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FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

A TEN-YEAR CROSS SECTIONAL STUDY OF TRENDS OF LABORATORY-CONFIRMED MALARIA IN THE REPUBLIC OF SOUTH AFRICA

BY

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Science in Epidemiology in the field of Epidemiology and Biostatistics

Johannesburg, April 2012

DECLARATION

I, Beatrice Lydia Mwagomba, hereby declare that this research report is my own work. It is being submitted for the degree of Master of Science in Epidemiology in the field of Epidemiology and Biostatistics at the University of Witwatersrand, Johannesburg. It has not been previously submitted entirely or partially for examination at this or any other University.

Signature:  Date: 25th April 2012

DEDICATION

I dedicate this work to my lovely baby, Caleb Shaddai Mwagomba, who endured mum's sleepless nights and restless weekends through assignments, examinations and the research project, while in utero and after birth. May his life be a testimony of God's sufficient grace upon women who are committed to career as well as family development.

ABSTRACT

Introduction

Malaria is a vector-borne parasitic disease with heterogeneous distribution in time and space. The sub-Saharan African region harbours the largest proportion of the global malaria cases and contributes over 90% to the deaths due to malaria. The present study aimed to identify trends of laboratory-confirmed malaria in both malaria endemic and non-endemic areas of South Africa over a period of ten years (January 2000 to December 2009). The association between malaria and demographic characteristics was also explored.

Materials and methods

This analytical cross-sectional study used secondary malaria surveillance data obtained from eight South African provinces through the National Health Laboratory Service. A population subset that utilised public health care facilities during the study period was included. Chi-square test of proportions was used to test if there were significant differences in the distribution of demographic and temporal characteristics among the laboratory-confirmed malaria cases. Annual parasite incidence of malaria was calculated to estimate malaria incidence in the population. Logistic regression models were constructed to determine the association between malaria and demographic characteristics.

Results

There were 175,069 suspected malaria cases from the endemic provinces of which 26,367 (15.1%) were laboratory confirmed; 130,980 (40.2%) suspected cases were from non-endemic provinces of which 42,488 (32.4%) were diagnosed as malaria. The overall malaria positivity rate was 21.4%. There were more cases of malaria among males (62.9%) than females, among individuals aged 25-44 years (44.0%) than individuals in any other age-group and among those living in non-endemic provinces (60.8%) than those living in endemic provinces.

A linear downward trend in malaria incidence was observed over the ten-year period ($p<0.001$). Thus, malaria incidence declined from an overall API of 64 per 100,000 population in 2000 to 50 per 100,000 population in 2009. The incidence of malaria in both endemic and non-endemic provinces was highest in the month of January (15 per 100,000 and 24 per 100,000 respectively).

The following demographic factors were found to be independently associated with increased malaria incidence: male gender (adjusted odds ratio (aOR) 1.54, CI: 1.51-1.57, $p<0.001$) and non-endemic province-type (aOR 2.68, CI: 2.63-2.73, $p<0.001$). Age was inversely associated with malaria incidence. Individuals in 45-64 and $\geq$ 65 year age-groups were 20% (aOR 0.80, CI: 0.77-0.82, $p<0.001$) and 51% (aOR 0.49, CI: 0.46-0.53, $p<0.001$) less likely to have malaria respectively.

Conclusion

There was a high incidence of laboratory-confirmed malaria in previously malaria non-endemic parts of South Africa especially Gauteng and North West provinces in the past decade. Targeted information, education and communication (IEC) to all travelers during the annual festive and holiday seasons should be reinforced to minimize importation of malaria into non-endemic areas.

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May God richly bless my husband, Kondwani Mwagomba, for selflessly standing by my side and amazingly filling the gap for our precious children. May a hard working spirit be imparted upon my first born son, Josua Wamaka Mwagomba, who endured life transitions at a tender age. I am also truly grateful for all the understanding and support from my parents and parents-in-law.

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ACRONYMS

ACT	Artemisinin-based Combination Therapy
aOR	Adjusted odds ratio
API	Annual parasite incidence
CDW	Corporate Data Warehouse
DDT	Dichlorodiphenyltrichloroethane
EC	Eastern Cape province
FS	Free State province
GP	Gauteng province
HIV	Human Immunodeficiency Virus
KZN	KwaZulu-Natal
LP	Limpopo province
LSDI	Lubombo Spatial Development Initiative
MP	Mpumalanga province
NC	Northern Cape
NHLS	National Health Laboratory Service
NICD	National Institute for Communicable Diseases
NW	North West province
OR	Odds ratio
RDT	Rapid Diagnostic Test
SA	South Africa
SADHS	South African Demographic and Health Survey
SOPs	Standard Operating Procedures
Stats SA	Statistics South Africa
SP	Sulphadoxine-pyrimethamine
USA	United States of America
WC	Western Cape province
WHO	World Health Organization

CHAPTER 1: INTRODUCTION

This chapter gives background information on the burden of malaria worldwide and in South Africa (SA). In addition the chapter includes a statement of the problem, justification for the study as well as study objectives

.

1.1 Background

Malaria is a vector-borne parasitic disease that occurs in tropical and subtropical regions of the world. The disease is caused by plasmodial parasites. There are four species of plasmodia that cause human malaria: *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae,* and *Plasmodium ovale. P. falciparum* and *P. vivax* are the most common while *P. falciparum* is also the most deadly [1]. Parasites are transmitted exclusively through the bites of certain *Anopheles* mosquitoes. The management, treatment outcomes and prognosis of infection due to the various species are different. Like most vector-borne infectious diseases, malaria has heterogeneous distribution in time and space [2]. Thus, the incidence of malaria varies between geographical areas which could be as small as villages or as big as provinces.

Globally, it is estimated that the number of cases of malaria rose from 233 million in 2000 to 244 million in 2005 but thereafter decreased to 225 million in 2009. Furthermore, the number of deaths due to malaria decreased from 985 000 in 2000 to 781 000 in 2009 [3]. Eleven countries in Africa reported marked decreases (>50%) in the number of malaria cases between 2000 and 2009. In all countries that showed this success, the decreases were associated with intense malaria control interventions. Even though there are reported decreases in malaria burden

worldwide, particularly noted in the European Region [3], malaria remains a major public health problem in sub-Saharan Africa. This region harbours the largest proportion of malaria cases (85%) as well as associated malaria deaths (89%) [4]. Nonetheless, southern Africa had four countries, including South Africa (SA), which showed a greater than 50% reduction in reported malaria cases between 2000 and 2009 [3].

South Africa's malaria transmission is mostly confined to the low altitude areas (below 1000 meters) [5] of Limpopo, Mpumalanga and north-eastern KwaZulu-Natal provinces. These areas form the south-eastern extremity of the tropical and subtropical malaria belt of Africa. The geographical locations of these areas within South Africa and in relation to other Southern African countries are shown in Appendix 1. Neighboring countries such as Mozambique and Zimbabwe are malaria hyper-endemic. Thus, SA has relatively low malaria transmission with epidemic-prone malaria infections since it is located along geographical margins of an endemic region [6]. The country's peak transmission period varies but transmission is limited to the summer months ranging from September to May [7].

The success in malaria confinement to the north-eastern border areas of South Africa is mainly attributed to the in-door residual spraying (IRS) of Dichlorodiphenyltrichloroethane (DDT) [8], which combats *Anopheles funestus,* a major pyrethroid-resistant malaria vector [9]. The introduction of DDT and other long-lasting insecticides from 1945 resulted in dramatic interruption of malaria transmission from most parts of SA [8].

The numbers of malaria cases and deaths reported through routine surveillance systems are used to inform core indicators for tracking the progress of malaria control programmes. However, not all malaria cases reported are laboratory confirmed, such that some of the cases reported as

malaria may possibly be other febrile illnesses. To minimize overestimation of the burden of malaria, the World Health Organization (WHO) recommends the use of parasitologically confirmed cases either by microscopy or by rapid diagnostic test (RDT) for monitoring trends of malaria in communities [10].

1.2 Statement of the problem

Despite SA's success in confinement of malaria transmission, a high number of cases are still being reported from malaria non-risk areas. For instance, Gauteng province, a non-risk area for malaria, has previously been observed to contribute greatly to reported malaria cases ranking third after Limpopo and Mpumalanga provinces [11]. However, published data on trends and patterns of parasitologically confirmed malaria cases for both risk and non-risk areas are scarce at national level. Very few malaria studies have been documented in SA's non-endemic provinces [12-15] and to our knowledge long term malaria trends have not been studied in these areas. Therefore, it is not known whether or not the observed reduction in SA's reported malaria cases in the past decade [3] can be reflected in both endemic and non-endemic areas. It is also not known how demographic characteristics like age, gender and location are associated with malaria in SA.

1.3 Justification

The drivers of malaria in endemic and non-endemic areas are different; hence the malaria control measures in these areas might not necessarily be standard. For endemic areas, the risk of malaria transmission is expected to be high due to environmental factors including greater precipitation

and higher temperatures that favour the breeding of Anopheline species and malaria parasite reproduction [2,6,7,16-20]. The non-endemic areas under study have for a long time been believed to have no risk for malaria infections [21-22] and hence the national focus for malaria treatment and control has been in the endemic areas.Therefore, knowing the prevailing trends and patterns in all areas nationally would be useful to inform policy for appropriate interventions at all levels.

