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Using Geographical and Malaria Information Systems for Enhanced Malaria Control

Marlize Coleman

A dissertation submitted to the Faculty of Science, University of the Witwatersrand, in fulfillment of the requirements of the degree of Doctor of Philosophy

Johannesburg, 2008

DECLARATION

I declare that this thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other University.



M. Coleman

10th day of October 2008

ABSTRACT

Introduction

The use of information systems to understand the dynamics of malaria disease and inform decisions on control proved valuable to a malaria control programme. Development of simple practical and sustainable information system tools has been slow in coming for many resource-poor environments. This thesis addresses many issues relating to the conceptual development and implementation of simple tools and their integration into operational malaria control to support decision making and advocacy.

Methods

A basic Microsoft Access malaria data collection and repository tool has been in existence since 1997 focussing mainly on case reporting alone. Better utilization of data and further expansion to include outbreak identification and response, cluster detection and intervention monitoring has been the main focus over time.

Eight years of retrospective malaria case data from Mpumalanga Province, South Africa were used to explore disease dynamics including spatial as well as temporal variation in malaria epidemiology. The identification of specific risk areas and the confirmation of the unstable nature of malaria occurrence lead to the conceptualization and development of an outbreak model using binomial statistics. The novel three tier outbreak identification and response system was field tested over a two season period to establish acceptance and the ability to

direct resources in times of elevated case loads. Comparison against other existing malaria outbreak systems was conducted.

SaTScan freely available software was used to detect spatial and space-time disease clusters within towns in the highest risk area of the province.

A malaria case control study was conducted in seven localities/towns/villages to explore risk and protective characteristics of household structure and practices, including the use of impregnated nets. The micro economic status of households as a determinant of malaria risk was also explored.

A spray operations component as part of the malaria information system was developed and implemented during the time to allow for routine monitoring and historical exploration of indoor residual spray activities.

Results

Retrospective malaria case data analysis identified heterogeneity of malaria risk in the Province and spatial analysis identified significant clusters at small geographical area resolution rejecting the hypothesis that malaria is homogeneously distributed over space and time.

The importance of intervention monitoring to identify low coverage areas, over or under application of insecticides, and assessment of the productivity of spray operators was identified.

The outbreak identification and response system was successfully implemented, integrated and sustained with a set of response activities developed for implementation at defined threshold levels. The outbreak systems can be considered for utilization in other low transmission settings.

Results of the case control study indicated that malaria risk was associated with living in traditional housing and the practice of re-opening windows at night when peak biting behaviour of the main mosquito vector, *Anopoheles arabiensis* is expected. Higher household socio economic status (SES) profile was associated with a lower risk of malaria.

Conclusions

The conceptualization, development and implementation of operationally feasible malaria information management tools in a rural African environment proved useful for enhancing malaria control. The novel malaria outbreak identification and response, cluster detection as well as the spray monitoring systems were successfully implemented and adopted as an integral part of the routine malaria control programme monitoring and surveillance system. This research has enabled more informed real-time decision-making for effective programme management.

For my Mum and Dad

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Presentations

Oral

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2. Parasitolgical Society of Southern Africa
Malelane, South Africa
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Poster

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Authors: Booman, M[1]. **(Coleman, M)**, Sharp, B.L.[6], Martin, C.L.[6], Manjate, B.[7], La Grange, J.J.P.[3], Durrheim, D.N.[2]

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Peer reviewed publications

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Coleman, M[1,a,b,c,d]., Coleman, M[5,b]., Mabuza A.M[3,c]., Gerdalize Kok[3,c], Coetzee M.[4,b], Durrheim D.N.[2,a,b,d] (2008). Evaluation of an operational malaria outbreak identification and response system in Mpumalanga province, South Africa. *Malaria Journal*,**7**. PubMed Central. Available via http://www.malariajournal.com/content/7/1/69.

Coleman, M.[1,a,b,c,d], Coleman, M.[5,b]., Mabuza A. M[3,c]., Kok, G[3,c],Coetzee, M.[4,b], Durrheim, D. N.[2,a,b,d] (2008), Using the SaTScan method to detect local malaria clusters for guiding malaria control. *Malaria Journal,*, submitted for publication.

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Autor’s Contributions

[a]Conceptual
[b]Preparation of the written publication
[c]Field management and quality control
[d]Data analysis

CONTENTS PAGE

DECLARATION ..... **II**

ABSTRACT ..... **III**

ACKNOWLEDGEMENTS ..... **VII**

LIST OF FIGURES ..... **XIII**

LIST OF TABLES ..... **XVI**

NOMENCLATURE AND ABBREVIATIONS ..... **XVII**

CHAPTER 1 ..... **1**

1. Introduction **1**

1.1 Historical overview of malaria **1**

1.2 Global importance of malaria **2**

1.2.1 The social and economic impact of malaria 3

1.2.2 Sub-Saharan Africa as the central problem area 4

1.2.3 The magnitude of the malaria problem in South Africa 6

1.2.4. Recent control and management initiatives and new vector control possibilities 9

1.3 Malaria in Mpumalanga province, South Africa including community knowledge, attitude and practices **13**

1.4. Information Technology tools for disease surveillance and control **16**

1.5 Aim and objectives **21**

CHAPTER 2 ..... **23**

2. Epidemiology of malaria in Mpumalanga province **23**

2.1 Introduction **23**

2.2 Methodology **24**

2.3 Results **26**

2.3.1 Malaria cases and deaths, 1997/1998 to 2004/2005 season 26

2.3.1.1 Cases by month 27

2.3.1.2 Case reporting 28

2.3.1.3 Source of infection 30

2.3.2 Population malaria incidence and case fatality ratios (CFR), 1997/1998 to 2004/2005 season 33

2.3.2.1 District incidence 33

2.3.2.2 Municipal incidence within Ehlanzeni district 35

2.3.2.3 Town (locality) incidence 37

2.3.2.4 Gender specific incidence 37

2.3.2.5 Age specific incidence 39

2.3.3 Case fatality 39

2.4 Discussion **42**

CHAPTER 3 ..... **50**

3. Development and use of a computerized management system for malaria intervention monitoring **50**

3.1 Introduction **50**
3.2 Methods **53**
3.2.1 Spray cards and forms 53
3.2.2 Database design and data capture 54
3.2.3 Data retrieval and query tools 55
3.2.3 Spatial platform 59
3.2.4 Security and data backup 60
3.2.5 Data analysis 60
3.2.6 Intervention area 61
3.3 Results and use of the management information system **62**
3.3.1 Comparing spray activity data from the 1999/2000 to 2005/2006 seasons for Mpumalanga province and where indicated southern Mozambique 62
3.4 Discussion **69**

CHAPTER 4 ..... **72**

4. Outbreak identification and response **72**

This chapter has been accepted for publication in the *Malaria Journal.* **72**
4.1 Introduction **72**
4.2 Methodology **74**
4.2.1 Study region 74
4.2.2 Threshold calculation 74
4.2.3 Description of the outbreak identification and response system 75
4.2.3.1 Tier 1 75
4.2.3.2 Tier 2 76
4.2.3.3 Tier 3 77
4.2.4 Comparison 78
4.3 Results **78**
4.4 Discussion **82**

