end of the 1980s and over 1100 in the mid-1990s when there were several outbreaks, often caused by heavy rains (Sharma, 1996; Lal et al., 2000). Since then better control measures have brought the toll down to below 700, but it is still a persistent problem and malaria control absorbed a quarter of the national health budget from 1977–1997, with most of the money being spent on insecticides (Dhingra et al., 1998). However, these figures may well under-state the actual death toll from malaria in India, which was estimated by the WHO as 9400 in 2002, or just under 0.1% of all deaths.

During the 1990s, a renewed effort was made to reduce the burden from malaria, with major initiatives in research. The Multilateral Initiative on Malaria was started in 1997, following an initial meeting in Dakar in January and a further meeting of potential donors in Den Haag in July, but money built up rather slowly at first (Butler, 1997; Gallagher, 1997; Pennisi, 1997). Much more money has subsequently been forthcoming (Davies, 1999; Marshall, 2000; Butler, 2003; Das, 2003), particularly for research in Africa (Kilama, 2001; Ntoumi et al., 2004), and this seems to have had some positive results (Anon, 2002). Other initiatives include the Roll Back Malaria Project; the Global Fund for HIV, Tuberculosis and Malaria (the Global Fund); the Medicines for Malaria Venture; and the Malaria Vaccine Initiative (Alilio et al., 2004). The focus has been on high-tech approaches, such as the development of vaccines (Hagmann, 2000; Anon, 2001; Gulland, 2003) and the sequencing of the malaria genome (Gavaghan, 1994; Anon, 1996; Horrocks et al., 2000; Gardner et al., 2002; Holt et al., 2002). These approaches have been criticised because more conventional methods may be much more cost-effective and produce results more quickly (Curtis, 2000; Enserink, 2004). Moreover, social science research may also have a substantial role to play in the fight against malaria (Williams et al., 2002). The other methods include the promotion of insecticide-treated bednets (ITNs) (Anon, 2003; Anon, 2005) and the spraying of interior walls with DDT, which has recently been encouraged by the World Health Organization (Mandavilli, 2006) despite the opposition of some environmentalists and the Bayer Crop Science company, who had a rival (and more expensive) insecticide (Beattie, 2005).

In this paper, we have examined the outputs of malaria research over the quarter-century from 1980 to 2004, as revealed by papers recorded in the Science Citation Index (SCI). Quantitative surveys of malaria research have been undertaken before, but mainly as a means to estimate the financial resources going into malaria research (Anderson et al., 1996; Beattie et al., 1999; Lewison et al., 2002). An exception is the survey of malaria research in Brazil by Rodrigues et al. (2000), which compared its geographical distribution with that of cancer and cardiovascular research. We have analysed the malaria research papers in our database geographically, and compared national outputs of malaria papers with their production of biomedical papers overall so as to show their relative commitment to malaria research – this comparison to some extent compensates for biases in the SCI against tropical countries.

We have also analysed the database of papers in terms of the approaches being researched for malaria control. These include the study of mosquitoes and their habitats; spraying with DDT and other insecticides; the use of bednets; vaccine development; and genetic approaches. We have also looked at five sets of drug-based methods of attack: quinine; chloroquine; mefloquine; pyrimethamine; and the new artemisinins. There are major differences between countries in the relative emphasis that they give to these ten approaches. This diversity may well be highly desirable, but it is not clear that the national research profiles necessarily relate to the local situation. In fact, as we shall see, the large majority of the malaria research, as covered in the SCI, comes from high-latitude industrial countries with very little malaria.

Finally, we speculate that a high relative commitment to malaria research may well generate dividends in the form of a reduced burden from the disease, probably because a research-based healthcare environment is likely to lead to the adoption of appropriate control methods and the allocation of sufficient resources to make them effective, through more detailed examination of one particular country that has been in the forefront of the battle (Thailand).