1.4 Literature review

1.4.1 Malaria patterns in Sub-Saharan Africa

Malaria transmission intensity is directly correlated with breeding of *Anopheles* mosquitoes and varies with different vector species. In a meta-analysis done in sub-Saharan Africa, the heterogeneity of malaria transmission was found to result in large differences in malaria prevalence in humans living in different areas [23]. The prevalence ranged from 3% in an urban area to 81% in peripheral areas [23] in Brazzaville. This geographic variation in malaria occurrence is presumed to exist in all African countries.

A systematic review of data from 13 sub-Saharan African hospitals and two from the Arab peninsular, showed that a greater proportion of malaria admissions in children older than five years was associated with declining malaria transmission intensity [24]. Therefore, there is need to understand malaria distribution patterns in South Africa where malaria transmission has been reduced to elimination phase (<1 indigenous case/1000 population at risk).

1.4.2 History of malaria in South Africa prior to the study period

South Africa's national malaria incidence started showing declining trends in late 1940s. The successful decline and localization of malaria transmission was due to the vector control programmes that used DDT for indoor residual house spraying [25]. This strategy led to the elimination of the two major malaria transmission vectors: *Anopheles gambiae* and *Anopheles funestus*, leaving *Anopheles arabiensis* as the major vector in malaria risk areas of South Africa [5].

In the mid-1990s to 2001, a five-fold increase in malaria cases was seen in KwaZulu-Natal (KZN) province [26]. Factors contributing to this increase were seen to be parasitic resistance to chloroquine and sulphadoxine/pyrimethamine (SP), Human Immunodeficiency Virus (HIV) infection, mosquito resistance to pyrethroid insecticides and malaria importation [26]. The use of DDT was therefore re-introduced and scaled up since 2000 [27], in order to combat insecticide-resistant *An. funestus* in KZN and in the other malaria endemic provinces.

1.4.3 Trends and patterns of malaria in South Africa

A survey conducted in hospitals throughout Gauteng province in 2006 found a malaria incidence of 17.54 per 100,000 population [14]. This malaria incidence rate was said to be higher than previously reported in Gauteng province. However, the burden of malaria in Gauteng has not been compared to the burden in other non-endemic provinces.

In Kwa-Zulu Natal province, a retrospective analysis of malaria incidence rates between 1986 and 1999, showed an increase in incidence with uneven spatial distribution [28]. Signs of increase in high risk malaria areas were seen and geographic expansion of malaria transmission

in South Africa was suggested [28]. However, it is not known whether the increase was only within KZN province or extended to other provinces.

In Limpopo province, a descriptive study by Gerritsen *et al.* [29] found a statistically significant decline in trends of malaria incidence over the years 1998 to 2007. In the same study, the incidence rate was found to be low in 0–4 year olds and in those aged 40 years or more, and highest in the 35 to 39 years age group [29]. It is not known if such trends and patterns of malaria were existent in other parts of South Africa over the last decade.

1.4.4 Potential drivers of malaria case occurrence

1.4.4.1 Meteorological factors

Meteorological factors that affect the malaria include land cover, rainfall, altitude and temperature. These factors have been used to predict malaria transmission risk as they favour both the vector and the parasite [16-20]. A study done in Ethiopia, a country with unstable and seasonal malaria, found a significant association between malaria incidences and meteorological variables [30]. Low altitude areas are presumed to have different meteorological factors from high altitude areas, thus different risk levels for malaria. However, the recent global climate change is expected to influence malaria through changes in temperature, rainfall, and relative humidity. Thus, the behavior and geographical distribution of malaria vectors as well as the length of the life cycle of the parasite are expected to be directly modified. Evidence for the presumed change in distribution and behavior of the vector has already been documented [31]. Therefore, there is need to study trends and patterns of malaria in both the areas known to have malaria-risk and those previously known as malaria-free.

1.4.4.2 Non-meteorological factors

Human factors such as migration and land use play an important role in the epidemiology of malaria. Migration complicates measures for the control of malaria by contributing to the spread of malaria infection and exposing non-immune people to risk of infection [32]. Evidence of re-introduction of malaria in areas previously known to be free of malaria risk has been documented. For instance, since the 1980s a series of *Plasmodium falciparum* epidemic malaria has occurred in the western Kenyan highlands [33-36]. In such areas, migration was found to be significantly associated with both uncomplicated and complicated malaria [37-38].

In South Africa specifically, travel to an endemic area has previously been documented for individuals who present with malaria in a non-endemic area [15,39]. In a retrospective review of malaria cases seen in Pretoria, a malaria non-endemic area, Dube and colleagues [13] found that 96% of smear positive malaria patients had a positive travel history to malaria endemic countries in southern Africa, predominantly (71%) Mozambique. Only 4% of those who traveled received malaria chemoprophylaxis during their travel [13]. In another malaria non-risk area, Cape Town, Gray *et al*. [12] showed that pediatric and adolescent malaria was predominantly high among new and returned immigrants from other African countries [12]. Therefore, it is evident that malaria infections in non-endemic areas of South Africa are attributable to movement of people to and from malaria risk areas either as immigrants from neighbouring malaria endemic countries or internal migrants.

1.4.5 Prevalence of malaria species

In Japan, a study that looked at types of imported malaria found that 45% were *P. falciparum* and 45% were *P. vivax* [40]. Sub-Saharan Africa's malaria infections are predominantly caused

by *P. falciparum* and only 5% to 10% of malaria infections are said to be caused by non-falciparum plasmodial species [8]. A province-wide hospital-based prospective survey by Weber *et al.* [14] in Gauteng, South Africa, found that 96% of malaria infections were caused by *P. falciparum*, 2% by *P. malariae* and <1% each by *P. ovale* and *P. vivax*. However, there is limited documentation on the extent of non-falciparum malaria in endemic and non-endemic provinces.

In summary published documentation of recent trends and patterns of malaria as well as its associated demographic risk factors are scarce at national level. As such this study aimed at identifying trends of laboratory-confirmed malaria using data reported to the National Health Laboratory Service over a decade (2000 to 2009) from both endemic and non-endemic areas of South Africa.

1.5 Objectives

i. To describe patterns and trends of laboratory confirmed malaria cases by demographic characteristics in both endemic and non-endemic areas of South Africa over the period 2000 to 2009.

ii. To determine the relative proportions of malaria parasite species among the laboratory-confirmed malaria cases in South Africa for the period 2000 to 2009.

iii. To determine the association between laboratory-confirmed malaria and demographic characteristics in South Africa.

CHAPTER 2: MATERIALS AND METHODS

This chapter describes the setting in which the study was conducted as well as the study design, population, measurements used, data management, statistical analysis and ethical considerations applied.

2.1 Study design and period

The study was a cross-sectional exploratory analysis of secondary malaria data obtained from a national, laboratory-based surveillance system. The data were collected over a period of ten years from January 2000 to December 2009.

2.2 Study setting, population and data source

2.2.1 Study setting

The study was conducted in South Africa, one of the four sub-Saharan African countries designated for malaria elimination [41]. Thus, South Africa is in the phase of reducing the incidence of locally acquired malaria infection to zero through deliberate efforts [41].

Over the study period, a number of changes occurred in the national malaria control programme. Firstly, the vector control strategy resumed in-door residual spraying with DDT in 2000 [8]. Then the treatment policy changed in 2001with artemether-lumefantrine (LA) replacing sulphadoxine-pyrimethamine (SP) as first line treatment for uncomplicated *P. falciparum* infections. The treatment change followed the development of significant SP resistance [22].

Implementation process for the new treatment policy was not uniform nationally. Among the malaria endemic provinces, KwaZulu-Natal was the first to implement from 2001 while Mpumalanga used a different ACT using SP-artesunate in the public sector instead of LA from 2001 until January 2006 when LA became available. However, by December 2004, all the three malaria endemic provinces had replaced SP with ACTs for the treatment of uncomplicated malaria in the public sector [22]. The non-endemic provinces had no provision for the implementation of the WHO recommended ACT policy since the national guidelines recommended in-hospital treatment with quinine plus doxycycline/clindamycin for every malaria case seen in non-malaria areas [22].

The guidelines for diagnosis remained the same throughout the study period. However, there was increasing availability of rapid diagnostic testing (RDTs) for malaria screening at primary health care level [22].

2.2.2 Study population and sample

SA's total population was about 44 million people in 2000 and about 50 million people in 2009. Data from eight of the nine provinces were included. These were: Eastern Cape (EC), Free State (FS), Gauteng (GP), Limpopo (LP), Mpumalanga (MP), Northern (NC), North West (NW) and Western Cape (WC). One province, KwaZulu-Natal (KZN), was excluded because it was using a different laboratory information system from the other provinces during the study period.

The study population was a proportion of the population in the eight provinces that used public health care facilities during the study period. Annual population figures by province, gender and age were extrapolated from census data of 1996 and 2001 as reported by Statistics South Africa (Stats SA). An average annual growth rate (AGR) of 1.5% was used in estimating total population size per year. Study population estimates per year were calculated as a proportion of the total annual population per demographic characteristic using public health service utilization rates as reported by South Africa Demographic Health Surveys (SADHS) of 1998 and 2003. The population that did not report use of public health care facilities during the study period was excluded.

