

## Malaria research: preliminary findings of a bibliometric approach

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### Abstract

The object of the ongoing research reported here is to analyze and comprehend the international research efforts in malaria research derived from numerous programs and international initiatives, such as published and indexed articles by the major scientific databases. Our objective is to map the international and Brazilian research production, skills and competence along with the key research topics and themes of malaria research in the world and in Brazil. We also aim to identify the pattern of malaria research funding, which should provide subsidies to improve public policies in the field. References on the subject obtained from the Science Citation Index (SCI) and PubMed Medline (web edition) databases for the period 1997-2007 are analyzed and show that the research takes place mainly in Europe and North America, not the peripheral countries who are directly affected by the disease. Internationally, the most substantial funding for malaria research came from the National Institutes of Health (NIH), and World Health Organization (WHO). In Brazil, these were The National Council for Scientific and Technological Development (CNPq) and the State of São Paulo Research Foundation (FAPESP). These data are preliminary and we intend to extend the searches to other databases and also use network analysis to detect collaborative research groups or communities in this area.

### Introduction

With a history that merges with the own trajectory of mankind, malaria has reached the twenty-first century no longer a challenge restricted to developing countries in tropical regions. Approximate figures show that half the world population is at risk of malaria and that an estimated 243 million cases led to nearly 863.000 deaths in 2008, which places malaria as a major public health problem in the international arena (World Health Organization, 2009). Indicative of this centrality was its inclusion in the Millennium Development Goals: which argues that by 2015 the dissemination of malaria should be stable and epidemics controlled (United Nations, 2010). Consequently, since the late nineties of the last century, malaria research has been the focus of numerous programs and international efforts, such as the Roll Back Malaria Partnership (RBM), The Multilateral Initiative on Malaria, Medicines for Malaria Venture, The Global Fund to Fight HIV, Tuberculosis and Malaria and the Malaria Vaccine Initiative (World Health Organization, 2009). New models, new drugs and vaccines, especially in genomics with support of biotechnology, are some promises for the future. Therefore, to analyze and comprehend the international research efforts in malaria research derived from these initiatives, such as published and indexed articles by the major scientific databases, is the object of the ongoing research reported here. The project is also part of a research program on neglected diseases, coordinated by the National Institute on Science and Technology for the Management of Innovation on Neglected Diseases (INCT-IDN), based at the Oswaldo Cruz Foundation (<http://www.cdts.fiocruz.br/AnnualActivityReport/?p=home>) in Brazil. Therefore, the goal of this work is to map the international and Brazilian research

production, skills and competence along with the key research topics and themes of malaria research in the world and in Brazil. We also aim to identify the pattern of malaria research funding in the world and in Brazil, which should provide subsidies to improve public policies in the field.

### Methodology

To identify the studies developed in the world and in Brazil, its main actors (researchers and institutions) which are involved in the area, the selected databases for this study was Science Citation Index and PubMed Medline. Science Citation index is produced by the Thomson Reuters ISI Web of Science (ISI), the main source of globally recognized citation analysis (Meho, 2007) and also the main reference source for international coverage allowing the identification of the institutions from which all authors belong to. This database is available from many hosts such as Dialog and STN, but we utilized the versions offered in the Portal CAPES ([www.periodicos.capes.gov.br](http://www.periodicos.capes.gov.br)), a Brazilian virtual library funded by the Ministry of Education which provides the international scientific production to educational and research institutions free of charge. The version we utilized is also known as Web of Science (WOS). PubMed Medline database (web edition) is published by the National Library of Medicine (USA), also a leading English language abstracting and indexing service in the area of health and medicine. To define the search strategy, the hypothesis was that if an article is part to the area of malaria research, the authors should mention either the disease (malaria) or the vector (*Anopheles*) or the parasite (*Plasmodium*) in at least three search fields: either title, or keyword, or abstract. The study period was 1997-2007. Why this period? As explained above, after the late 1990's a coalition of organizations and individuals, was initiated on 1997 with the objective to strengthen and sustain, through collaborative research and training, the capability of malaria-endemic countries to carry out research required to develop and improve strategies for malaria control. After the searches, without time restriction in WOS, 26.949 references were identified during the study period of 1997 to 2007. Of this total, editorials, conferences and other works of this nature were excluded, which resulted in a total of 19.158 articles, scattered over 1.822 different journal titles. In PubMed, 25.416 references were found. We also excluded conferences and other works as in WOS, resulting in a total of 23.436 articles in 1.748 journal titles. From this initial universe, 1.225 articles from Brazilian institutions were identified in WOS, compromising 2% of the total and in PubMed, 356 articles were found, compromising 1.5%. The table below shows the global and Brazilian production of malaria research in WOS and PubMed for the period of 1997-2007.