2. Methodology

The malaria research papers were identified within the SCI (CD-ROM version) by means of a filter, developed by Andres de Francisco and Stephen Lipworth, on the basis of selected title words; details are given in Lewison et al., 2002. Only articles, notes and reviews were chosen, and their bibliographic details (authors, title, full source, document type and addresses) were downloaded to a file and then analysed using MS Excel. There were a total of 23,916 papers so listed, covering the 25 years 1980–2004, though a few 2004 papers would have been absent because of late processing for the SCI.

The addresses on the papers were analysed by country on both an integer and a fractional count basis using a macro written by Philip Roe. Integer counts give unity credit to each country listed in an address on the paper, and fractional counts divide up the unity credit equally to each address. Thus, a paper with one address in Germany, one in Thailand and two in India would count unity for each of the three countries on an integer count basis, but 0.25 each for Germany and Thailand, and 0.5 for India, on a fractional count basis. Because of international collaboration, integer counts will sum to more than 100% of the fractional count/actual total, and the ratio between a country's fractional and integer counts affords a simple measure of the amount of international co-authorship.

Interest in malaria research is very widespread, and some 155 countries (out of 192 members of the World Health Organization) were represented among the addresses on the papers. The papers were also classified by their research level on the basis of the journal in which they were published and the pres-

Table 1
Some leading journals used by malaria researchers with their research levels for 2000–2004

Journal	Papers	RL
Bulletin of the World Health Organization	307	1.03
Lancet	201	1.24
Transactions of the Royal Society of Tropical Medicine and Hygiene	1257	1.28
Journal of the American Mosquito Control Association	799	1.42
American Journal of Tropical Medicine and Hygiene	1443	1.59
Acta Tropica	289	1.70
Indian Journal of Medical Research	197	1.94
Journal of Medical Entomology	459	2.16
Memorias do Instituto Oswaldo Cruz	215	2.27
Journal of Parasitology	289	2.58
Parasitology	305	2.76
International Journal for Parasitology	178	3.28
Science	134	3.52
Proceedings of the National Academy of Sciences of the USA	259	3.70
Journal of Biological Chemistry	238	3.93

RL1: clinical observation; RL4: basic research.

ence of "clinical" or "basic" words in the titles of papers in that journal (Lewison and Paraje, 2004). Research level (RL) is a decimal number between 1.0 = clinical observation and 4.0 = basic research. (The scale is the one used by CHI Research Inc. (now IPIQ) to categorise biomedical research journals for the biennial US National Science and Engineering Indicators; the intermediate levels were labelled "clinical mix" and "clinical investigation". However, CHI only used these four categorical levels.) Table 1 shows some examples of the RLs of leading journals.

We were interested to see the amount of national research activity in malaria compared with each country's biomedical research output in all subject areas. For this purpose, an address-based filter was used (Lewison and Paraje, 2004) that identified biomedical research papers, and the (integer counts) of leading countries in biomedical research were determined from the SCI. The ratio of the percentages of a country's presence in malaria research to its presence in biomedical research then gave its relative commitment to malaria research. This was, of course, much higher than unity for many countries affected by the disease, and was mostly below unity for countries not so affected. The papers in the file were also sub-classified by subject area within malaria research, mostly on the basis of the presence of particular title words, but for two of the 10 subject areas (vaccines and genetics), also on the basis of papers in relevant journals. The 10 subject areas, each of which was given a three-letter (trigraph) code for ease of reference, with their corresponding title words, were as shown in Table 2.

The relative commitment to each of these 10 subject areas for the leading countries was calculated relative to their presence in world malaria research overall, again as a number that could be either above or below unity.

Finally, some comparisons were made with the burden of disease from malaria in selected countries, so that their malaria

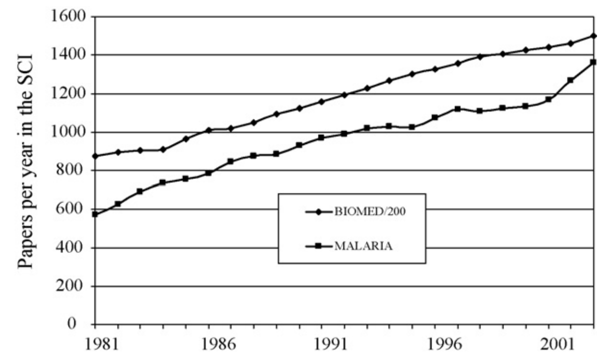

Fig. 1. Numbers of biomedical papers (divided by 200) and malaria research papers in the SCI, 1980–2004 (three-year running means).