The study used convenient sampling method. The sample comprised of all people whose specimens were taken for malaria diagnostic testing in public health facilities with subsequent recording of results in a laboratory database from 2000 to 2009.

2.2.3 Data source

The study utilized malaria data from a database of the National Health Laboratory Service (NHLS). These data were collected from laboratories which were linked online to the NHLS's corporate data warehouse (CDW) through a laboratory based information system called DISA*LAB. All malaria specimens handled by the reporting laboratories were recorded in the database regardless of results. Only the data from laboratories whose specimens came from public health facilities were included in the dataset used for this study as an attempt to achieve data completeness. The data available from a few private facilities which reported to the NHLS during the study period were excluded.

2.3 Laboratory methods

A blood sample from every suspected malaria case was examined to confirm or exclude malaria diagnosis [22]. Two main methods were used to test the presence of malaria parasites: oil immersion microscopy using Giemsa stain and rapid antigen detection using rapid diagnostic test (RDT) kits which contain histidine-rich protein 2 or lactate dehydrogenase or aldolase [22]. Use of the rapid antigen detection test was basically a screening tool especially for early diagnosis in health facilities where microscopy was not immediately available. Thus, the RDT positive cases were further confirmed microscopically.

Standard operating procedures (SOPs) were available for malaria antigen detection, Giemsa staining technique, malaria microscopic investigation and quantitation of malaria parasitaemia. Quality control tests were run on all reagents as one way of assuring quality of test results. This study assumed that similar malaria diagnostic procedures were followed in all NHLS-linked laboratories during the entire study period.

2.4 Study variables and definitions

The dataset contained the following information: province, health district, health sub-district, location name (health facility), age (years, months and days), gender, laboratory number (unique identifier), plasmodium antigen (positive or negative), malaria (presence or absence on microscopy), number of parasites, percent of infestation, malaria count, red cell count, month,

year and comments. The malaria parasite species detected was indicated under either malaria presence or comments.

2.4.1. Outcome variable

The outcome variable was malaria test result, a binary variable with positive or negative values. The outcome of interest was a parasitological malaria case which in this study was defined as a positive malaria test result confirmed in a laboratory. Ascertainment of a positive result was by either positive plasmodium antigen or presence of malaria parasites on microscopy.

2.4.2. Explanatory variables measured

All explanatory variables measured in this study were categorical and were defined as follows:

- Gender: defined as participant's sex, either male or female
- Age-group: defined as a category of completed years of age. The age-groups were either below 5 years or any 20 year band within 5 to 64 years or 65 years and above. The <5 years age-group was considered separately as a recommended strategy in monitoring trends of malaria in communities [10]. All ages of ≥65 years were aggregated to increase the accuracy of the estimates since their population numbers are relatively small.
- Province: defined as a political and government administrative area in which the reporting health facility is located.
- Province type: defined as a category of malaria risk to which a province belongs based on prior knowledge. It was categorized as either endemic i.e. a province with known risk of malaria transmission or non- endemic i.e. a province without known risk of malaria

transmission. Endemic provinces under study were LP and MP while non endemic provinces were EC, FS, GP, NW, NC and WC.

- Year: defined as time in calendar year (January to December)
- Year category: defined as categorized time in two calendar year intervals.
- Season: defined as either hot and rainy season in the months of September to May or winter season in the months of June to August.
- Malaria species: defined as malaria parasite species i.e. *P. falciparum, vivax, ovale* or *malariae.*

2.5 Data management

2.5.1 Data extraction and cleaning

The data collected and reported from laboratories were stored in a single Microsoft Structured Query Language (MS-SQL) database at NHLS's Corporate Data Warehouse (CDW). SQL scripts were written to extract data from the database to Microsoft excel spreadsheets. Data were then exported into STATA version 11.0 (StataCorp.2009, College Station, Texas, USA) for data cleaning, coding and statistical analyses. Determination of malaria incidence and generation of all graphs was done using the Microsoft excel software package.

Cleaning of the data involved checking for duplicate entries, outliers, missing and inconsistent values. All inconsistent values were corrected accordingly e.g. plasmodium antigen "present" was replaced with "positive" and age values recorded in months or days only were replaced with

equivalent complete years. All missing values were excluded from statistical tests involving their respective variables. Duplicate entries and repeated tests were identified using the unique laboratory number and were dropped.

2.5.2 Descriptive analysis

Chi-square test was used to compare differences in proportions of all variables since they were all managed as categorical. Differences were considered statistically significant at $p<0.05$.

Measures of frequency used were: Annual Parasite incidence (API) and malaria positivity rate. API was defined [42] and calculated as:

$$\frac{\text{Number of parasitological malaria cases in 1 year}}{\text{Estimated population per year}} \times 100{,}000^{*}$$

*API was expressed per 100,000 persons in this study instead of per 1000 persons [3] as a result of SA's low malaria prevalence.

Malaria positivity rate was defined as a proportion of positive malaria test results among all specimens examined per 100 persons. Trends of the calculated APIs were graphed over time and Chi-square test for trend was used to test linearity of the trends.

2.5.3 Inferential analysis

Logistic regression analysis was done to find out the existence of any association between the explanatory variables under study and malaria. Thus, exploratory logistic univariate and multivariable regression models were constructed with odds ratio (OR) as a measure of effect.

Despite a previous recommendation on variable selection [43], inclusion of factors into the multivariable model was set at 10% significance level after considering the limitation on the number of variables that were assessed. The multivariable models had the precision of estimate set at 5% significance level**.** The explanatory variables included in the multivariable model were tested for fitness in the model using the Chi-square log likelihood ratio test for individual parameters. All estimates were measured at 95% confidence level.

2.5.4 Ethical considerations

The study was approved by the Human Sciences Research and Ethics Committee of the University of Witwatersrand with an ethical clearance certificate number M10M101108.

CHAPTER 3: RESULTS

This chapter gives the results of analysis of laboratory-confirmed malaria cases for the ten year duration in South Africa. Descriptive time trends as well as logistic regression models for the association of demographic characteristics and malaria incidence are presented.

3.1 Overall distribution of the study sample

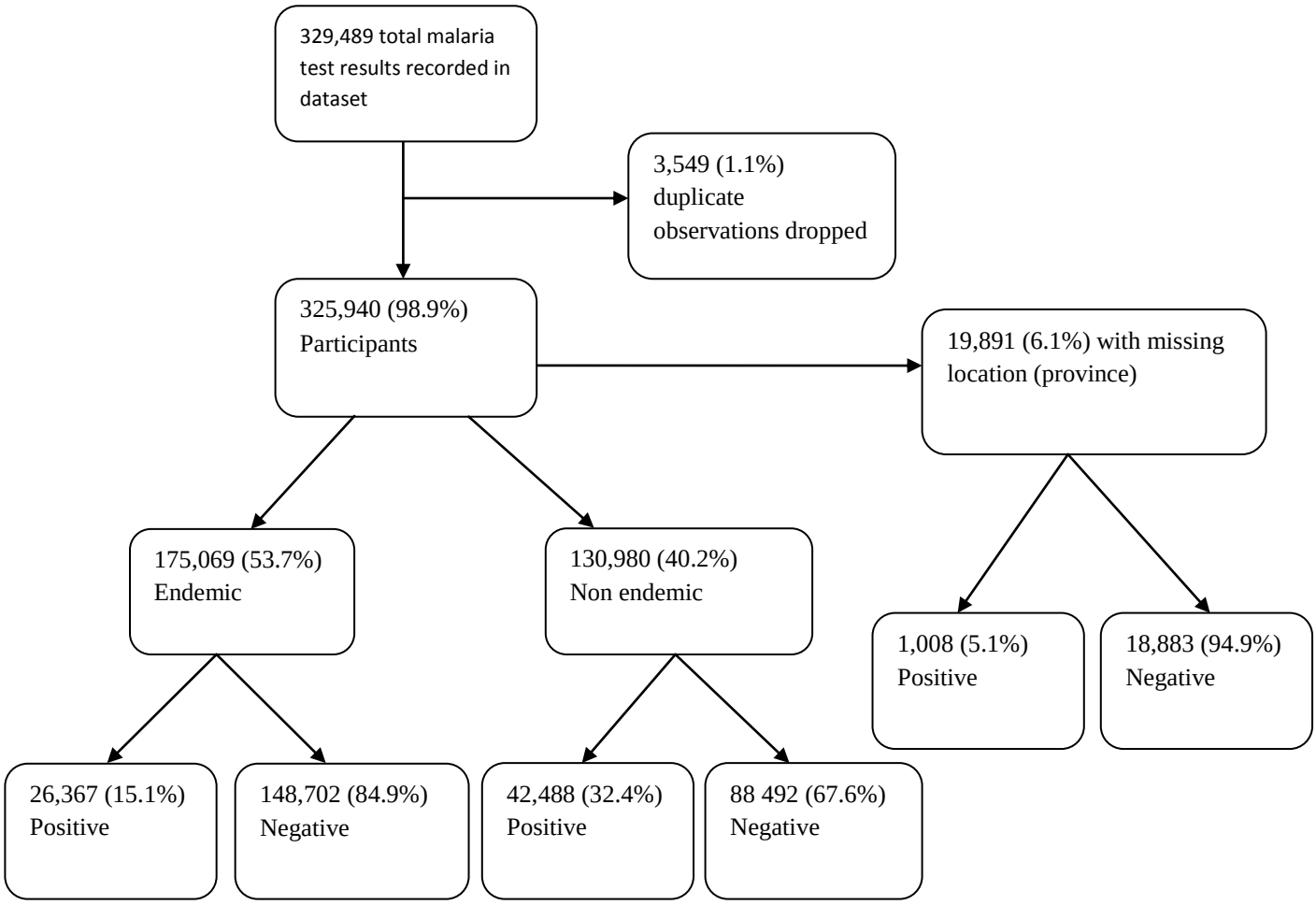


Figure 1: Distribution the of the study sample

A total of 325,940 suspected malaria cases were tested and reported from public health facilities in eight of the nine South African provinces between 2000 and 2009. 175,069 (53.7%) were from endemic provinces of which 26,367 (15.1%) were laboratory confirmed cases and 130,980 (40.2%) were from non-endemic provinces of which 42,488 (32.4%) were laboratory confirmed cases (figure 1).