**Table 1. Malaria scientific production, 1997-2007.**

<i>Publication Year</i>	<i>PubMed</i>		<i>Web of Science</i>	
	<i>World</i>	<i>Brazil</i>	<i>World</i>	<i>Brazil</i>
1997	1543	19	1351	30
1998	1633	19	1280	41
1999	1763	24	1473	48
2000	1814	28	1473	54
2001	1849	26	1480	42
2002	2072	31	1684	69
2003	2283	34	1877	63
2004	2360	39	1713	53
2005	2575	46	2231	76
2006	2698	41	2342	88
2007	2846	49	2254	101
	23.436	356	19.158	665

The references obtained were processed and analyzed using VantagePoint software, developed by GeorgiaTech and marketed by U.S. company SearchTechnology (<http://www.thevantagepoint.com>). Institute of Scientific and Technological Communication and Information in Health (ICICT-Fiocruz) has an academic license since 2007. A process of standardization was carried out to bring together the various different names of a particular author or institution and a VantagePoint thesaurus for names and addresses was created in order to process additional name and address lists. This process helped to cut out unnecessary data variation and redundancy (Porter & Cunningham, 2005, p. 324).

## Results

### *Key communication channels*

The results of malaria research have been disseminated mainly through scientific journals at an international and national level. Nonetheless, the most productive journals identified originate from countries which do not have the pathology, such as the American Journal of Tropical Medicine and Hygiene, Acta Trop, Molecular and Biochemical Parasitology, Transactions of the Royal Society of Tropical Medicine and Hygiene, and the Tropical Medicine & International Health.

**Table 2. Ranking of journal titles in the database**

<i>WOS</i>		
<i>Journals</i>	<i>N. Articles</i>	<i>Impact Factor</i>
Am. J. Trop. Med. Hyg	1894	2.795
Acta Trop	957	2.221
Mol. Biochem. Parasitol	781	2.939
Trans. Roy. Soc. Trop. Med. Hyg	684	2.553
Trop. Med. Int. Health	581	2.328
Infect. Immun	536	4.205
Malar. J	410	2.995
J. Infect. Dis	401	5.865
Lancet	387	30.758
Ann. Trop. Med. Parasitol	376	1.368
<i>PubMed</i>		
Am. J. Trop. Med. Hyg	1219	2.795
Mol. Biochem. Parasitol	667	2.939
Trans. Roy. Soc. Trop. Med. Hyg	647	2.553
Trop. Med. Int. Health	575	2.328
Infect. Immun	473	4.205
Malar. J	471	2.995
J. Infect. Dis	469	5.865
Lancet	402	30.758
Ann. Trop. Med. Parasitol	362	1.368
Southeast Asian J Trop Med Public Health	343	0

It is striking that there are no journal titles from countries where the burden of malaria is highest. Although it is a local and neglected disease, the production is still noticeably international. This reflects the historical preponderance of scientific production of International Health, also known as Global Health, tropical medicine, among others in the area of parasitology by world regions such as Europe and North America. These results are in accordance with the few bibliometric studies reported in the literature of malaria research, such as Lewinson (2002), Falagas *et al* (2006), Garg *et al* (2006), and Fialho & Srinivas

(2004), which also shown that most of the prolific institutions are located in central and developed countries.

#### *Communication channels in Brazil*

The Brazilian authors, or the institutions which are located in Brazil, publish their work on the subject specifically on the journals listed in the table below; the vast majority of whom are international. Three of the titles are among the international journals with the most published articles in WOS: American Journal of Tropical Medicine and Hygiene, Molecular and Biochemical Parasitology and Transactions of the Royal Society of Tropical Medicine and Hygiene. It is interesting to notice that the American Journal of Tropical Medicine and Hygiene is the only journal present in both WOS and PubMed, placing first in the later. Among the Brazilian publications: Memórias do Instituto Oswaldo Cruz, Revista da Sociedade Brasileira de Medicina Tropical, Revista de Saúde Pública e a Revista do Instituto de Medicina Tropical of São Paulo, are the leading national journals for consultation on the issue. Also interesting is the fact that all of these journals, both for the international and Brazilian publications, reflect the overall area of tropical medicine research of which malaria belongs, with a relative overall low impact factor. Most, are not higher than 3 with the exception of The Lancet, Infection and Immunity, The Journal of Infectious Diseases and Insect Biochemistry and Molecular Biology.