research activity could be viewed in context. This burden can be calculated in terms of disability-adjusted life years (DALYs) or in terms of deaths. The World Health Organization publishes on its website estimates for both these numbers for all its member countries for the year 2002; for some countries the numbers of deaths from various diseases, including malaria, are given over a span of years. Each of these indicators should also be compared with overall DALYs and overall deaths, respectively: this can show if a country is over- or under-researching malaria compared with the need to combat the disease (among others). This is, of course, a rather crude comparison because in many tropical countries the biggest health burdens are attributable to a lack of good food, potable water and effective sanitation, which are not primarily susceptible to being tackled with more research.

3. Results

Malaria research is a small sub-field and currently represents about 0.4% of biomedical research output in the SCI, though it was only about 0.3% in the early 1980s. (The calibration factor of the filter was determined as 0.91, meaning that it over-estimated the number of malaria papers, because of a lack of precision, by about 9%.) Fig. 1 shows the growth of the gross numbers of malaria and biomedical research papers over the quarter-century,

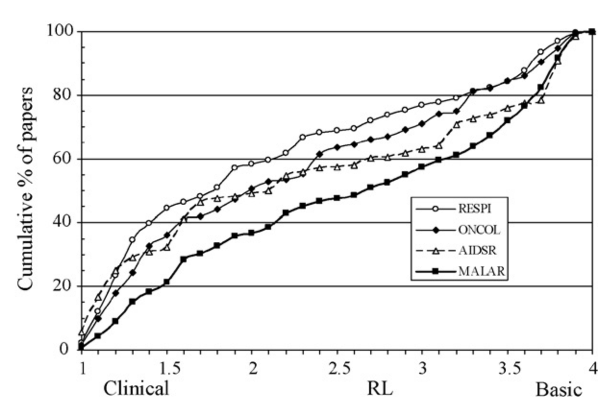

Fig. 2. Distribution of research level (journal) of papers in four biomedical sub-fields: MALAR: malaria, 1980–2004; AIDSR: AIDS research, 1997–2001; ONCOL: cancer research, 2000; RESPI: respiratory medicine, 1999–2001. RL1: clinical; RL4: basic.

Table 2
List of 10 subject areas within malaria research, with trigraph codes, title words used to identify papers, and numbers of papers found in the file

Subject area	Code	Title words	*N*
Artemisinins/qinghaosu	AAQ	Artemether, artemisinin, artesunate, qinghaosu	828
Bednets	BED	Bednets	91
Chloroquine	CHL	Chloroquine	2073
DDT and other insecticides	DDT	DDT, dieldrin, insecticid*	342
Genetics	GEN	Chromosom*, gene, genes, genetic*, genom* + Genetics jnls	1613
Mefloquine	MEF	Mefloquine, lariam	475
Mosquito habitats and control	MOS	Mosquito*	3701
Pyrimethamine	PYR	Fansidar, pyrimethamine	522
Quinine and quinidine	QUI	Quinidine, quinine	248
Vaccine development	VAC	Immuniz*, vaccin* + Vaccine	840

with the latter divided by 200, and three-year running means to smooth out annual variations.

Fig. 2 shows the distribution of the research levels of the malaria papers, with, for comparison, papers in three other biomedical sub-fields – AIDS, cancer and respiratory medicine. As can be seen the malaria papers are the most basic of the four, with a median value of RL of 2.66 compared with 2.10 for AIDS, 1.98 for cancer and 1.77 for respiratory medicine. This suggests that much still has to be learned about the fundamentals of the disease, whereas for the other research sub-fields, the emphasis of research is very much on the development of new and better drugs.