CHAPTER 5 ..... **86**

5. Using the SaTScan method to detect local malaria clusters for guiding malaria control **86**

This chapter has been submitted for publication to the *Tropical Medicine and International Health* journal. **86**
5.1 Introduction **86**
5.2 Methodology **87**
5.2.1 Study area 87
5.2.2 Active malaria case investigation 89
5.2.3 Spatial and temporal clusters 89
5.3 Results **90**
5.3.1 Malaria incidence 90
5.3.2 Case clustering 91
5.3.3 Cluster detection to guide control activities 91
5.4 Discussion **94**

CHAPTER 6 ..... **97**

6. Household and micro-economic factors associated with malaria **97**

This chapter has been submitted for publication to the *International Health and Geography* journal. **97**
6.1 Introduction **97**

6.2 Methodology **98**
6.2.1 Study area 98
6.2.2 Study design 99
6.2.3 Case household enrolment 99
6.2.4 Data collection 99
6.2.5 Data analysis 100
6.2.6 Ethics 101
6.3 Results **101**
6.4 Discussion **104**

CHAPTER 7 ..... **108**

7. General discussion and conclusion **108**

APPENDICES **115**

REFERENCES **121**

LIST OF FIGURES PAGE

Figure 1.1 *Plasmodium falciparum* Malaria Risk defined by annual parasite incidence (top), temperature, and aridity (bottom) 3
Figure 1.2 Malaria Risk Map, South Africa and bordering countries, 2004/200510
Figure 1.3 Malaria case and death notifications, 1971 – 2005, South Africa 11
Figure 1.4 Malaria case incidence by province, 1999/2000 to 2004/2005 season, South Africa 11
Figure 1.5 Malaria fatality ratio by province, 1995/1996 to 2004/2005 season, South Africa 11
Figure 1.6 Mpumalanga orientation map 14
Figure 2.1 Notified malaria cases and deaths, 1997/1998 to 2004/2005 seasons, Mpumalanga province 27
Figure 2.2 Number of malaria cases notified by month, 1997/1998 – 2004/2005 seasons, Mpumalanga province 29
Figure 2.3 Notified malaria cases and average temperature by month, July 1997 to June 2005, inclusive, Mpumalanga province 29
Figure 2.4 Notified malaria cases and average rainfall by month, July 1997 to June 2005, inclusive, Mpumalanga province 31
Figure 2.5 Number of malaria cases by reporting type, 1997/1998 – 2004/2005, Mpumalanga province 31
Figure 2.6 Malaria case reporting percentages by primary health care facilities and hospitals, 1997/1998 – 2004/2005, Mpumalanga province 32
Figure 2.7 Seasonal proportion of cases notified by reporting category, 1997/1998 to 2004/2005 season, Mpumalanga province 32
Figure 2.8 Local and imported malaria cases, 1997/1998 to 2004/2005 season, Mpumalanga province 33
Figure 2.9 Average case incidence by municipal area, 1997/1998 to 2004/2005 season, Ehlanzeni district 36
Figure 2.10 Relative risk ratios by season, Nkomazi municipality compared to Mbombela, Umjindi and Thaba Chweu municipalities combined, 1997/1998 – 2004/2005 season, Ehlanzeni District, Mpumalanga province 36

Figure 2.11 Average case incidence by town, 1997/1998 to 2004/2005 season, Nkomazi municipal area, Ehlanzeni district 38
Figure 2.12 Relative risk ratios by season, comparing towns bordering Mozambique and towns bordering Swaziland, 1997/1998 – 2004/2005 season, Nkomazi municipality, Mpumalanga province 38
Figure 2.13 Gender specific incidence rate per 1 000 population, 1997/1998 – 2004/2005 season, Mpumalanga province 39
Figure 2.14 Age specific incidence per 10,000 population, 1997/1998 – 2004/2005 season, Mpumalanga province 40
Figure 2.15 Malaria case fatality ratio (%), 1997/1998 to 2004/2005 season, Mpumalanga province 40
Figure 2.16 Number of malaria deaths by age group, 1997/1998 to 2004/2005 season, Mpumalanga province 41
Figure 2.17 Malaria case incidence per 1,000 population, 1997/1998 to 2004/2005 season and malaria control intervention changes 49
Figure 3.1. List of paper based spray data capture forms, 1975 to 1998 53
Figure 3.2 Spray database navigation switchboard window 56
Figure 3.3 SP2 data entry window 56
Figure 3.4 Entity relationship diagram 58
Figure 3.5 Reports list database window 58
Figure 3.6 Report range database window 59
Figure 3.7 Mpumalanga provincial boundary including spray sector boundaries 61
Figure 3.8 Scatter plot to show linear association between incidence rate per 10 000 population and coverage rate (%) per municipal area, ... 64
1999-2000 to 2005/2006 seasons 64
Figure 3.9 Spraying progress map by sector, 2005/2006 season, Mpumalanga province 65
Figure 3.10 Example of a spraying progress map by town, Zone 1, first round spraying, southern Mozambique, 2000 68
Figure 3.11 DDT insecticide application rate by season, 2000/2001_2005/2006 seasons 69

Figure 4.1 Clinics/hospital and towns/villages under outbreak surveillance in the Nkomazi and Thaba Chweu municipal areas, 2004/2005 –2005/2006, Ehlanzeni District, Mpumalanga province 75
Figure 4.2 Example of the outbreak detection chart 76
Figure 5.1. Location of the seven towns selected for detailed GIS surveillance, Nkomazi municipal area, Mpumalanga. 88
Figure 5.2. Malaria case incidence per 1,000 population by town, 2002/2003 – 2004/2005 seasons, Nkomazi municipal area 90
Figure 5.3 Spatial malaria case clusters, 2002/2003 - 2004/2005 seasons, Albertsnek town 92
Figure 5.4 Space time malaria case cluster, 2004/2005 season, Albertsnek town 92
Figure 5.5 Space time malaria case cluster, 2004/2005 season, Thambokulu town 93
Figure 5.6 Space malaria case cluster, 2002/2003 - 2004/2005 seasons, Thambokulu town 94

LIST OF TABLES

Table 2.1 Notified malaria cases by district, 1997/1998 to 2004/2005 seasons, Mpumalanga province..... 29
Table 2.2 Deaths notified by reporting category, 1997/1998 to 2004/2005 season, Mpumalanga province..... 33
Table 2.3 Locally acquired cases by source district, 1997/1998 to 2004/2005 season, Mpumalanga province 34
Table 2.4 Malaria case incidence per 100,000 population by district, 1997/1998 – 2004/2005, Ehlanzeni District, Mpumalanga province 35
Table 2.5 Malaria case incidence per 10,000 population by municipal area, 1997/1998 season, Ehlanzeni District..... 35
Table 2.6 Malaria case fatality ratio (%) by district, 1997/1998 to 2004/2005 season, Mpumalanga province 41
Table 3.1 SP2 table, field names and descriptions 57
Table 3.2 Spray data for structures sprayed, 1999/2000 – 2005/2006 seasons..... 62
Table 3.3 Productivity results for spray activities, 1999/2000 – 2005/2006 seasons 66
Table 4.1 Example of outbreak identification threshold table for field use..... 77
Table 4.2 Malaria outbreaks by month, 2004/2005 season..... 79
Table 4.3 Malaria outbreaks by month, 2005/2006 season..... 80
Table 4.4 Summary of health facility survey responses regarding the outbreak identification chart, 2004/2005 and 2005/2006 seasons, Tonga health area..... 81
Table 5.1. Cluster and outbreak profile by town, 2002/2003 – 2004/2005 season91
Table 6.1. Univariate analysis showing the frequency of potential risk factors and protective factors among cases and controls, odds ratios (OR) and confidence intervals (CI) for the association with malaria. 102
Table 6.2. Multivariate analysis showing selected variables with their odds ratios (OR) and confidence intervals (CI) for the association with malaria. 104

NOMENCLATURE AND ABBREVIATIONS

Active case detection
Follow up activity triggered by a malaria case passively reported from a health facility or a health practitioner. Malaria case investigator visits index case household and all neighbouring households to perform a rapid diagnostic test for all symptomatic individuals and take a blood smear from non symptomatic individuals to detect malaria cases at community level. All positive cases are notified and referred to a health care facility.