**Table 3. Ranking of journal titles published by Brazilians in the database.**

<i>WOS</i>		
<i>Journals</i>	<i>N. Articles</i>	<i>Impact Factor</i>
Mem. Inst. Oswaldo Cruz	70	2.097
Am J Trop Med Hyg	37	2.795
Mol Biochem Parasit	24	2.939
Exp Parasitol	23	1.773
J Med Entomol	22	1.921
Rev Saude Publica	22	1.006
Acta Trop	17	2.221
Insect Biochem Molec	16	3.117
Rev Soc Bras Med Tro	14	0.736
Trans R Soc Trop Med Hyg	12	2.553
<i>PubMed</i>		
Am J Trop Med Hyg	24	2.795
Exp Parasitol	15	1.773
Acta Trop	14	2.221
J Med Entomol	14	1.921
J Infect Dis	10	5.865
Mem Inst Oswaldo Cruz	10	2.097
Trans R Soc Trop Med Hyg	10	2.553
Malar J	8	2.995
Rev Inst Med Trop Sao Paulo	7	0.3741
Rev Saude Publica	7	1.006

#### *Researchers*

As for the authors, we listed below in table 4 the top ten researchers who published in the area of malaria. As a preliminary finding, we identified that the majority of the articles are published in collaboration, mostly with researchers from North-South collaborations and/or institutions, mainly Thailand and Kenya. Further analyses are necessary, but these findings

suggest that it is mostly through these types of collaborations that researches from the south become more “visible”.

**Table 4. Ranking of the most productive authors in malaria and origin**

<i>Author</i>	<i>Instances</i>	<i>Institution</i>	<i>Country</i>
Looareesuwan, Sorrnchai	285	Mahidol University	Thailand
White, Nicholas J	270	Mahidol University	Thailand
Kremsner, Peter Gottfried	204	Univ Tubingen	DE
Marsh, Kevin	169	Kenya Medical Research Institute; Institute of Molecular Medicine	Kenya, UKA
Hoffman, Stephen L	146	USN, Med Res Institute	USA
Snow, Robert W	135	Kenya Medical Research Institute; Wellcome Trust Collaborat Programme	Kenya, UKA
Nosten, Francois	133	Wellcome-Mahidol University Oxford Tropical Medicine Research Unit	Thailand <sup>1</sup>
Rosenthal, Philip Joseph	114	Univ Calif San Francisco	USA
Patarroyo, Manuel Elkin	112	Fdn Inst Immunol Colombia	Colombia
Cowman, Alan F	109	The Walther and Eliza Hall Institute of Medical Research	Austrália

<sup>1</sup> This Unit was formed as collaboration between the Faculty of Tropical Medicine, Mahidol University, Bangkok and The Centre for Tropical Diseases, Nuffield Department of Medicine, John Radcliffe Hospital, University of Oxford in 1979. It is supported by the Wellcome Trust of Great Britain and is based in Thailand (<http://www.tm.mahidol.ac.th/en/wellcome/index.html>).

As for the Brazilian authors, the most productive are researchers from the Universidade Estadual de São Paulo (USP), Fundação Oswaldo Cruz (Fiocruz), Instituto Evandro Chagas-IEC, Centro de Pesquisas de Medicina Tropical - CPMT e Universidade Federal do Estado de São Paulo (UNIFESP).

**Table 5. Ranking of the most productive Brazilian authors in malaria and origin.**

<i>PubMed</i>			<i>WOS</i>		
<i>Authors</i>	<i>N. Articles</i>	<i>Origin</i>	<i>Authors</i>	<i>N. Articles</i>	<i>Origin</i>
Ferreira, M. U.	37	USP	Ferreira, M. U.	40	USP
del Portillo, H. A.	26	USP	Daniel-Ribeiro, C. T.	27	Fiocruz
Daniel-Ribeiro, C. T.	25	Fiocruz	del Portillo, H. A.	26	USP
Krettli, A. U.	21	Fiocruz	Krettli, A. U.	24	Fiocruz
Povoa, M.M.	20	IEC	Garcia, C. R. S	23	USP
Wunderlich, G.	20	USP	Sallum, M. A. M.	22	USP
Forattini, O. P.	19	USP	Povoa, M. M.	21	IEC
Soares, I. S.	19	USP	Forattini, O. P.	19	USP
Kirchgatter, K.	18	USP	Rodrigues, M M	19	UNIFESP
Rodrigues, M. M.	17	Unifesp	Soares, I. S.	19	UNIFESP