3.2 Distribution of characteristics among the suspected malaria cases by outcome: South Africa, 2000 to 2009.

There were 69,863 participants who tested positive for malaria with a malaria positivity rate of 21.4%. The largest proportion of the positive outcome was from Gauteng (48.1%) while most of the negatives were from Limpopo (40.3%). The confirmed cases (44.0%) concentrated in the 25-44 year age-group and there were more malaria cases among males (62.9%) than females (33.3%) (Table 3.1).

Table 3.1: Demographic characteristics of suspected malaria cases by outcome: South Africa, 2000 to 2009.

Characteristic	Positive (n=69,863)	Negative (n=256,077)
	N (%)	N (%)
Gender		
Female	23,256 (33.3)	116,091 (45.3)
Male	43,963 (62.9)	132,795 (51.9)
Missing	2,644 (3.8)	7,191 (2.8)

Age-group in years		
0 – 4	7,095 (10.2)	25,669 (10.0)
5 – 24	16,913 (24.2)	65,912 (25.7)
25 – 44	30,751 (44.0)	100,520 (39.3)
45 – 64	6,528 (9.3)	31,228 (12.2)
≥ 65	945 (1.4)	8,658 (3.4)
Missing	7,631 (10.9)	24,090 (9.4)
Province		
EC	963 (1.4)	2,539 (1.0)
FS	1,481 (2.1)	2,576 (1.0)
GP	33,593 (48.1)	69,471 (27.0)
LP	7,511 (10.8)	103,088 (40.3)
MP	18,856 (27.0)	45,614 (17.8)
NW	4,680 (6.7)	7,400 (2.9)
NC	376 (0.5)	1,241 (0.5)
WC	1,395 (2.0)	5,265 (2.1)
Missing	1,008 (1.4)	18,883 (7.4)
Province type		
Endemic	26,367 (37.8)	148,702 (58.0)
Non-endemic	42,488 (60.8)	88,492 (34.6)
Missing	1,008 (1.4)	18,883 (7.4)
Time in years		
2000[#]	5,471 (7.8)	21,892 (8.5)
2001[#]	5,256 (7.5)	16,686 (6.5)
2002[##]	3,981 (5.70)	10,315 (4.0)
2003	8,078 (11.56)	21,349 (8.3)
2004	8,525 (12.2)	29,794 (11.6)
2005	8,859 (12.7)	33,480 (13.1)
2006	11,573 (16.6)	38,421 (15.0)
2007	6,307 (9.0)	29,970 (11.7)
2008	6,733 (9.6)	30,543 (11.9)
2009	5,080 (7.3)	23,626 (9.2)

Missing	0	1 (0)
Time in seasons		
Hot and rainy *(September - May)*	61,622 (88.2)	212,813 (83.1)
Winter *(June – August)*	8,241 (11.8)	43,263 (16.9)
Missing	0	1 (0)

3.3 Comparison of proportions of the characteristics among laboratory-confirmed malaria cases by province type

Demographic and temporal characteristics of 68,855 (98.6%) confirmed malaria cases with known location were analysed by province type. There were statistically significant differences in the distribution of malaria cases by gender, age, time and season ($p<0.001$) between endemic and non-endemic provinces. For instance, in the distribution by gender, the proportion of male malaria cases was higher in non-endemic provinces (67.0%) than in the endemic (62.6%).

A 49.3% reduction in the number of confirmed malaria cases was observed in endemic provinces from 3,787 in 2000 to 1,919 in 2009. On the other hand, an increase in the number of cases was observed in non-endemic provinces from 1,420 in 2000 to 3,138 in 2009 (Table 3.2).

Table 3.2: Comparison of proportions of the characteristics among laboratory-confirmed malaria cases by province endemicity: South Africa, 2000 to 2009.

Characteristic	Endemic N (%)	Non-endemic N (%)	P-value
Gender			
Female	9,587 (37.4)	13,385 (33.0)	
Male	16,070 (62.6)	27,208 (67.0)	<0.001
Age-group in years			
0-4	1,730 (7.3)	5,341 (14.2)	
5-24	7,112 (30.0)	9,551 (25.5)	
25-44	11,160 (47.0)	19,132 (51.0)	<0.001
45-64	3,131 (13.2)	3,189 (8.5)	
>=65	612 (2.6)	313 (0.8)	
Time in calendar years			
2000[#]	3,787 (14.4)	1,420 (3.3)	
2001[#]	2,004 (7.6)	3,096 (7.3)	
2002[##]	2,296 (8.7)	1,596 (3.8)	
2003	2,920 (11.1)	5,065 (11.9)	
2004	3,097 (11.8)	5,322 (12.5)	
2005	2,695 (10.2)	6,099 (14.4)	<0.001
2006	3,397 (12.9)	8,059 (19.0)	
2007	1,975 (7.5)	4,272 (10.15)	
2008	2,277 (8.6)	4,421 (10.4)	
2009	1,919 (7.3)	3,138 (7.4)	
Time in seasons			
Hot and rainy *(September - May)*	23,850 (90.5)	36,854 (86.7)	
Winter *(June – August)*	2,517 (9.6)	5,634 (13.6)	<0.001

[#] Data from two provinces (EC and WC) not included

[##] Data from one province (EC) not included

3.4 Distribution of malaria parasite species among the laboratory-confirmed malaria cases

Plasmodium falciparum was the only recorded malaria species, however only 41% of all observations had data on malaria species. There were statistically significant differences in the distribution of malaria species by gender, age, location and time ($p<0.001$) between cases that had *P. falciparum* and those that had no recorded malaria species (appendix 2).

3.5 The incidence of laboratory-confirmed malaria

The crude annual parasite incidence (API) of malaria ranged from 46 per 100,000 population to 115 per 100,000 with a median API of 66 per 100,000 over the ten year period. The API in 2009 (50 per 100,000) was 22% lower than that in 2000 (64 per 100,000).

3.5.1 Malaria incidence by age-group

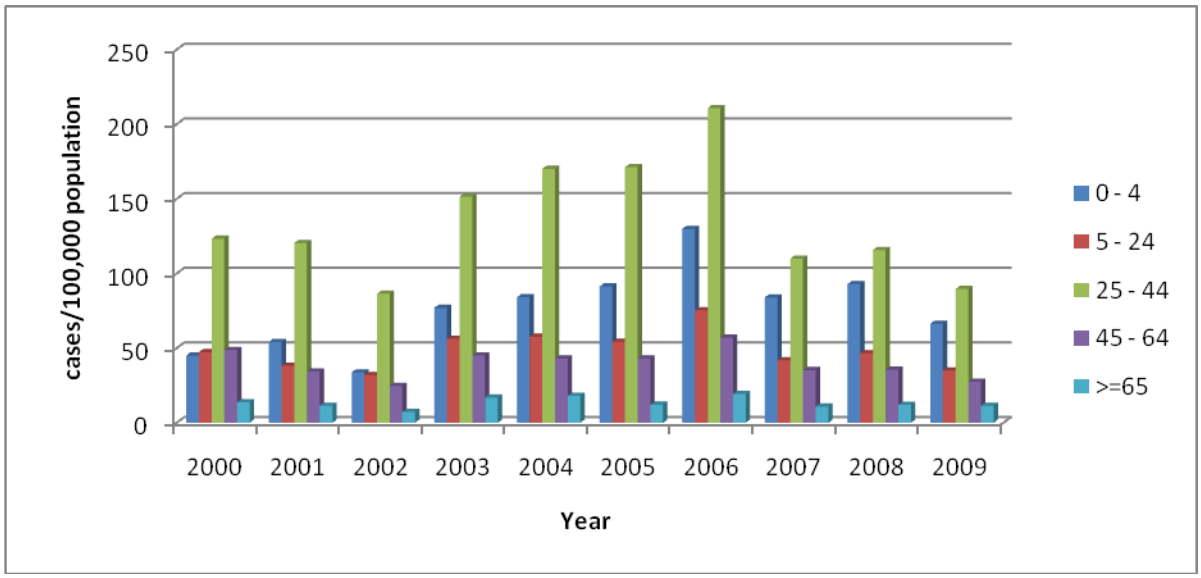


Figure 2: Age-specific malaria incidence by year, South Africa, 2000 - 2009.