Blanket indoor residual spraying
Targeting and spraying all structures with a residual insecticide within a defined area.

Chemoprophylaxis
The administration of a medication for the purpose of preventing disease or infection (Wikipedia, 2008a).

Epidemic
The occurrence of more cases of a disease than would be expected in a defined region during a given time period (Dirckx, 2006).

Holo-endemic
Parasite rate in infants constantly over 75% (World Health Organization, 1963)
Hypo-endemic
Parasite rate in children 2-9 years as a rule less than 10% (may be higher during part of year) (World Health Organization, 1963).

Imported malaria case

A malaria case in which the infection was acquired outside the area in which it is found, implying that its origin could be traced to a known malarious area (World Health Organization and UNICEF, 2005).

Integrated vector management
A strategy to reduce or interrupt transmission of disease and is a process of evidence-based decision-making procedures aimed at planning, implementing, monitoring, and evaluating targeted, cost-effective, and sustainable combinations of vector control measures (World Health Organization, 2005).

Larviciding
The activity where insecticide/s are used to specifically target the larval life stage of an insect (Wikipedia, 2008b).

Locality
A geographical area usually referred to as a town, village or defined categories such as farm and lodge.

Local malaria cases
A malaria case that is natural to an area or country, i.e. not imported. The term is applied to cases whose origin from local transmission cannot be disproved (World Health Organization and UNICEF, 2005).

Malaria season
A malaria season in South Africa is defined as the period from 1 July to 30 June the following year. This term is commonly used for data analysis and review.

Outbreak
A small, localized group of people or organisms infected with a disease. Such groups are often confined to a village or a small area. Outbreaks may also refer to epidemics, which affect a region in a country or a group of countries (Wikipedia, 2008c).

Seasonal malaria
Unstable malaria with variable prevalence of malaria typically showing great changes from one part of the transmission season to another. Epidemics and outbreaks are common and population shows little or no immunity (World Health Organization, 1963).

Stand
Delineated area of one residence, household or family. Can consist of more than one house structure. Also referred to as a plot or premise.

Strip indoor residual spraying
Targeting and spraying specific structures with a residual insecticide within a defined area.

AFRO:	World Health Organization Regional Office for Africa
AIDS:	acquired immunodeficiency syndrome
AS:	artesunate
BHC:	benzene hexachloride
CFR:	case fatality ratio
COARTEM:	artemether-lumefantrine
DDT:	dichlorodiphenyltrichloroethane
GIS:	geographical information system
GPS:	global positioning system
HIV:	human immunodeficiency virus
IMIS:	integrated malaria information system
IRS:	indoor residual spraying

ITN:	insecticide treated net
IVM:	integrated vector management
LRF:	long range forecasting
MARA:	Mapping Malaria risk in Africa
MEWS:	malaria early warning system
MIS:	malaria information system
MCP:	malaria control programme
MMCP:	Mpumalanga Malaria Control Programme
PCR:	polymerase chain reaction
PPGIS:	public participation GIS
PHC:	primary health care
RBM:	Roll Back Malaria
RDT:	rapid diagnostic test
SADC:	Southern African Development Community
SAMCP:	South African Malaria Control Programme
SD:	standard deviation
SES:	socio economic status
SP:	sulfadoxine-pyrimethamine
UNICEF:	United Nations Children's Fund
WHO:	World Health Organization

CHAPTER 1

1. Introduction

1.1 Historical overview of malaria

Malaria has been an integral part of civilizations since the beginning of recorded human history. The Chinese were the first to observe the association between fever and the enlargement of the spleen approximately 5000 years ago (Targett, 1992) and Hippocrates described malaria in the fourth century BC (Bell, 1995). The first therapeutic break-through was made during the middle of the seventeenth century when the therapeutic value of cinchona bark was observed. Additional therapeutic milestones included the application of chloroquine in the 1940s and qinghaosu (rediscovered, 1971) for treatment (White *et al.*, 1992). Alphonse Laveran discover the malaria parasite in the human host in 1880 (Ross, 1911). The mode of infection and disease was historically controversial and causal hypotheses ranged from inhalation “miasma”, ingestion of contaminated water and the possible involvement of mosquitoes (Ross, 1902). Ronald Ross eventually concluded in 1898 that mosquitoes were involved in the transmission (Celli, 1901) of bird malaria and Giovanni Battista Grassi confirmed this for human malaria later that year (Bradley, 1999).

The first large-scale mosquito control efforts commenced in 1899 in Cuba and the Panama Canal Zone. In the 1950s global eradication was considered feasible after the mass production of dichlorodiphenyltrichloroethane (DDT) became possible in 1942 (Russell, 1952). The effort was successful in some areas, mainly islands, but later abandoned by the World Health Organization after been recognized as an unrealistic goal (Bell, 1995).