Table 3 shows the numbers of papers in each quinquennium from 19 leading countries with both integer and fractional totals, in all cases as percentages of the world total. The integer counts are, of course, higher than the fractional ones, and the ratio between them gives a measure of the amount of international collaboration in a country's malaria research – the further the ratio is from unity, the more the collaboration. Although normally countries with less scientific output collaborate more internationally, it is striking that India collaborates so little with other countries – this finding applies to other fields of science as well. During the quarter-century, most countries among the leading 19 have increased their relative presence in malaria research, particularly Kenya and Brazil, but four (Israel, Nigeria, the USA and India) have decreased their presence. For Israel and the USA, malaria is not a domestic problem, but it certainly is for Nigeria, where malaria causes a burden (measured in DALYs) twice that in any other country and is responsible for over 11% of the total burden of disease (compared to 0.3% in India). Nigeria also tends to collaborate rather little with other countries.

Fig. 3 shows the relative commitment to malaria research (on a log scale) of these 19 countries during the last 10 years (1995–2004). As would be expected, the countries most committed to malaria research in relation to their biomedical research output are all ones affected by the disease, but Kenya, Thailand and Nigeria are in a different group from India, South Africa and Brazil. Among the industrial countries, Australia, Switzerland

Table 3
Percentages of world total papers in each of five quinquennia, 1980–2004, for 19 leading countries in malaria research, integer and fractional counts and ratio between them over 25 years

	Integer counts					Fractional counts					FR/IN
	80–84	85–89	90–94	95–99	100–104	80–84	85–89	90–94	95–89	100–104	
USA	40.7	38.1	33.9	30.6	32.1	38.1	33.6	28.0	23.8	23.6	0.82
UK	14.2	13.5	16.6	19.4	19.7	12.7	10.9	11.4	12.3	11.3	0.68
France	4.8	7.3	9.5	9.2	10.2	4.2	5.7	7.1	6.4	6.5	0.72
India	6.9	4.9	4.6	5.0	5.8	6.7	4.8	4.4	4.7	5.4	0.95
Australia	2.7	5.0	6.4	6.5	7.4	2.4	4.3	5.2	4.9	5.1	0.77
Germany	3.4	4.2	4.3	5.3	7.5	2.8	3.6	3.3	3.3	4.5	0.69
Thailand	3.1	4.4	5.1	5.4	6.0	2.2	3.0	3.1	3.2	3.3	0.60
Japan	2.5	3.0	2.5	3.8	5.1	2.3	2.6	2.3	2.9	3.7	0.80
Switzerland	2.6	3.1	4.8	5.0	4.7	2.1	2.1	2.8	2.5	2.1	0.56
Netherlands	2.1	2.7	3.9	5.1	3.7	1.9	2.1	2.4	3.0	1.7	0.61
Brazil	0.6	1.3	2.4	2.8	3.2	0.5	1.0	1.8	2.1	2.4	0.75
Sweden	1.7	2.5	2.9	2.5	2.3	1.5	1.9	2.0	1.6	1.4	0.69
Canada	2.4	1.6	2.1	2.4	2.3	2.3	1.4	1.5	1.8	1.5	0.75
Nigeria	2.4	2.3	2.0	1.5	1.4	2.1	2.0	1.7	1.2	1.0	0.83
Kenya	1.1	1.4	2.2	3.3	4.8	0.8	0.9	1.4	1.6	2.0	0.51
China	1.3	2.0	1.5	1.7	1.9	1.2	1.8	1.0	1.4	1.5	0.82
Italy	0.9	1.1	2.1	2.4	2.6	0.7	0.8	1.3	1.5	1.5	0.61
Israel	1.6	1.9	1.8	0.9	0.9	1.5	1.6	1.5	0.7	0.6	0.81
South Africa	0.9	0.8	1.1	1.4	1.8	0.8	0.7	1.0	1.0	1.2	0.78
Total papers	3164	4114	5006	5415	6217	3164	4114	5006	5415	6217	