The malaria incidence was consistently higher in the 25-44 year age-group followed by the 0-4 year age-group. The incidence was lowest in the ≥65 year age-group (Figure 2).

3.5.2 Malaria incidence by gender

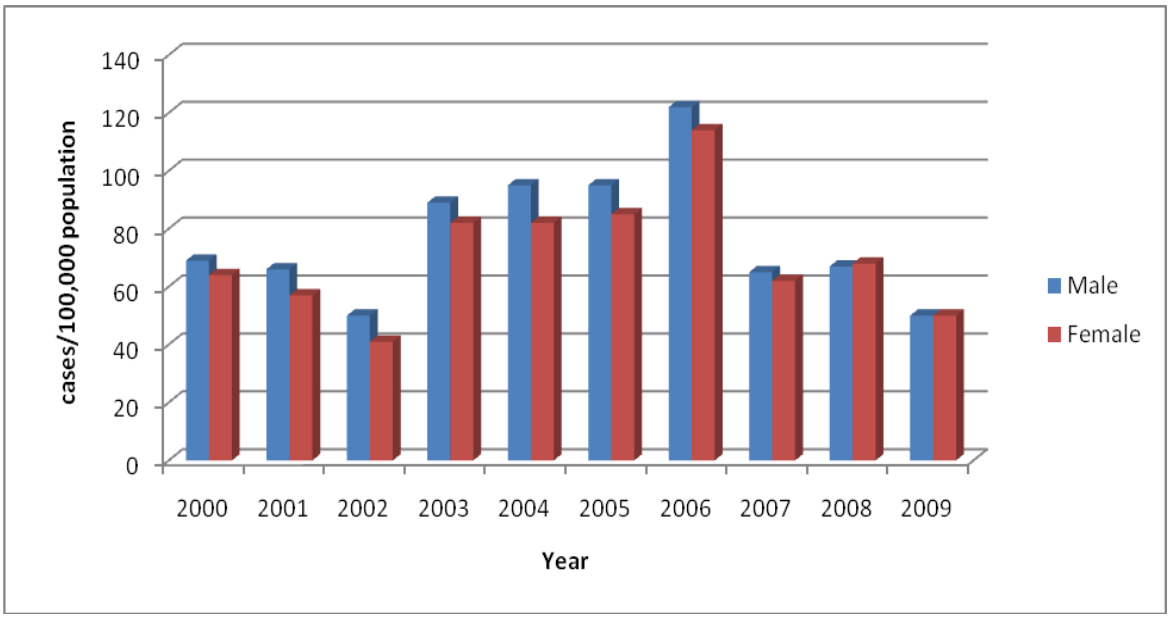


Figure 3: Malaria incidence by year and gender, South Africa, 2000-2009.

The incidence of malaria was generally higher in males than females. The highest incidence of malaria was in 2006 (API 120 and 115 per 100,000 population for males and females respectively). The incidence of malaria in both sexes declined to 50 per 100,000 in 2009 (Figure3).

3.5.3 Malaria incidence by province

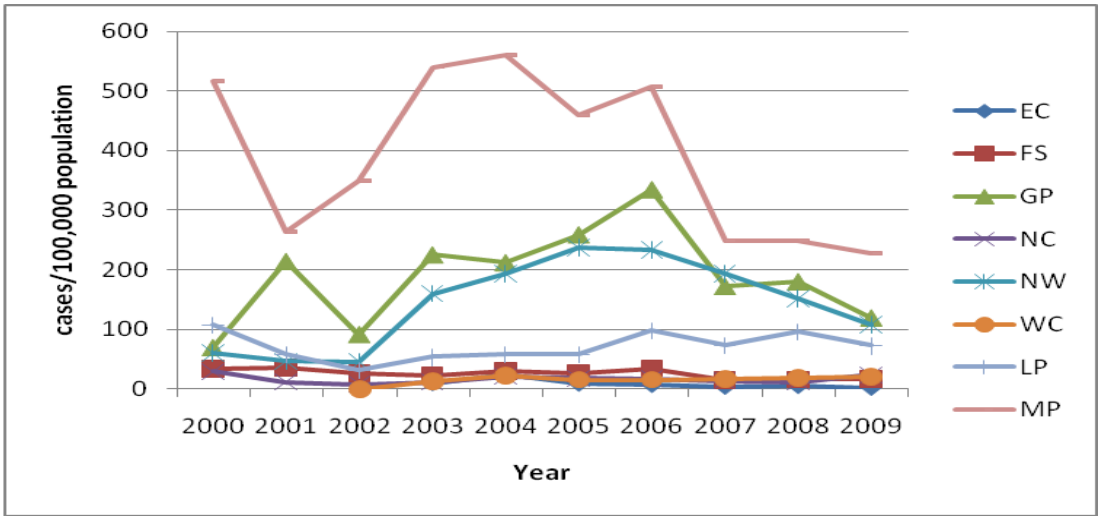


Figure 4: Malaria incidence by year and province, South Africa, 2000-2009

The burden of malaria was highest in Mpumalanga province which had consistently the largest annual parasite incidence. This was followed by Gauteng and North West, both malaria non-endemic provinces (Figure 4).

3.5.4 Malaria incidence by province-type

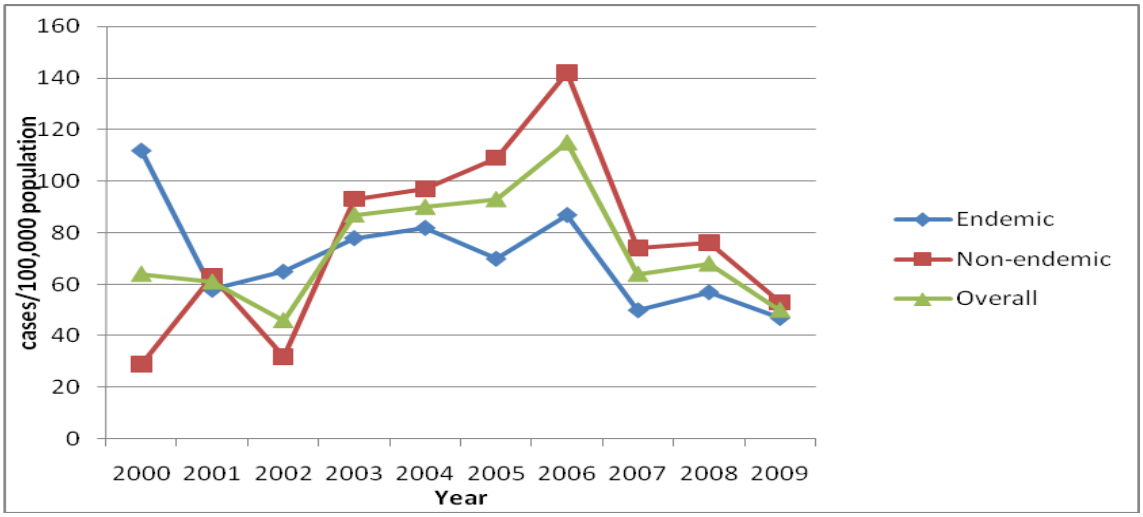


Figure 5: Malaria incidence by year in endemic and non-endemic provinces, South Africa, 2000-2009

In endemic provinces, there was a sharp decline of malaria incidence in the year 2001 followed by an increasing trend (though *below the 2000 level*) until 2005 when there was another drop. From 2003, the non-endemic provinces had a continuously increasing malaria incidence to a peak of 140 per 100,000 population in 2006. There was no observable difference in the trend of the incidence of malaria between endemic and non-endemic provinces from 2007 to 2009 (Figure 5). There were statistically significant linear trends of odds of malaria occurrence over time, both overall and stratified by malaria endemicity (X^2 trend test $p<0.001$); (appendix 3).

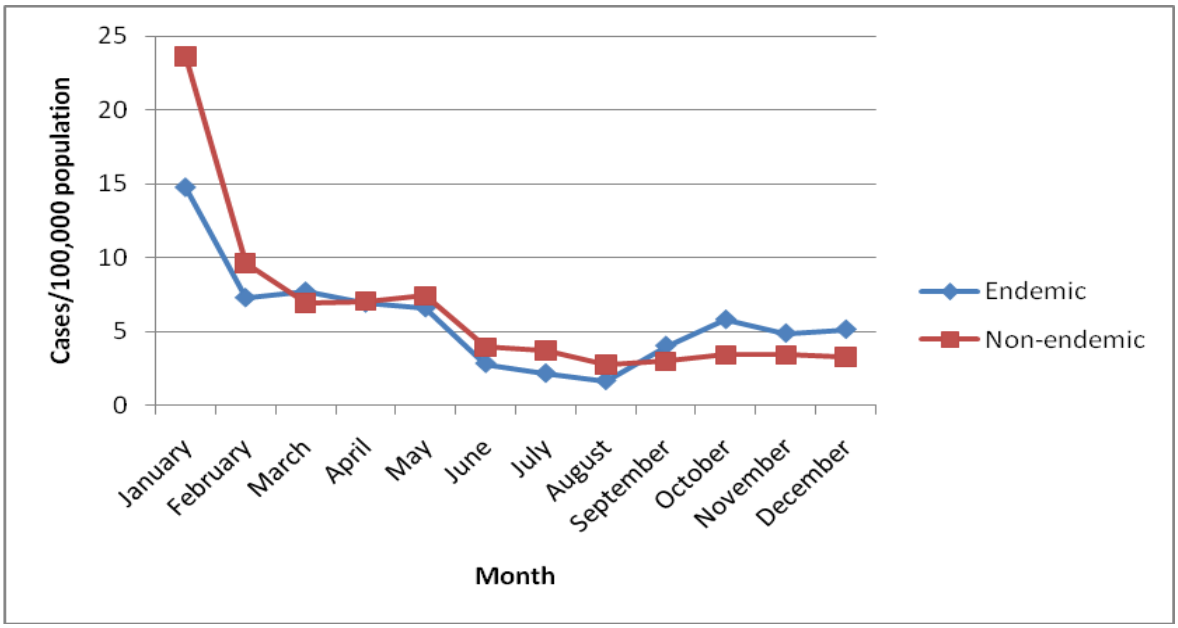


Figure 6: Mean incidence of malaria by calendar month in endemic and non-endemic provinces, South Africa, 2000 -2009