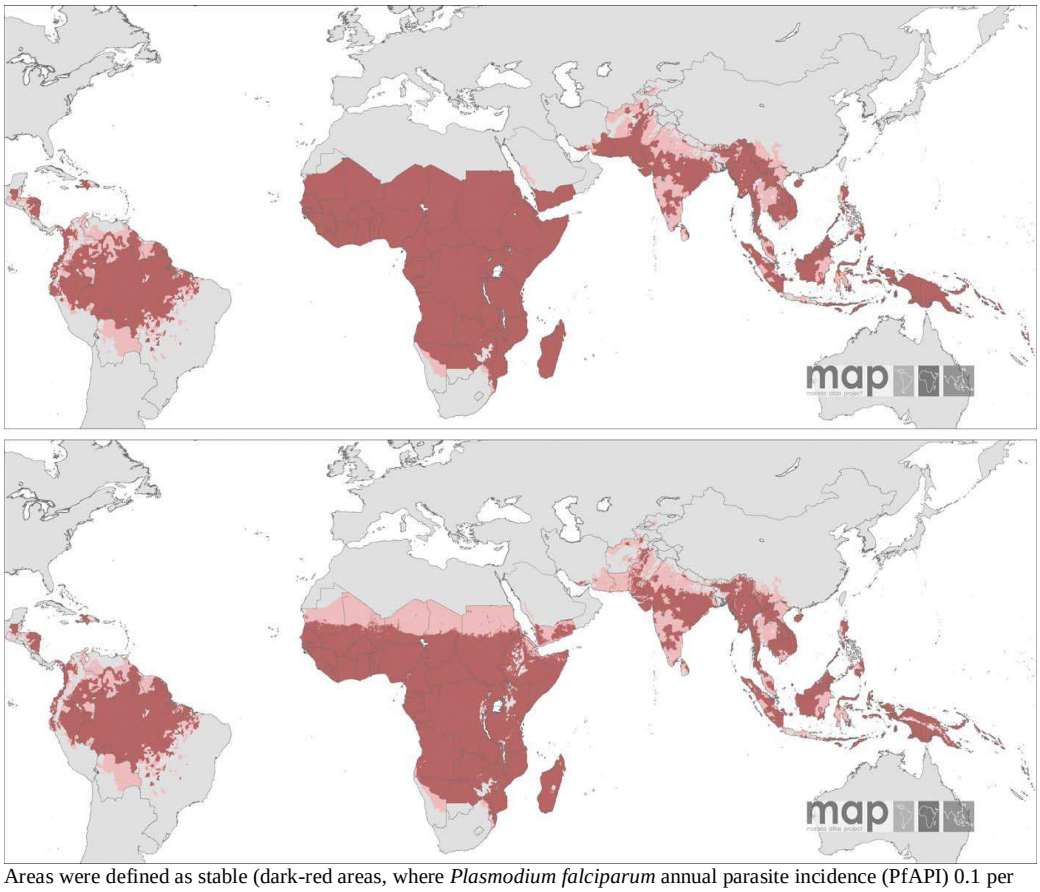
1.2 Global importance of malaria

The global burden of malaria is not equally distributed. Tropical and sub-tropical zones are most affected and developing countries suffer the most from the consequences of endemic malaria and malaria epidemics (Sachs & Malaney, 2002). Prevailing temperature, rainfall, humidity and altitude are considered the dominant factors in explaining the geographical distribution of malarial disease and risk of transmission (Sachs & Malaney, 2002) (Fig. 1.1). Geographical variation in vectorial capacity influences the extent to which the distribution of malaria falls short of its limiting isotherms . Ninety percent of world malaria infections occur in Africa south of the Sahara, but malaria is also a major public health problem in parts of Asia, Latin America, the Middle East, Eastern Europe and the Pacific region. Epidemics in India are frequently reported in areas where malaria has not formerly been endemic. Brazil accounts for 50% of all cases reported in the Americas. South East Asia is severely affected by high levels of resistance to multiple anti-malarial drugs (WHO and UNICEF, 2005). In Asia, Africa and the Americas malaria poses a serious problem in frontier areas of economic development and regions of social disruption (World Health Organization, 1993). War stricken countries are at particular risk since health service infrastructure is largely non-existent. Afghanistan and Sierra Leone are typical examples where war has impacted negatively on the malaria situation. In Kenya and Ethiopia several epidemics have occurred recently in highland areas previously not prone to malaria transmission. The possibility that these unexpected epidemics are related to climatic aberrations has been postulated

(Brooker *et al.*, 2004; Brooker *et al.*, 1999; Ernst *et al.*, 2006; Hay *et al.*, 2003a; Hay *et al.*, 2002; Ministry of Health, 1999).

Malaria endemicity, seasonality and risk vary from one area to another. The complexity of the disease, due to interacting environmental and social determinants, its control and surveillance warrant continued research and global collaboration to lessen the burden of disease.

Figure 1.1 *Plasmodium falciparum* Malaria Risk defined by annual parasite incidence (top), temperature, and aridity (bottom)



Areas were defined as stable (dark-red areas, where *Plasmodium falciparum* annual parasite incidence (PfAPI) 0.1 per thousand pa), unstable (pink areas, where PfAPI , 0.1 per thousand pa), or no risk (light grey). The few areas for which no PfAPI data could be obtained, mainly found in India, are coloured in dark grey. The borders of the 87 countriesdefined as P. falciparum endemic are shown. Highland areas where risk was excluded due to temperature appear in light grey. The aridity mask excluded risk in a step-wise fashion, reflected mainly in the larger extents of unstable (pink) areas compared to the top panel, particularly in the Sahel and southwest Asia (southern Iran and Pakistan) (Guerra *et al.*, 2008).

1.2.1 The social and economic impact of malaria

It is estimated that malaria threatens the lives of 40% of the world's population and is a public health problem in more than 90 countries (World

Health Organization, 1993). Malaria is an important public health problem with 300 to 500 million clinical cases reported annually. It has been estimated that a child dies of malaria every 40 seconds with a global loss of 2 000 young lives each day (Sachs & Malaney, 2002). The majority of deaths occur among the poorest fifth of the world's population and in sub-Saharan Africa malaria contributes to a loss of 15% of all disability-adjusted life-years (Guerrant *et al.*, 2002). Poor people living in poor quality housing, usually in rural areas, are at increased risk of disease and also have less access to medical facilities and personal protection (World Health Organization, 2001a). Sub-standard housing can create opportunities for vector mosquitoes to enter the houses and increase possible contact between infected vectors and humans. Malaria has thus been characterized as a "social disease" and thus amenable to human intervention.

There is a direct ecological correlation between malaria and poverty. Comparisons of incomes in malarious and non-malarious countries indicate that the average gross domestic product (GDP) of the former is more than five times lower. Loss in productivity, the cost of treatment and lack of access to effective treatment are direct contributory factors. Investment and tourism are also threatened in these areas and possible income thus lost for indigenous population. Malaria affects many aspects of social and economic endeavours including fertility, savings and investments, agricultural choices, schooling and mobility (Sachs & Malaney, 2002).

1.2.2 Sub-Saharan Africa as the central problem area

The degree of efficiency of malaria vectors to transmit malaria from one human to another is an important factor defining the distribution of malaria in

Africa. *Anopheles gambiae* is predominantly found in sub-Saharan Africa and has the reputation of being a very effective vector (Gallup & Sachs, 2001).

The upsurge of malarial disease following systematic programme neglect recently resulted in large African malaria epidemics (Nchinda, 1998). The Southern Africa Development Community (SADC) Malaria Control Strategy (Durrheim *et al.*) and the Abuja Declaration (2000) was initiated to enable countries to strategically tackle malaria and implement evidence based interventions (World Health Organization, 2004).

Malaria intensity in the southern region of Africa varies from holo to hypo endemic. Seasonal variation and epidemics characterize unstable malaria while intense transmission throughout the year is typical in areas of stable malaria. IN sub-Saharan Africa, up to 30% of outpatient and 40% of inpatient episodes are due to malaria infection. Children under 5 years and pregnant women are the worst affected by malaria in stable malaria areas of sub Saharan Africa (World Health Organization, 2004).

High-level chloroquine resistance in Africa is widespread but chloroquine is still used in some countries as first line treatment (Kaona & Tuba, 2003; White *et al.*, 1992). Effective, cheap drugs are needed and combination therapy is currently considered as the best alternative. The use of Artemisinin derivatives is currently being explored and this raises hope of future effective malaria therapy (Barnes *et al.*, 2002; Koornhof, 1999). Multiple control interventions have been attempted in this part of the world due to the massive burden of the disease with limited success. The HIV/AIDS epidemic in Africa has also strained primary health care services to the limit.