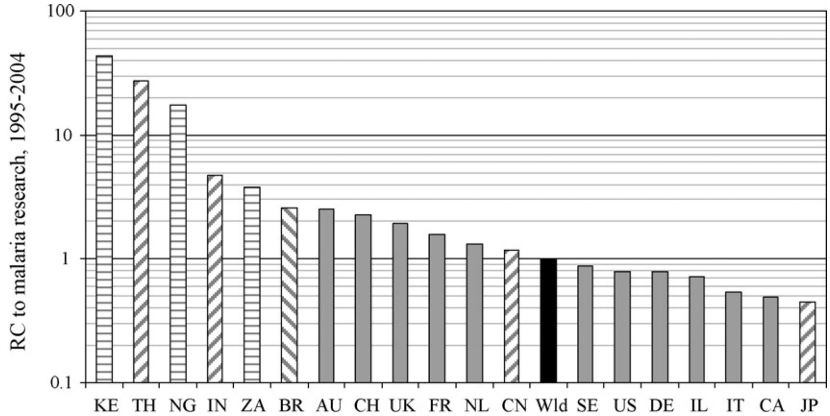

Fig. 3. Relative commitment of 19 leading countries to malaria research, 1995–2004 (log scale). Asian countries shaded diagonally to upper right; African countries shaded horizontally; industrial countries solid grey; Latin American country shaded diagonally to upper left. For country codes, see Table 4.

and the UK are relatively the most active, followed by France and the Netherlands, most of them for historical reasons.

The leading countries vary also in the type of research that they undertake. Some do mainly basic research, and some, mainly clinical observation; Fig. 4 shows the distribution of mean RL values. (Although basic biomedical research is taking place that may ultimately benefit the fight against malaria, these papers will not be included in the database unless they appear relevant to malaria and have a "malarial" title word. The "basic" work considered here was primarily genetics and secondly vaccine development.) The most basic research appears to be done in three Asian countries (Japan, Israel and China) but this may be an artefact of the SCI, which may not cover the clinical journals from Japan and China, and perhaps not those of Israel if they are written in Hebrew. The three African countries, Nigeria, Kenya and South Africa are clearly doing very clinical work, which is likely to be of immediate benefit to their populations, which is appropriate.

Ten subject areas within malaria research were identified, as shown in Table 2. They comprised between 40% and 45% of all malaria papers. Although Table 2 shows the overall numbers of papers in each subject area, there were some noticeable variations with time in the popularity of the subjects. Figs. 5 and 6 show these variations for four of the five non-pharmaceutical

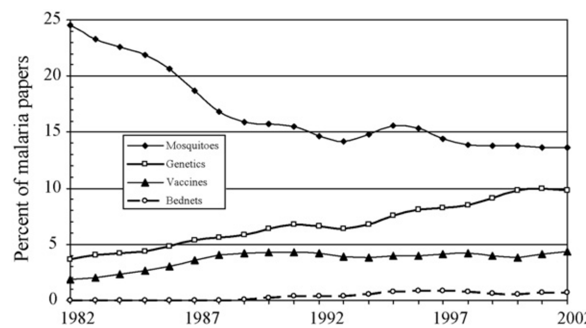

Fig. 5. Variation with time of research articles on four non-pharma approaches to malaria control, 1980–2004 (five-year running means), as percent of all malaria research: worldwide.

and pharmaceutical approaches (the others, not shown, are small and relatively constant). There has been a steady relative decline in the amount of attention given to mosquitoes and their habitat, but, as might be expected, an increase in the relative effort devoted to genetics. Vaccines research increased in the 1980s, and has remained at about 9% of the total. Work on bednets is still sparse, probably because the technology is by now well understood and the main questions are how best to distribute them (in some African countries, they are still taxed by the govern-