The highest monthly incidence of malaria in both endemic and non-endemic provinces was in January. During the summer months of September to December, the monthly incidence of malaria was higher in endemic provinces than in non-endemic provinces. However, the malaria incidence for the month of January was greater in the non-endemic provinces than in the endemic provinces (24 per 100,000 versus 15 per 100,000) (Figure 6).

3.6 Factors associated with the occurrence of malaria

3.6.1 Univariate analysis

The following factors were significantly associated with increased likelihood of malaria occurrence in univariate analysis: 25-44 year age-group (odds ratio (OR) 1.11, CI: 1.07 – 1.14, p<0.001); male gender (OR 1.65, CI: 1.62-1.68, p<0.001); non-endemic province type (OR 2.71,

CI: 2.66-2.76, p<0.001); calendar years 2002-2003 (OR 1.36, CI: 1.33-1.41, p<0.001); hot and rainy season (OR 1.52, CI: 1.48-1.56, p<0.001). The factors were included in a multivariable logistic regression model (table 3.4).

3.6.2 Multivariable analysis

In multivariable logistic regression analysis, the following factors were found to be independently associated with increased incidence of malaria:

i. Gender: Males were 54% more likely to have malaria than females (adjusted OR (aOR) 1.54, CI: 1.51-1.57, p<0.001).

ii. Province type: Individuals located in non-endemic provinces were 2.68 times more likely to have malaria than those who were located in the endemic provinces (aOR 2.68, CI: 2.63-2.73, p<0.001).

iii. Season: hot and rainy months of September to May had 68% more likelihood of malaria occurrence compared to the winter months of June to August (OR 1.68, CI: 1.64-1.73, p<0.001)

On the other hand factors that were found to be independently associated with reduced incidence of malaria were:

i. Age: Compared to 0-4 year age-group, individuals in 45-64 and ≥ 65 year age-groups were 20% (aOR 0.80, CI: 0.77-0.82, p<0.001) and 51% (aOR 0.49, CI: 0.46-0.53, p<0.001) less likely to have malaria respectively.

ii. Time in calendar years: Years 2006-2007 and 2008-2009 were associated with 31% (aOR 0.69, CI: 0.67-0.71, p<0.001) and 43% aOR 0.57, CI: 0.54-0.58, p<0.001) less likelihood of malaria occurrence respectively compared to 2000-2001.

Table 3.3: Logistic regression analysis for unadjusted and adjusted association of malaria occurrence and demographic characteristics

Explanatory factor	Univariate models			Multivariable model		
	OR	95% CI	P value	aOR	95% CI	P value
Age-group (years)						
<5	1.00	Reference	-	1.00	Reference	-
5-24	0.93	[0.90-0.96]	<0.001	1.04	[1.01-1.08]	* 0.021
25-44	1.11	[1.07-1.14]	<0.001	1.04	[1.01-1.07]	* 0.013
45-64	0.76	[0.73-0.79]	<0.001	0.80	[0.77-0.82]	<0.001
≥65	0.39	[0.37-0.42]	<0.001	0.49	[0.46-0.53]	<0.001
Gender						
Female	1.00	Reference	-	1.00	Reference	-
Male	1.65	[1.62-1.68]	<0.001	1.54	[1.51-1.57]	<0.001
Province-type						
Endemic	1.00	Reference	-	1.00	Reference	-
Non-endemic	2.71	[2.66-2.76]	<0.001	2.68	[2.63-2.73]	<0.001
Time category (calendar years)						
2000-2001	1.00	Reference	-	1.00	Reference	-

2002-2003	1.36	[1.33-1.41]	<0.001	1.11	[1.08-1.15]	<0.001
2004-2005	0.99	[0.96-1.02]	0.387	-		
2006-2007	0.94	[0.92-0.97]	<0.001	0.69	[0.67-0.71]	<0.001
2008-2009	0.78	[0.76-0.81]	<0.001	0.57	[0.54-0.58]	<0.001
Time in seasons						
Winter (*June - August*)	1.00	Reference	-	1.00	Reference	-
Hot and rainy season *(September - May)*	1.52	[1.48-1.56]	<0.001	1.68	[1.64-1.73]	<0.001

OR: odds ratio; aOR: denotes adjusted odds ratio; CI: confidence interval

*P value not considered due to non-significance of the result based on the confidence interval which is including values approximate to 1, a point of no difference

CHAPTER 4: DISCUSSION

This chapter gives a discussion of the main findings of this study. The study strengths and limitations are also highlighted. Additionally, suggestions for further studies and recommendations are outlined.

The study aimed at identifying trends of laboratory-confirmed malaria in South Africa over a ten-year period (2000 to 2009). We found that there was a decline in the trend of malaria incidence from 64 per 100,000 population to 50 per 100,000 population over the study period. There were more cases of malaria in the 25-44 years age group particularly among males. The incidence was higher in non-endemic provinces than in the endemic with a steeper decline in endemic provinces over the study period. The incidence of malaria was evidently higher during the month of January in both endemic and non-endemic provinces. Male gender and non-endemic province were independently associated with an increased likelihood of malaria occurrence. Age ≥45 years showed an inverse relationship with malaria. The summary of findings presented above will further be discussed in detail.

4.1 Distribution of malaria by demographic characteristics

4.1.1 High incidence of malaria among adults of economically productive age

The incidence of malaria was highest in the 25-44 year age-group, a subset of the economically productive age-group (15-64 years). This finding is consistent with previous studies in SA whereby high malaria levels were found among adults of economically productive age [14, 29].

A study conducted in Bhutan, a country with low malaria transmission intensity like SA, also found that most malaria infections occurred in the economically productive age-group [44]. This age pattern of malaria might be explained by the fact that economically productive individuals are likely to migrate to and from malaria risk areas in search of employment opportunities. This could be supported by previous documentation that migrant remittances form the main source of household income for both male and female migrants [45]. Therefore, these findings are suggestive that imported malaria contributes substantially to the malaria burden in SA and other low transmission areas.

In both endemic and non-endemic provinces, the age distribution pattern of laboratory-confirmed malaria cases found in this study was consistent with expected age patterns in populations that lack malaria immunity [46]. Even provinces that are traditionally known as malaria endemic did not show the predominance of ≤5 year-old children among the cases as would be expected in areas of high malaria endemicity [47]. Thus, South African residents of all ages, children and adults alike are at risk of contracting malaria infections.

4.1.2 High incidence of malaria among males

The incidence of malaria was higher in males than females throughout the study period except for the 2008-2009 calendar years. The finding of high incidence of malaria among males is consistent with previous findings in SA [13-14, 29] and in Bhutan [44]. This could be attributed to labour-related in-country and cross-country migration between malaria endemic and non-

endemic areas. The finding also supports a previous documentation that cross-border migration in the Southern African Development Community (SADC) region remains dominated by men [45]. Males are more likely to migrate to cities and other areas with employment opportunities, e.g. gold mines, to earn a living for their families.

This finding however, is in contrast to the finding of a study done in Cameroon where there was no significant difference in the prevalence of malaria between males and females [48]. The different findings might be due to the fact that Cameroon has higher malaria endemicity and hence less influence of migration on overall malaria incidence than SA.

The reasons for the change in gender distribution pattern of malaria between males and females in years 2008 - 2009 are however not clear. To our knowledge, there were no documented changes in in-country or cross-country migration patterns between males and females in those years.

4.1.3 High incidence of malaria in the non-endemic provinces

The incidence of malaria was predominant in non-endemic provinces. Gauteng and North West provinces had distinctly high malaria incidence rates. The incidence in each of these two provinces which are known to be malaria risk-free was even higher than in Limpopo, a known malaria risk province. The high incidence of malaria in GP could be related to its centrality in domestic and international travel [49]. Reasons for such a high malaria incidence in NW province are not clear.

It is important to note that the recommended ACTs for the treatment of uncomplicated malaria were not available in public facilities of non-endemic provinces during the period under study [13-14]. It has previously been reported that most of the malaria patients in non-endemic areas present with uncomplicated malaria and are mostly treated with quinine [13-14]. Compliance to quinine treatment might be questionable as it has a longer dosage period. Therefore, this study's finding of a high malaria incidence in non-endemic provinces coupled with non-availability of ACTs might indicate a higher burden of malaria (more severe complications) on provincial health systems in non-endemic areas than in the endemic. However, neither the severity of the malaria infections nor its complications could be determined by the current study.