Insecticide treated nets and residual house spraying have been the major vector control interventions implemented in malaria endemic areas of Africa. The latter intervention has been evaluated as being more cost-effective in areas with low seasonal risk (Guyatt *et al.*, 2002). A problem facing malaria control programmes is the rapid development of insecticide resistance. Resistance of *Anopheles funestus* to pyrethroids impacted dramatically on malaria in South Africa (Hargreaves *et al.*, 2000). Although insecticide treated bed nets appear to play a role in reducing malaria morbidity and mortality, they do not have a mass killing effect on village populations of *Anopheles gambiae* (Quinones *et al.*, 1998). Nets treated with insecticides have been found to be more effective than untreated nets, as observed in Ubwari, Tanzania (Maxwell *et al.*, 1999).

Control interventions introduced should be sustainable, as interruption in control can have devastating effects where immunity has been compromised (Teklehaimanot & Bosman, 1999).

1.2.3 The magnitude of the malaria problem in South Africa

Malaria in South Africa attracted little attention until the building of the Pretoria-Delgoa Bay railway line in the early 1900s. A loss in production due to malaria resulted in the South African Railways investigating and implementing control interventions in 1904. These included the screening of houses, drainage of water and environmental manipulation. Durban health authorities began to tackle the malaria problem in a similar way and also introduced disinfectants to control larvae. Paraffin was used for the treatment of deep pools implicated in mosquito breeding. Mosquito brigades implemented these measures in 1905 with great success (Ross, 1911).

These efforts lead to the evolution of malaria control programmes in the 1920s with oil and Paris green being used for larval control as the major intervention (Ingram & De Meillon, 1927). This remained the focus of control until 1946 when the focus shifted to adult mosquito control.

The severity of malaria in KwaZulu-Natal and Mpumalanga during the early 1930s affected socio-economic, agricultural and industrial development and growth (Sharp & Le, 1996). Malaria mortality in KwaZulu-Natal for the period November 1931 to June 1932 was estimated at 22 132 (Sharp & Le Sueur, 1996).

Malaria in South Africa remains a public health problem in the north-eastern part of the country that includes the low altitude areas of the Limpopo Province, Mpumalanga and north eastern KwaZulu-Natal (KZN) (Figs. 1.1, 1.2). Before the introduction of large scale spraying of DDT in the 1940s and 1950s, malaria was prevalent from Port Shepstone in southern KZN to Gauteng in the northwest and even included parts of the Northern Cape (Maharaj *et al.*, 1998). The use of Pyagra (pyrethrum and kerosene) indoor insecticide spraying in the 1930s (De Meillon, 1936) preceded the introduction of organochlorines and DDT. In 1956 major anti larval activities were terminated. In the same year malaria was declared a statutory notifiable disease. During 1958 the spraying of all malaria areas in South Africa was achieved by using DDT inside dwellings (Sharp & Le Sueur, 1996). However the use of DDT became problematic for several reasons. People plastered their walls because of the white marks deposited by DDT (Mnzava *et al.*, 1998). Resistance and excitation of bedbugs by DDT resulted in increased biting activity of the bugs that has been linked to diminished community compliance (Newberry *et al.*, 1984). Environmental concerns, such as

concentrations of DDT found in piscivorous tigerfish (Bouwman *et al.*, 1990a), contributed to a negative perception of DDT.

Synthetic pyrethroids were considered an acceptable alternative to DDT when its ongoing use was challenged due to environmental concerns and adopted by the MCP (Malaria Control Programme) during the mid 1990's with their replacement of DDT in certain areas. Most synthetic pyrethroids are more expensive per square meter of application than DDT insecticide (Tren & Bate, 2004). When resistance of *An. funestus* to pyrethroids in South Africa was discovered it led to the reintroduction of DDT (Hargreaves *et al.*, 2000).

The effect of discontinuing the use of DDT was most severely experienced in KwaZulu-Natal with an increase from approximately 8000 cases in 1996 to 41 786 cases in 2000 (National Department of Health, 2006).

Microscopic examination of finger-prick thick blood smears was historically the method of choice for malaria diagnosis. Rapid card tests were introduced in the late 1990s as a result of field confirmation of their value for prompt and accurate malaria diagnosis (la Grange *et al.*, 1999).

The incidence of malaria in South Africa is low thus protective immunity does not develop in populations at risk. The epidemiology of malaria varies in the three provinces affected by malaria.

Trends in malaria notifications in South-Africa during the past 35 years showed a clear peak during 2000 (National Department of Health, 2006) (Fig. 1.3) corresponding to major floods in the neighbouring country of Mozambique.

Although the malaria burden has decreased dramatically since the 1999/2000 season 4 million people are still at risk of contracting malaria in South Africa (Tren & Bate, 2004).

During the 1999/2000 epidemic season the incidence rate for KwaZulu-Natal province (70 per 1 000 population) was the highest ever recorded since the electronic capturing of malaria case data followed by Mpumalanga (10 per 1 000 population) and Limpopo (5 per 1 000 population) (Fig. 1.4). High case fatality ratios were seen for KwaZulu-Natal (0.8 deaths per 100 cases) closely followed by Limpopo (0.7 deaths per 100 cases) and Mpumalanga province reported an acceptable level of 0.4 deaths per 100 cases (Fig. 1.5).

The decline in case incidence since the epidemic season is speculated to be due to a combination of factors including the change to effective therapy, the reintroduction of DDT for vector control and the southern Mozambique residual indoor spraying activities.

1.2.4. Recent control and management initiatives and new vector control possibilities

Malaria's impact on human life and social well-being has again captured global attention. It has also been recognized that effective control of malaria requires collaboration of neighbouring countries and the global community (Durrheim *et al.*, 1998b). The Roll Back Malaria (RBM) initiative was founded by WHO, UNICEF, World Bank and UNDP in 1998 with the objective to halve the global malaria burden by 2010. The core strategies selected included rapid malaria detection and effective treatment, limiting mosquito bites by the use of insecticide

treated nets (ITNs), preventing malaria in pregnancy, and detecting and responding to epidemics (World Health Organization, 2001c).