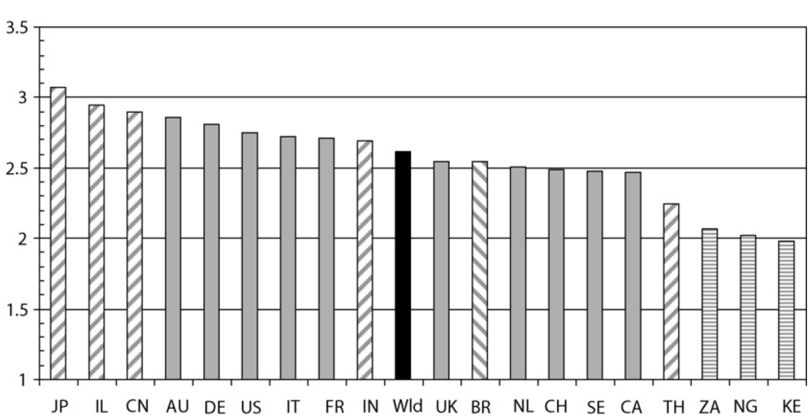

Fig. 4. Mean research level of malaria papers in SCI from 19 countries, 1980–2004. (1: clinical observation; 4: basic research). Industrial countries (not much affected directly by malaria) shown in gray. For country codes, see Table 4.

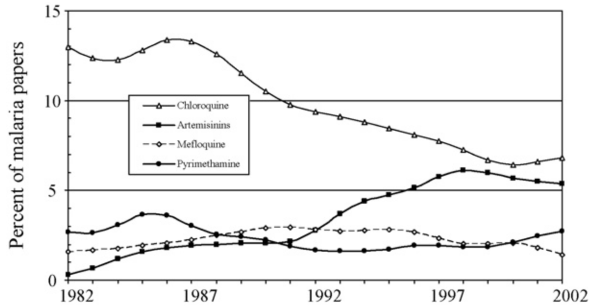

Fig. 6. Variation with time of research articles on four pharmaceutical approaches to malaria control, 1980–2004 (five-year running means), as percent of all malaria research: world-wide.

ment). Among the pharmaceutical approaches, it is striking how the amount of research on chloroquine has declined (although relatively rather than absolutely, and it may now be making a comeback: Vogel, 2006) whereas that on the artemisinins has increased from almost none in the early 1980s to around 6% in the 21st century.

There are some big differences between individual countries in the amount of research effort that they devote to these subject areas. Table 4 shows the relative commitment (in relation to their number of malaria research papers overall) of the 19 leading countries over the whole period. Values of RC greater than unity indicate that more research is undertaken than the world average, and *vice versa*. Different fonts are used to identify countries and subject areas with particularly high RC values. Among the non-pharma approaches, mosquito control research is undertaken most by the USA and Canada. South Africa concentrates heavily on the insecticidal approach (and maintained the use of DDT for the internal spraying of houses when it was proscribed in other African countries), and Kenya and the UK on the bednet approach. Malaria vaccines have been most favoured by Switzerland (led by F Hoffmann La Roche sa and the Swiss Tropical Institute), although Colombia (not shown in Table 4) has a RC of 5.5 to this subject area, largely because of the work of Manuel Patarroyo, who published 33 papers on malaria vaccines. Among the pharmaceutical approaches, the new artemisinins have (not surprisingly) principally engaged the attention of the Chinese, followed by the Thais. Chloroquine research has been the main interest of Nigeria, and mefloquine research in Thailand, Switzerland, Nigeria and Sweden. Nigeria has also been active in work on pyrimethamine (as has Kenya), and Thailand in work on the traditional remedy for malaria, quinine, which is now making something of a comeback as resistance develops to some of the newer drugs.

So the pattern of research interests can be seen to reflect the actual policies used to combat malaria in many of the countries affected.

4. Malaria research and deaths in Thailand

Thailand, together with other south-east Asian "tiger" countries, has been making a determined effort to modernise its economy through investment in science. This has borne fruit in the form of published scientific papers, whose numbers in the SCI have risen from fewer than 240 per year in the early 1980s to more than 1250 per year in the early 2000s. More than 60% of these papers are biomedical, and malaria research accounts for about one in eight of them. This compares with one in 250 biomedical papers worldwide, showing that Thailand's average relative commitment to malaria research is almost 36 times its "expected" value. It was even higher than this in the 1980s and early 1990s, during which time the Wellcome Trust tropical medicine unit was developed under the direction of Professor Nick White FRS, who is a pioneer of and enthusiast for the new drug, artesunate (a qinghaosu derivative), one of the artemisinins, which were subject to clinical trials and animal studies in China in the early 1980s and were tried out in Thailand from 1994 onwards (Marshall, 2000).