4.2 Temporal variations in the incidence of malaria

4.2.1 Temporal variations in endemic provinces

There is clear evidence of a decline in the number of reported confirmed malaria cases as well as annual parasite incidence between 2000 and 2009. The endemic provinces showed a decline of malaria API from 112 per 100,000 population in 2000 to 46 per 100,000 population in 2009. This reduction rate (59%) agrees with the previously documented >50% reduction of reported malaria from South Africa over the same period [3]. Furthermore, the significant decreasing trend of malaria incidence found in this study is in keeping with previous findings in Limpopo province [29]. The numbers of notified malaria cases that were reported by Limpopo and Mpumalanga provincial departments of health also showed declines between 2000 and 2009.

The decline is attributed to the re-introduction of DDT for indoor residual house spraying and introduction of ACT as first-line treatment for uncomplicated malaria in these malaria endemic provinces [8].

This study has also shown that the greatest decline of malaria incidence in endemic provinces was in 2001 when API decreased to 60/100,000 population from 112 per 100,000 population in 2000. However, the decline in the two endemic provinces included in the current study is substantially lower than that documented in KZN. In KZN, a 99% decline in absolute cases was observed by the year 2003 [50]. The difference may be attributable to earlier malaria control interventions in KZN province compared to Mpumalanga and Limpopo provinces. Thus, KZN was the first to be fully covered with the cross-border Lubombo Spatial Development Initiative (LSDI) malaria control programme [51]. Resistance of *Anopheles funestus* to pyrethroid insecticides in SA was first discovered in KZN followed by an early re-introduction of DDT. KZN also implemented the roll out of ACT as early as 2001 for the treatment of uncomplicated malaria [8].

Another drop in the incidence of malaria in the endemic provinces was observed in the year 2005. This might be attributed to the roll out of ACTs since all the three SA's malaria endemic provinces had replaced SP with ACTs for the treatment of uncomplicated malaria in the public sector by December 2004 [22].

The observed overall rate of malaria API decline of 22% in both endemic and non-endemic provinces is lower than the decline observed in endemic provinces alone. Therefore, limiting the monitoring of malaria trends to provinces with known malaria risk could mask the actual country level challenges and successes in malaria control.

4.2.2 Temporal variations in non-endemic provinces

An increasing trend of malaria incidence was found in non-endemic provinces between 2003 and 2006. A number of factors might have contributed to this increase. First, there could be increased reporting of cases from the non-endemic provinces as a result of the establishment of the NHLS's laboratory information system. However, this arte factual rise might only explain the increase observed in 2003 since NHLS reporting from the provinces became complete by 2003. Influx of migrant workers especially to Gauteng province, a beehive for both domestic and international travel [49], might also have contributed to the increase in malaria incidence in these traditionally malaria risk-free areas.

A sharp decline in malaria incidence rate occurred in non-endemic provinces between 2006 and 2007. This could be attributed to the re-introduction of indoor residual spraying with DDT by Mozambique's National Malaria Control Programme in 2006 and its enhancement by the President's Malaria Initiative (PMI) in 2007 [52]. Evidence of the majority of malaria cases in non-endemic parts of SA being imported from Mozambique, a neighbouring malaria hyper-endemic country has been previously found [13-14]; hence the possibility of a flow over effect of the malaria control programme in Mozambique that might have led to reduction in the incidence

of malaria in SA. Since the two greatest tourist and labour attraction cities, Johannesburg and Capetown [49] are within the non-endemic provinces, this indirect effect is more likely to be seen in the non-endemic than endemic provinces. Furthermore, the significant decline of malaria incidence in SA's endemic areas by 2005 might have contributed to the incidence reduction in non-endemic areas between 2006 and 2007.

Thus enhanced control measures in the malaria endemic provinces as well as in the neighbouring hyper-endemic countries would likely lead to a significant reduction in the overall incidence of malaria in South Africa.

4.3 Seasonal variations in malaria incidence

This study has produced evidence in support of previous findings that the majority of malaria cases occur during the hot and rainy months [7, 14, 48]. The seasonality trends of malaria incidence in endemic provinces are directly attributable to mosquito breeding patterns which favour hot and wet weather [7]. Evidence of seasonality trends in earlier decades being explained by climatic factors has previously been documented [53].

The current study also showed that monthly malaria incidence was predominantly high in the month of January. This is in line with a previous study that was done in Gauteng, a non-endemic province, which also found a distinct peak in January [14]. This might be due to increased external and internal migration to and from malaria endemic areas around the Christmas and

New Year festive season when a majority of people take annual holidays and are likely to travel to malaria endemic areas in the country and the region. The association of malaria epidemics and seasonal migration has been documented in Kenya [54].

4.4 Demographic factors associated with Laboratory-confirmed malaria

The study has for the first time documented the association between demographic characteristics and laboratory-confirmed malaria at a population level in South Africa.

4.4.1 Age

The likelihood of having laboratory-confirmed malaria was statistically significantly reduced in adults aged ≥45 years. The risk was much less for individuals aged ≥65 years than those in the 45-64 years age-group. This might be attributable to differences in health seeking behavior since the study used facility level data. Thus, the elderly people might be less likely to present to a health facility for diagnosis than those in younger age-groups. Furthermore, the elderly people do not travel as much as the younger people do; hence their reduced risk of contracting malaria.

The 25-44 year age-group was found to have the greatest incidence of malaria. However, belonging to this age-group alone does not entail increased likelihood of getting a malaria infection compared to belonging to the 0-4 years age-group. Other factors like gender and location might confound the association between this age-group and malaria. However, such potential confounding effect was controlled for in the multivariable regression analysis.

4.4.2 Gender

The male gender had 54% more likelihood of having laboratory-confirmed malaria than the female gender. Although this could be attributed to labour-related in-country and cross-country migration between malaria endemic and non-endemic areas, there is need to explore other associated behavioral factors that might explain the effect of gender on malaria occurrence [27].

4.4.3 Location

Individuals located in non-endemic provinces were 2.7 times more likely to have laboratory confirmed malaria than those who were located in the endemic provinces. A number of factors might have confounded this unexpected finding. Firstly, the finding might be due to the fact that residential location was measured using a proxy variable, health facility location. There is therefore a possibility of individuals presenting to health care facilities in provinces other than their residential province. They may also present in locations other than where they visited two weeks prior to getting sick. Thus, the non-endemic province might not be the actual place where malaria infection was acquired.

Secondly, the finding may be attributable to differences in thresholds for suspicion of a malaria case between health care providers in endemic and those in non-endemic provinces. Thus, compared to their colleagues in non-endemic provinces, clinicians in endemic provinces might have a lower threshold for suspecting malaria probably due to the known malaria risk in their provinces, resulting in relatively more negative outcomes in endemic provinces. On the other

hand, clinicians in endemic areas may be more likely to treat malaria presumptively than in non-endemic areas. Thus, only severe or uncertain suspects might be sent to the laboratory for diagnosis confirmation leading to lower number of recorded cases in the laboratory system. However, the malaria treatment guidelines for SA are clear that every suspected malaria case be parasitologically confirmed [22].

4.5 Study strengths

This study used a large surveillance dataset collected over a ten year period thereby increasing the power of the study to perform such an analysis. Chances for incidence under-estimation were minimized by use of data from public health care facilities only. Thus, public health utilization rates were used as the denominator for calculation of malaria annual parasite incidence rates.

The study also ensured that a standard case definition of malaria was applied during the study period through the use of laboratory data.

4.6 Study limitations

The following limitations should be taken into consideration when interpreting the findings of this study:

i) The use of secondary data that were collected for other purposes and not specifically for this study limited the ability to investigate other explanatory variables like actual residential location and travel history. As such we could not perform an effective

geospatial analysis to establish the actual place where malaria transmission occurred for the confirmed cases.

ii) The study used data from the public health facilities only. The erratic availability of data in the NHLS DIS*LAB information system limited the inclusion of private health facility users in this study. There is a likely inherent bias in the attendance of public health facilities towards people of lower socio-economic status (SES). This could limit the generalisability of results to the whole South African population since human behaviours that potentially influence malaria acquisition are likely to differ. For instance, utilization of preventive measures that have an attached monetary cost might be more among the higher SES group than their counterparts.

iii) Some variables especially malaria species, province and age had missing data points. Consequently, the study failed to determine the relative proportions of malaria parasite species since cases with recorded malaria parasite species seemed to be different from those with unrecorded malaria species in all demographic characteristics. This limits the ability to generalise findings of our study on prevalence of malaria parasite species to the target population.

iv) There was disparity in commencement of reporting among provinces as reporting using DISA*LAB system in the eight provinces under study became complete only in 2003. This therefore introduces an element of information bias into our study even though the resultant potential bias would be non-differential as both positive and negative outcomes were equally affected.

v) Data were only analysed at provincial level. This generalises findings to all areas in a province yet it is known that malaria transmission is spatially variable. Thus the findings in this study might not reflect the real malaria situation in some areas within a province.