Figure 1.2 Malaria Risk Map, South Africa and bordering countries, 2004/2005

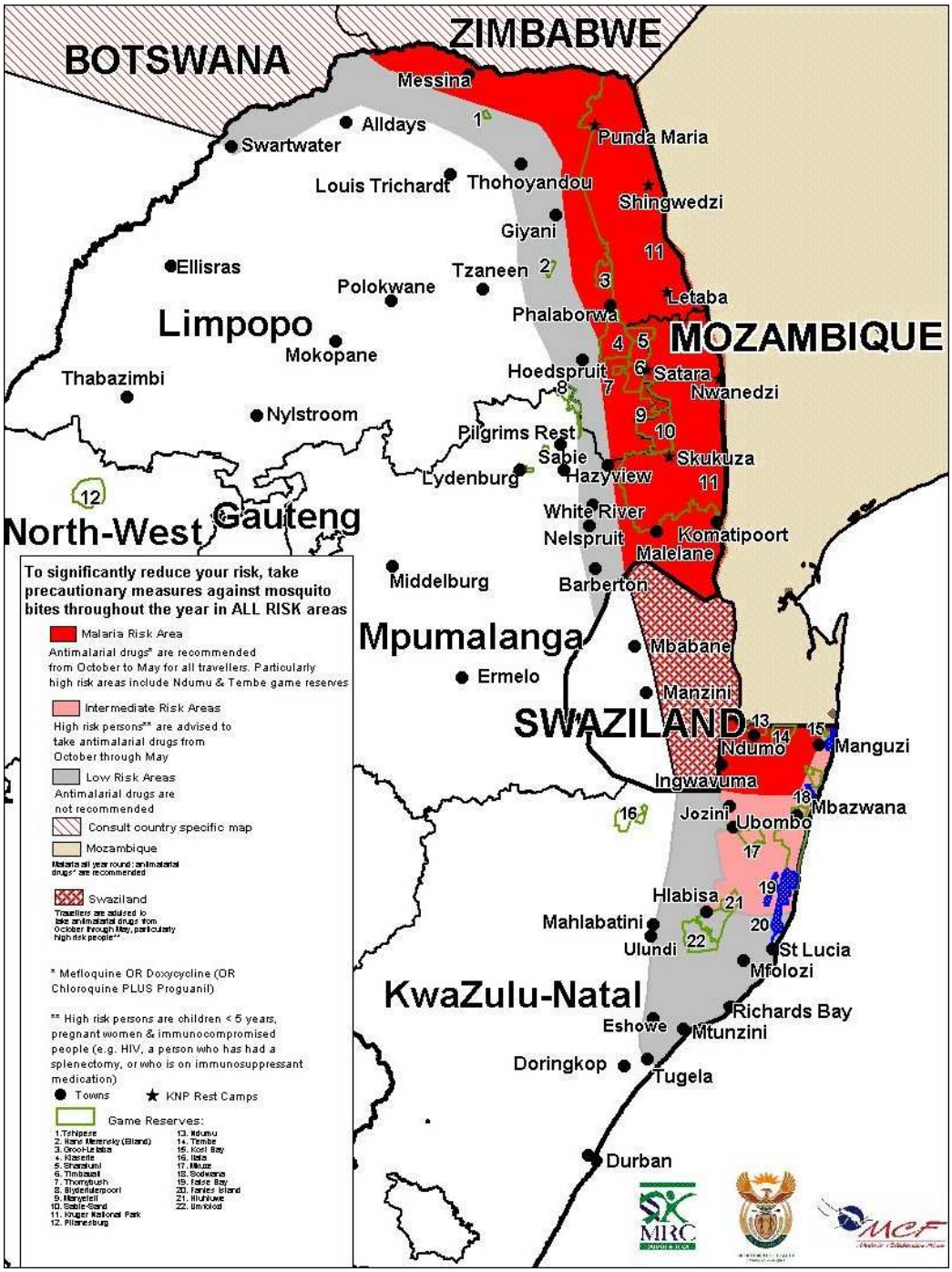


Figure 1.3 Malaria case and death notifications, 1971 – 2005, South Africa

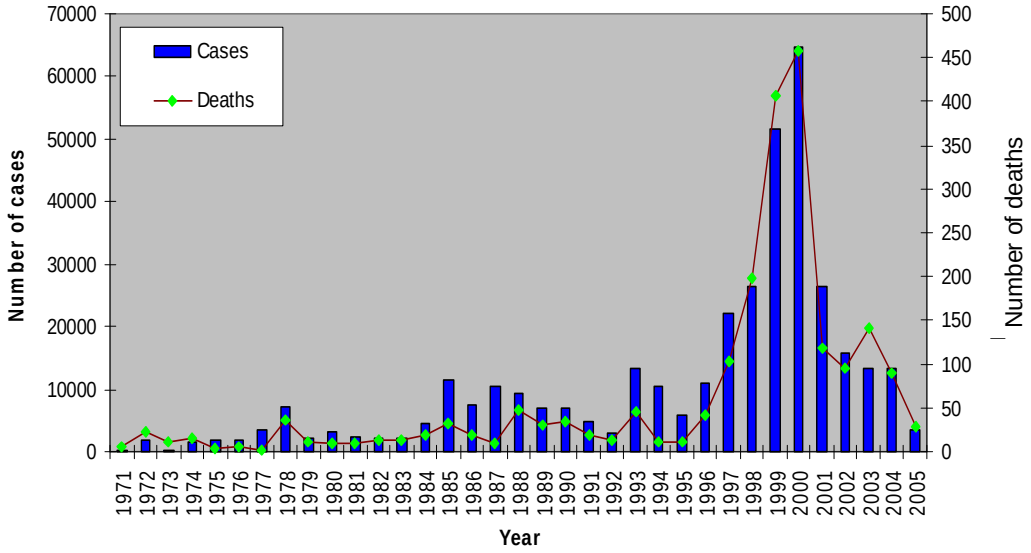


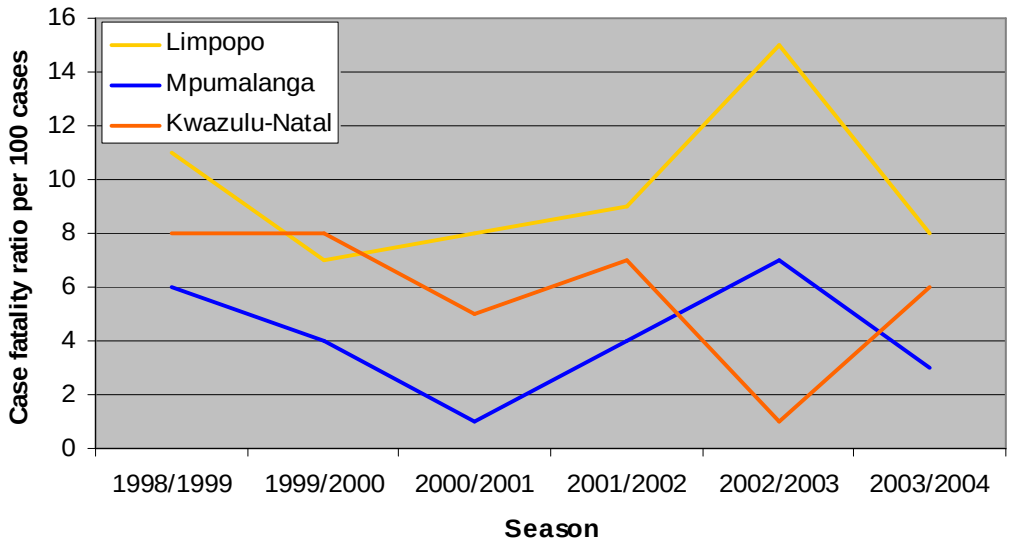
Figure 1.4 Malaria case incidence by province, 1999/2000 to 2004/2005 season, South Africa

The Multilateral Initiative on Malaria (MIM) (Multilateral Initiative on Malaria, 2002) was also established in 1998 and is a global alliance of organizations and individuals, with objectives including international public awareness campaigns, promotion of global communication and cooperation, development of sustainable malaria research capacity in Africa, and a commitment to ensure that research findings are applied to malaria treatment and control (Multilateral Initiative on Malaria, 2002).