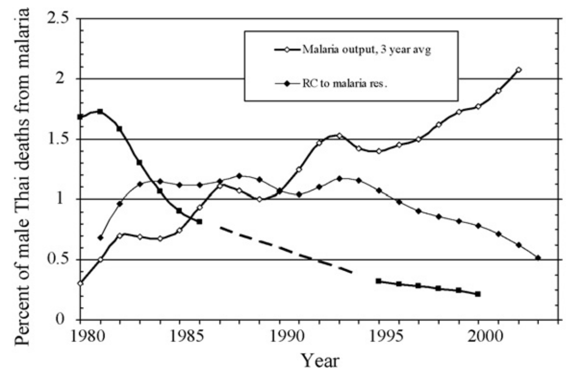

Fig. 7. Malaria research in Thailand, numbers of papers per year (running three-year mean) and relative commitment to malaria research (running five-year mean), right scale; and percentage of male deaths from malaria (WHO country data), 1979–2000. Note: malaria death rates have also been estimated at ten times these values in WHO DALY country estimates for 2002.

The death rate from malaria has dropped sharply, and does not seem to have suffered the recent rises that occurred in India as a result of heavy rain and a relaxation of controls. However, it is hard to be sure because the WHO data for deaths in Thailand (for which there is a long series available, from 1979 to 2000, with only a short break from 1988 to 1993), shown in Fig. 7, are much lower than the WHO estimate for 2002, which is just under 4000 deaths, about 1.0% of all Thai deaths in that year. (This is an order of magnitude higher than the recorded number, which probably refers only to registered deaths.) The figure also shows the RC to malaria research and the annual number of malaria papers, which has continued to rise. One would hardly expect that research *per se* would directly affect the death rate from malaria, but a national culture that places a high value on such research will also be favourable to well-chosen approaches to malaria control. Moreover, the prestige of the internationally connected malaria research community is likely also to be influential in the securing of appropriate resources for control and treatment.

5. Malaria research and control measures in India

By contrast, the situation in India is less favourable. In the 1950s and 1960s, as a result of the eradication programme, malaria cases were reduced to below 100,000 and deaths almost eliminated. Malaria became a rural disease and it was negligible

Table 4
Relative commitment of 19 leading countries to different subjects within malaria research (for codes, see Table 2), 1980–2004

		AAQ	*BED*	*CHL*	*DDT*	*GEN*	*MEF*	*MOS*	*PYR*	*QUI*	*VAC*
US	U S A	0.68	0.21	0.65	0.57	1.18	0.45	1.64	0.53	0.39	1.46
UK	U K	0.69	2.48	0.68	1.71	1.32	0.70	0.66	0.98	1.32	0.91
FR	France	0.91	0.29	1.33	1.51	1.23	1.47	0.66	0.68	1.41	0.66
IN	India	1.09	1.23	0.87	1.80	0.67	0.25	1.12	0.45	0.26	0.51
AU	Australia	0.56	0.38	0.60	0.24	1.14	0.60	0.73	0.74	0.47	1.66
DE	Germany	0.56	0.09	1.49	0.00	0.76	1.19	0.35	0.68	0.61	0.54
TH	Thailand	3.15	0.00	0.40	0.63	0.65	**4.72**	0.47	1.61	**4.24**	0.28
JP	Japan	0.30	0.00	0.84	0.55	0.94	0.19	1.32	0.96	0.29	0.67
CH	Switzerland	1.36	1.02	0.65	0.97	0.72	2.84	0.33	1.57	0.50	2.71
NL	Netherlands	1.92	0.49	1.14	0.65	1.11	1.23	0.50	1.03	0.88	0.78
BR	Brazil	0.55	0.00	0.51	0.60	0.91	1.38	0.69	0.54	1.58	1.51
SE	Sweden	1.96	0.00	2.51	0.05	0.61	2.71	0.43	1.73	2.34	0.85
CA	Canada	0.36	0.00	1.16	0.54	0.74	0.77	1.78	0.13	0.82	0.12
NG	Nigeria	0.85	0.00	**5.09**	0.29	0.10	2.78	0.17	3.36	2.30	0.25
KE	Kenya	0.30	**8.47**	0.96	1.56	0.59	0.34	0.60	2.79	1.71	0.43
CN	China	**9.70**	1.58	0.79	0.31	0.76	1.00	0.78	1.29	0.58	0.62
IT	Italy	0.59	0.27	1.03	0.91	1.83	1.16	0.53	0.55	1.16	0.21
IL	Israel	0.20	0.00	1.14	0.00	0.52	1.23	1.02	0.40	1.09	0.00
ZA	S'th Africa	0.93	1.90	1.66	**6.11**	0.65	0.56	0.66	1.09	1.47	0.00