4.7 Suggestions for further study

In view of the findings and limitations observed in this study, further research is needed to investigate both demographic and behavioral factors associated with malaria in the South African population using a tailored questionnaire to capture all necessary information i.e. travel history and other clinical details.

Further work is also recommended to look at malaria trends and associated factors at sub-provincial and health district levels since the incidence of malaria is spatially variable even between small areas.

4.8 Conclusion

In conclusion, this study has shown that there has been a consistently significant downward trend of malaria incidence in malaria endemic provinces of South Africa between 2000 and 2009. The overall decline in malaria incidence over the ten year period was 22%. The malaria non-endemic Gauteng and North West provinces had a high burden of malaria infections. Therefore, the malaria non-endemic provinces ought to be closely monitored and appropriate anti-malarial treatment drugs should be made readily available in order to manage the cases effectively in these areas.

4.9 Recommendations

The findings of this study have implications on national and provincial health care delivery systems. We therefore make the following recommendations:

i. There is need for continuity of the malaria control activities to sustain the successes of the past decade.

ii. Authorities in the provincial departments of health in the malaria non-endemic provinces ought to be aware of the magnitude of malaria cases presenting to their facilities in order to plan for appropriate case management interventions.

iii. Mass sensitization campaigns need to be carried out in all communities to improve awareness of the malaria risk areas in and outside South Africa, symptoms as well as preventive measures.

iv. There is need for targeted information, education and communication (IEC) to migrant workers and all travelers during the annual festive and holiday seasons. The messages ought to emphasize the availability of non-drug and chemo-prophylactic malaria preventive measures as well as the importance of good adherence to such measures.

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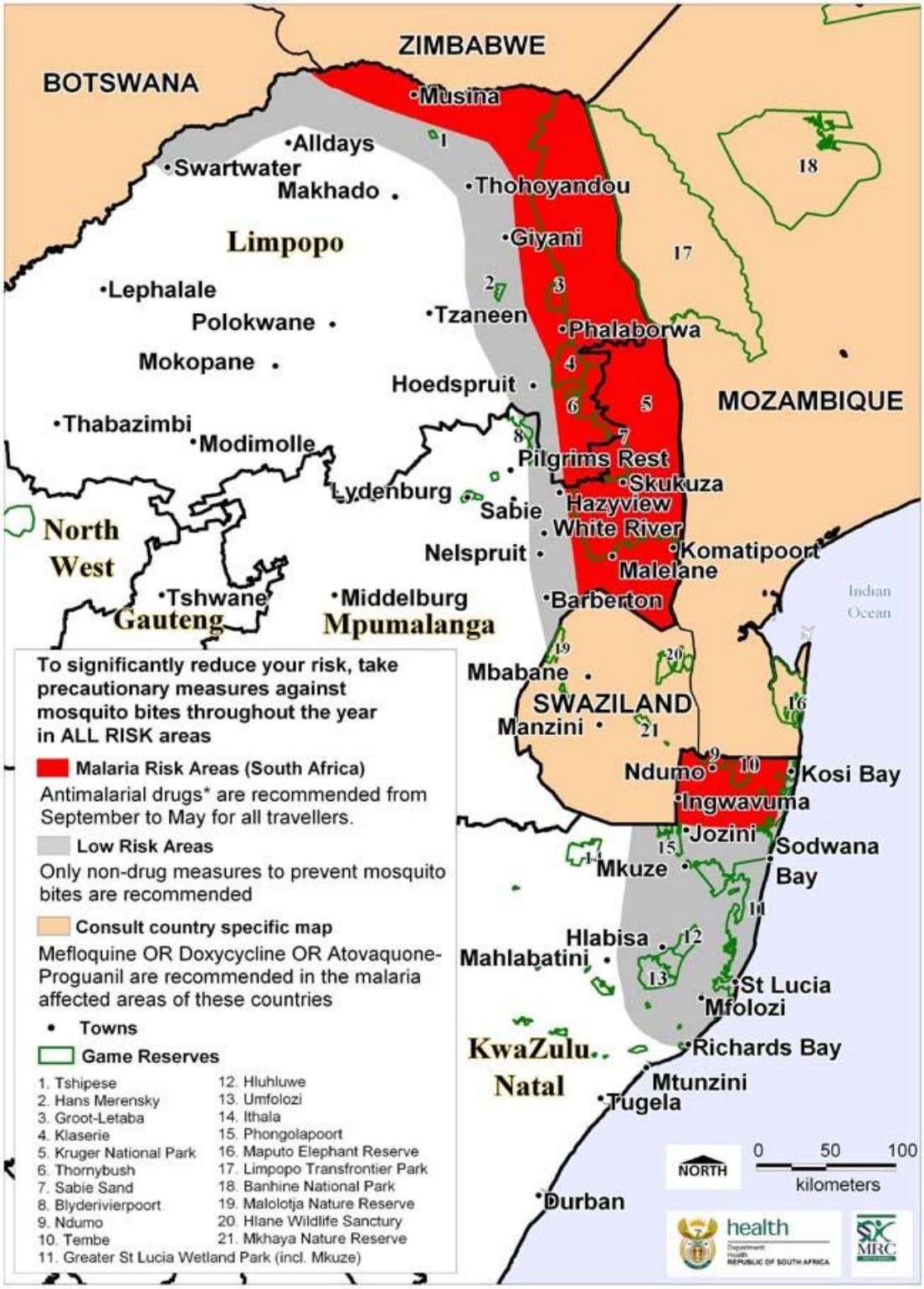
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Appendix 1: Map of malaria risk areas in South Africa



Source: *http://www.malaria.org.za/Malaria_Risk/Risk_Maps/risks_maps.html*

Appendix 2: Comparison of demographic characteristics between laboratory-confirmed malaria cases with *Plasmodium falciparum* and those with non-reported malaria species: South Africa, 2000-2009

Characteristic	*Plasmodium falciparum* N (%)	Non-reported N (%)	P-value
Gender			
Female	9,189 (32.81)	14,067 (38.88)	<0.001
Male	18,820 (67.19)	25,143 (64.12)	
Age-group in years			
0 – 4	2,991 (11.48)	4,104 (11.34)	
5 – 24	6,906 (26.52)	10,007 (27.65)	
25 – 44	13,079 (50.22)	17,672 (48.83)	<0.001
45 – 64	2,718 (10.44)	3,810 (10.53)	
≥ 65	350 (1.34)	595 (1.65)	
Time in calendar years			
2000[#]	1,970 (6.80)	3,501 (8.56)	
2001[#]	2,865 (9.90)	2,391 (5.84)	
2002[##]	1,428 (4.93)	2,553 (6.24)	
2003	3,376 (11.66)	4,702 (11.49)	
2004	3,574 (12.34)	4,951 (12.10)	<0.001
2005	3,479 (12.02)	5,380 (13.15)	
2006	4,923 (17.00)	6,650 (16.25)	
2007	2,561 (8.85)	3,746 (9.16)	
2008	2,755 (9.52)	3,978 (9.73)	
2009	2,021 (6.98)	3,059 (7.48)	
Time in seasons			
Hot and rainy *(September - May)*	25,571 (88.32)	36,051 (88.12)	0.416
Winter *(June – August)*	3,381 (11.68)	4,860 (11.88)	

[#] *Data from two provinces (EC and WC) not included;* [##] *Data from one province (EC) not included*

Appendix 3: Time-trend analysis for occurrence of malaria

Time trend analysis of occurrence of laboratory-confirmed malaria in South Africa over ten year period: 2000 - 2009 using chi ^{2} test of trend

	Odds of occurrence of positive malaria case per calendar year-category						
	2000 -2001	**2002–2003**	**2004-2005**	**2006-2007**	**2008-2009**	**Homogeneity P-value (5%)**	**trend P-value (5%)**
Province type							
Endemic	0.25	0.32	0.15	0.13	0.14	<0.001	<0.001
Non-endemic	0.52	0.58	0.56	0.49	0.34	<0.001	<0.001
Overall	0.28	0.38	0.28	0.26	0.22	<0.001	<0.001

Appendix 4: Ethical clearance certificate for the study

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Beatrice L Mwagomba

CLEARANCE CERTIFICATE	**M10M101108**
PROJECT	A ten-Year Cross-Sectional Study of Trends of Laboratory-Confirmed Malaria in the Republic of South Africa
INVESTIGATORS	Dr Beatrice L Mwagomba.
DEPARTMENT	School of Public Health
DATE CONSIDERED	26/11/2010
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 26/11/2010 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof M Coetzee

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix 5: Protocol Approval letter

Faculty of Health Sciences
Medical School, 7 York Road,
Parktown, 2193
Fax: (011) 717-2119
Tel: (011)717-2075/6

Reference: Ms Tania van Leeve
E-mail: Tania.vanleeve@wits.ac.za

24 November 2010

Person No: 502907
Dr BL Mwagomba Thyolo District Hospital
P O Box 21
Thyolo
0000
Malawi

Dear Dr Mwagomba

Master of Science in Epidemiology in the field of Biostatistics and Epidemiology: Approval of Title

We have pleasure in advising that your proposal entitled "*A ten-year cross-sectional study of trends of laboratory-confirmed Malaria in the Republic of South Africa"* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn

Faculty Registrar

Faculty of Health Sciences