A noteworthy initiative in southern Africa, is the malaria control component of the Lubombo Spatial Development Initiative. It aims to control malaria across the borders of Swaziland, Mozambique and South Africa through collaborative efforts and "protect communities, enhance development and protect economic investment" (Medical Research Council, 2005). All regions experienced a reduction in cases particularly KwaZulu-Natal, which experienced a reduction of 88% in parasite prevalence after the introduction of control in southern

Mozambique, including the introduction of combination antimalarial therapy and residual indoor spraying (Medical Research Council and University of Cape Town, 2004).

Figure 1.5 Malaria fatality ratio by province, 1995/1996 to 2004/2005 season, South Africa



Blanket and strip spraying with residual insecticides and distribution of insecticide treated nets (ITNs) are the major approaches used in the southern African region to control malaria vectors. The only countries utilizing ITNs on a large scale are Botswana and Tanzania followed by limited implementation in Angola, South Africa, Swaziland and Zimbabwe (South African Malaria Control Programme, 2001).

The integrated vector management (IVM) strategy has been adopted as the preferred approach by WHO/AFRO and its partners, with IVM defined "as a process of evidence-based decision-making procedures aimed at planning, implementing, monitoring, and evaluating targeted, cost-effective, and sustainable combinations of vector control measures" (Manga *et al.*, 2004). The aim is to

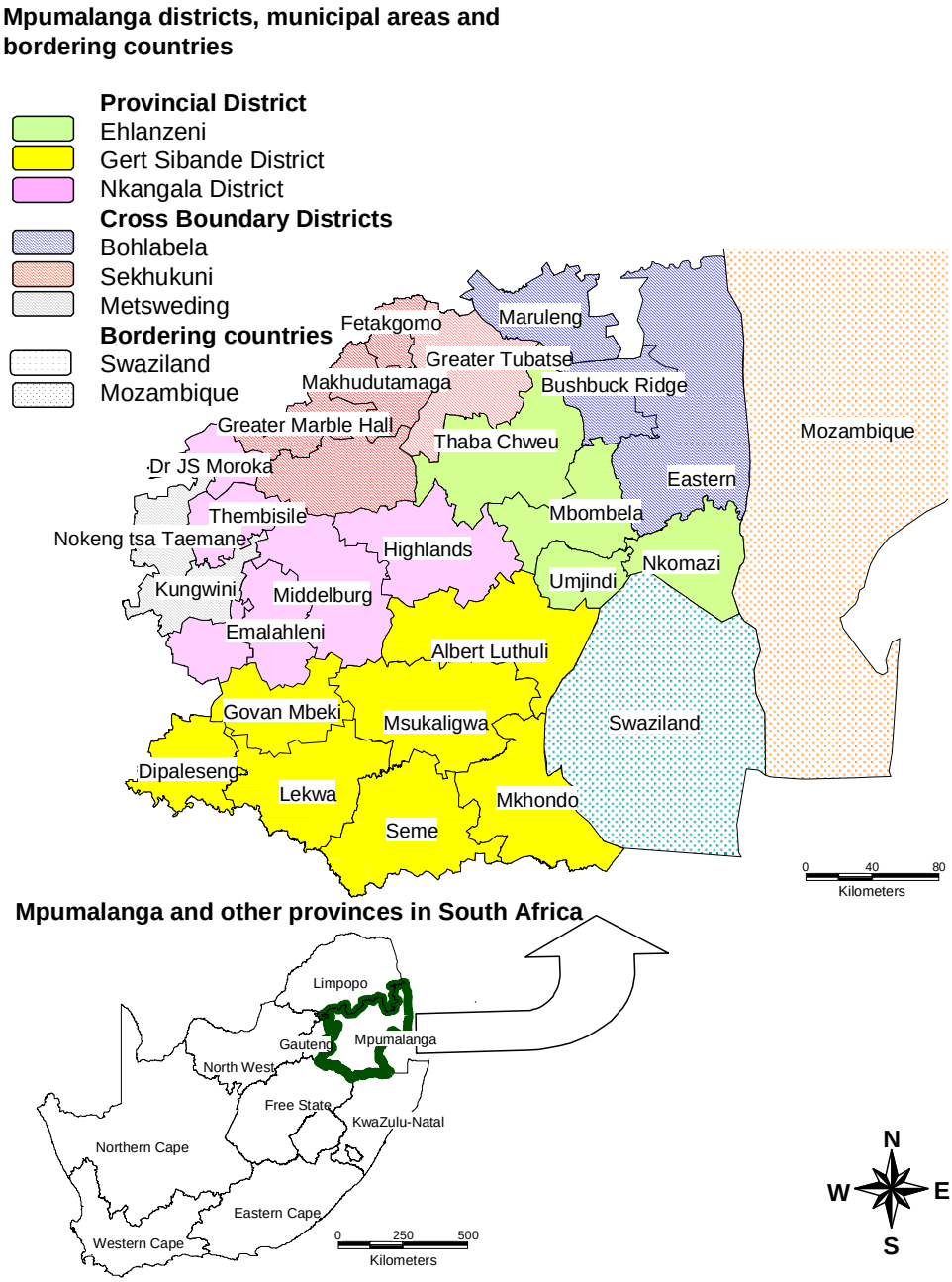
reduce the reliance on DDT through its gradual phasing out. IVM projects differ between regions being influenced by vector population dynamics and socio economic factors. Targeted control methods can include natural larviciding, for example with *Baccillus thuringensis* (Bt), removal of breeding sites, changed agricultural practices, better town/village planning away from possible breeding sites, screening of houses, personal protective measure and use of ITNs (Africa Fighting Malaria, 2005). There is general acceptance that high resolution mapping of disease risk at household, town or village level may assist in prioritizing and targeting areas for IVM implementation at local level.

1.3 Malaria in Mpumalanga province, South Africa including community knowledge, attitude and practices

Malaria in Mpumalanga is mainly confined to the eastern Ehlanzeni region with the highest risk Tonga area, bordering Mozambique in the east and Swaziland in the south (Mpumalanga Malaria Control Programme, 2005).

The remaining districts, Nkangala and Gert Sibande are non-malarious areas but passive surveillance is maintained as occasional focal outbreaks occur (Mpumalanga Malaria Control Programme, 2005). The highest malaria case incidence (12/1000 population) in the past two decades occurred during the 1999/2000-malaria season (July 1999 to June 2000). These figures only include local malaria case numbers where infection was acquired within Mpumalanga province. All other cases from outside the boundary of the province are imported cases and contributed towards 30% of the cases notified in the Province during this period. The majority of the imported cases originated from Mozambique.

Figure 1.6 Mpumalanga orientation map



Malaria occurs seasonally in Mpumalanga with localized epidemics in towns in the highest risk areas in the east, bordering Mozambique (Mpumalanga Malaria Control Programme, 2006). The majority of the local population at risk are non-immune and live in rural and semi-rural settlements (Durrheim *et al.*, 1997). *Plasmodium falciparum* is responsible for 90% of the infections in the

area and diagnosis in primary health care centres is primarily by means of rapid card tests (la Grange *et al.*, 1999).