Values above 4 shown bold; values above 2 shown underscored; other values in normal type; values below 0.5 in light type.

in towns and cities. It was indeed neglected, and as a result of the relaxation of the main control measure, indoor residual spraying (IRS) with DDT and other new insecticides, it returned as a major public health problem, with over 6 million cases recorded in 1976, chloroquine-resistant strains being found in Assam and rising numbers of the more deadly falciparum malaria cases. In the rural areas, the primary health care system does not operate effectively and poor people are unable to afford the cost of treatment (a few US dollars for simple cases, but several hundred dollars for refractory ones). A further problem has been the environmental degradation associated with economic development, which has damaged the local ecology and created havens for the disease vectors. National development projects aimed at poverty alleviation have lacked proper health-impact assessments. As a result, Japanese encephalitis and dengue haemorrhagic fever have also increased rapidly.

In particular, epidemiological research was and is needed to understand the situation and devise appropriate public policies. What happened in the 1960s was that the reduction in malaria was attributable to the decline in *P. vivax* and not of *P. falciparum*, whose presence has now risen to over 50% in the 2000s and made control more difficult and more expensive.

6. Discussion

There are several interesting lessons to be drawn from this survey. First, despite all the international pleading about the need to combat malaria, there is little evidence that malaria research has increased significantly in recent years, although there are some signs of a small upturn since 2002. Second, the vast majority (74% on a fractional count basis) of all malaria research is still being carried out in developed countries. To some extent this high figure is an artefact of the journal selection process of the SCI, but it still represents a large proportion of the international literature. Third, it is clear that the strategies adopted by countries for their malaria research do take some account of national needs, with African countries performing clinical work and developed nations (including China) more basic work. Fourth, the major burden of malaria is suffered by Africa, with over 90% of the DALYs attributable to malaria, yet it performs less than 10% of world malaria research, see Table 5. This stark imbalance, which echoes the "10/90" gap described by the Global Forum for Health Research, means that Africa is lacking both researchers and advocates for more resources to be used for the control of the disease.

Table 5
The continents, with their burden of disease (Disability Adjusted Life Years, DALYs) from malaria and fractional counts of their malaria research papers, 1980–2004

Continent	DALYs	DALYs (%)	Mal res paps	Mal res (%)
Africa	31602	91.4	2276	9.6
Asia	2809	8.1	4035	17.0
Europe	3	0.0	7967	33.6
Latin America and Caribbean	141	0.4	989	4.2
North America	0	0.0	7135	30.1
Oceania	35	0.1	1293	5.5
World total	34590	100.0	23697	100.0

Research will not by itself reduce the death toll from malaria, though it may provide the knowledge base for appropriate public policies, provided that the authorities are aware of its outcomes and are prepared to listen. The example of Thailand given above shows that new drugs can be effective. In Kenya (Fegan et al., 2007) and Zanzibar (Bhattarai et al., 2007), the use of insecticide-treated bednets and the new artemisinin-based combination therapies (ACTs), has recently been shown to have beneficial results on both incidence and deaths. The former study showed that one death was averted for every 140 ITNs distributed. The latter showed that the strategy recommended by the Roll Back Malaria initiative, based on research findings, could be immensely effective and gave hope that "the Millennium Development Goals of reducing mortality in children under five and alleviating the burden of malaria are achievable in tropical Africa with high coverage of combined malaria control interventions".

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