### Main themes

As a preliminary finding, we identified the top ten themes present in the keywords specified by the authors. It is only natural that the most frequent keywords reflects the nature of the strategy utilized in the search, in our case, the disease (malaria), the vector (*Anopheles*) or the

parasite (*Plasmodium*). In WOS, one may observe that in relation to the parasite, the *Plasmodium falciparum* is approximately seven times more cited than *Plasmodium vivax*. Malaria is caused mainly by four species of *Plasmodium* parasites, of which *P. falciparum* causes most disease and death across sub-Saharan Africa, and *Plasmodium vivax* is the most prevalent parasite in most other malaria-endemic parts of the world. Vivax malaria has been historically categorized as benign; however, there are reports of increasing clinical severity and resistance to antimalarials in South America and Southeast Asia. Malaria, as a single entity, is recognized as a prominent neglected disease, without much research and development investment devoted to it. However, most of the activity is perhaps justifiably focused on *Plasmodium falciparum*, because of its more lethal consequences. Nevertheless, the important health and economic morbidity that *P. vivax* imposes upon a much larger number of people in certain areas requires more research (Lacerda et al, 2007). One may also note that, some otherwise singular subjects also appear, such as drug resistance and artemisinin. Antimalarial drug resistance is a major public health problem which hinders the control of malaria. Since 1960s the sensitivity of the parasites to chloroquine, the best and most widely used drug for treating malaria, has been on the decline. Newer antimalarials were discovered in an effort to tackle this problem, but all these drugs are either expensive or have undesirable side effects. Moreover after a variable length of time, the parasites, especially the *P. falciparum* species, have started showing resistance to these drugs also. Currently, artemisinin and its derivatives are a group of drugs that possess the most rapid action of all current drugs against malaria. The starting compound, artemisinin (a sesquiterpene lactone), is isolated from the plant *Artemisia annua*, a herb described in Chinese traditional medicine, though it is usually chemically modified and combined with other medications. Treatments containing an artemisinin derivative are now standard treatment worldwide for malaria. In PubMed, the major themes seem to revolve around broader subjects, such as specific population risk groups. These include humans, as opposed to malaria in animals, more specifically semi-immune pregnant women in areas of high transmission. Malaria can result in miscarriage and low birth weight, especially during the first and second pregnancies. Therefore, these themes are all very high on the priority lists of research agendas worldwide for malaria.

**Table 6. Ranking of the main keywords**

<i>WOS</i>		<i>PubMed</i>	
<i>Keywords (author's)</i>	<i>N. Articles</i>	<i>Keywords (author's)</i>	<i>N. Articles</i>
malaria	4078	Humans	17439
<i>Plasmodium falciparum</i>	1999	Animals	16668
<i>Plasmodium</i>	546	Female	7266
chloroquine	396	Male	5700
Mosquito	345	Adult	4343
<i>Anopheles gambiae</i>	315	Child	3457
<i>Plasmodium vivax</i>	281	Child, Preschool	3057
<i>Anopheles</i>	276	Adolescent	2880
Drug resistance	252	Molecular Sequence Data	2532
Artemisinin	195	Infant	2420

### Project Funding

In addition to this investigation, we also consulted the Lattes Database, a Curriculum and institutions database of Science and Technology areas in Brazil (<http://www.e.gov.br/defaultCab.asp?idservinfo=126&url=http://lattes.cnpq.br/>), in order to identify the national and international funding agencies obtained by the most productive authors. It was then identified that among the 68 most productive authors, 55% (37 authors)

received at least one type of financing in the period. National institutions that funded most projects were: The National Council for Scientific and Technological Development (CNPq) (46), State of São Paulo Research Foundation (FAPESP) (16), FAPEMIG (4), FAPEAM (1) and FAPESP (1). International funding agencies that funded projects were: NIH (5), WHO (2), World Bank (1), UNICEF (1). In other words, the vast research efforts in malaria in Brazil seem to not have been benefited by these external programs.

## Conclusion

This work covered the international and the Brazilian scientific production of malaria, covering the period of 1997-2007. References on the subject obtained from the Science Citation Index (SCI) and PubMed Medline (web edition) databases with 26.949 references in WOS and 23.436 articles in PubMed. The most substantial funding for malaria research was guaranteed by: the National Institutes of Health (NIH); the World Health Organization (WHO) in the US and The National Council for Scientific and Technological Development (CNPq) and the State of São Paulo Research Foundation (FAPESP) in Brazil. For future research, we intend to use network analysis to detect collaborative research groups or communities in this area (Morel *et al*, 2009). We also intend to extend the searches to other databases, since SCI does not index a large number of journals published from peripheral countries, such as Brazil, China and India. Therefore, research in malaria, which predominantly affects these countries and is of local interest end up becoming “invisible”. By extending our searches to other databases, such as Scientific Electronic Library (SciELO), Scopus, Chemical Abstracts Biological (CAB), among others, we will be able to have a better view of the malaria research output worldwide.

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