Mpumalanga is a popular tourist destination due to its mild climate and abundance of game reserves. There are approximately 2.5 million local and 1.1 million international visitors to the province annually. This industry contributes R8.7 billion to the gross geographic product of the province (Mpumalanga Tourism, 2004). The most popular attraction is the Kruger National Park, situated in the east of the province and this Park is visited by almost one million local and international visitors per annum. Although a low malaria attack rate of 4.5 cases per 10 000 visitors (1996) exists in the Kruger National Park perceptions of potential tourists are dramatically affected by reports of epidemics amongst the local population (Durrheim *et al.*, 1998a).

Malaria is considered by communities in the high-risk district as a major health risk and was ranked third after tuberculosis and AIDS in a cross-sectional community survey (Govere *et al.*, 2000a). The majority of these inhabitants reported that they would seek treatment for febrile disease at a local clinic or hospital.

DDT was reintroduced in August 2001 for indoor application in traditional structures while deltamethrin is currently reserved for western style structures. A granulated form of deltamethrin has been in use since the 2004/2005 season (la Grange, 2005). Rotational spraying is considered for the future and can potentially result in significantly increasing the cost of spraying operations. The logical insecticide of choice for rotational spraying is a carbamate due to vector

resistance and cross-resistance dynamics referring to target site mechanisms (Brogdon & Mc Allister, 1998).

The added burden of HIV-AIDS has resulted in decreased budget for other PHC activities and thus the need for targeting vector control to best utilized available resources.

1.4. Information Technology tools for disease surveillance and control

Information is a powerful tool for controlling infectious diseases. It allows managers to make informed decisions regarding type of disease interventions, where they should be focused and what the extent of resource investment should be. Planning, implementation and evaluation of public health programmes is unlikely to be effective without quality information. To enable collection, collation, storing, analysis, interpretation and distribution of health related data for disease surveillance, an information system is usually required (Centres for Disease Control and Prevention, 2001). Information technology is a critical part of this system but should not be considered synonymous with "The System".

A literature review from 1992 to 2002 relating to health information technology (IT) application in primary health care in developing countries indicated a general lack of evaluation of application of information technology (Tomasi *et al.*, 2004). Many failures were recorded with three major factors implicated:

- rational models disconnected from behavioural reality;
- private sector systems failing in transfer to the public sector;

- the transfer of a system from one country to another where economic status differed (Heeks *et al.*, 1999)

A uniform malaria surveillance system exists in the three malaria effected provinces of south Africa. Minor differences exist but a core dataset is maintained (Martin *et al.*, 2002).

The advancement in and improvement of surveillance systems now lends itself to accommodate detection components to ensure quick response to outbreaks and prevention of epidemics. The availability of database development tools to verify and query data even before acceptance in the system, input masks for data entry, fixed drop down list and a more user friendly user interfaces improves data quality. Decentralization of services and surveillance offices lessen time from notification to collection to data entry. The improvement and availability of communication technology and specifically mobile technology for outbreak notification provides an additional option to improved response time.

The unstable nature of malaria in South Africa warrants the implementation of an outbreak identification and response tool. In unstable situations, focal outbreaks and epidemics are expected from time to time. All age groups are at equal risk and the non-immune characteristic of the population can lead to serious disease (Bell, 1995). Even more reason to identify epidemics timely and reduce the risk of fatalities. Early detection, containment and prevention of malaria epidemics are an important element of the Global Malaria Strategy. The Roll Back Malaria Initiative advocates this activity and produced a comprehensive framework in this regard (World Health Organization, 2001c). Several methods to determine thresholds for early warning and outbreak alert

system have been tested and suggested for use. Retrospective analysis of disease epidemics and sensitivity of proposed thresholds to detect outbreaks and epidemics have been documented (Hay *et al.*, 2002; Kaninda *et al.*, 2000; Lewis *et al.*, 2001; Moore *et al.*, 1992; Teklehaimanot *et al.*, 2004). No province in South Africa had an outbreak detection system linked to their malaria surveillance system prior to this work. Lack of ownership and participation on all levels as well as the clear understanding of the advantages might be contributing factors. It is time for social scientists to move away from the written theoretical perspective and move toward the appropriate communication of practical suggestions for malaria control programme implementation (Williams *et al.*, 2002).

Geographical information systems (GIS) are an integral part of malaria surveillance systems in South Africa. GIS concept originated in Canada three decades ago and is now more generally applied by the public health sector as the demand for information increases. Historically the most celebrated example of mapping relating to disease was John Snow's attempt to demonstrate the association between cholera deaths and contaminated water supplies during the cholera outbreak in London in the 1840s (Mbarki *et al.*, 2004)

Analysis of the relationship between people, their environment and disease aetiology is important for effective public health intervention (De Savigny & Binka, 2004). It enables the modeling of data that provides new insights that support spatially informed decision-making to improve the allocation of health resources in relation to needs (Conrad, 2001).

In South Africa, the distribution of malaria was recorded on a map as early as 1938 by the Department of Public Health of the Union of South Africa in

collaboration with the Swaziland Administration (Strebel *et al.*, 1986). Drug resistance and the increase of malaria cases have necessitated the review and continual update of geographical malaria risk stratification in South Africa. The most novel malaria risk distribution model attempted is the mapping of risk in Africa. The MARA/ARMA project was planned to empower developing countries in Africa with information relevant for decision-making (Sharp *et al.*, 1998). The MARA/AMRA project was initiated in 1996 to address the lack of integrated risk data and sustained in the spirit of open collaboration. MARA aims to provide an atlas of malaria in Africa. MARA's objectives include gathering relevant information that will be used for rational and targeted malaria control interventions (Mara/Arma, 2005). However this has not yet been realized.

GIS has a wide range of applications in health. These include applications in environmental health (Snow *et al.*, 1998b), health systems management (Wilkinson & Tanser, 1999) and communicable disease control (Clarke *et al.*, 1996). Accessibility to and siting of health care facilities is an important aspect of health care provisioning and GIS technology has been applied to support decision-making in this area (Tanser, 2002). The variation in distribution patterns of vector mosquitoes can also be mapped using GIS technology (Hii *et al.*, 1997). The State of Pennsylvania has developed and implemented a fascinating State-wide West Nile surveillance and outbreak response system based on GIS technology in the past two years (Conrad, 2001) The system collects information on the presence of the virus in any vector, identifies mosquito-breeding areas and helps target control efforts. Web application enables data submission from State laboratories. E-mail messages alert decision-makers of any new data and detailed maps are generated

and posted on a secure Web site for review. The public has access to summary statistics to ensure dissemination of information at all levels. The system was initiated after the 1999 outbreak of West Nile virus in New York City when seven people lost their lives (Conrad, 2001).

GIS is not only a reality in developed countries. The development of GIS in the Third World has initiated new hope for informative decision making in diverse areas of management. Isabelle Nuttall (1994) describes the success of GIS management tools for the control of tropical diseases in Botswana, Senegal and Morocco. It is clear that the use of computers in health systems of development countries "is a need not a fashion" (Sepvulveda *et al.*, 1992).

Democracies have necessitated a new approach to decision-making in developing countries. The evolution of Public Participation GIS (PPGIS) is a move towards a bottom-up mode of planning that explicitly recognizes the role of effected people (Proctor J. 2002). The approach aims to make GIS and other spatial decision-making tools available and accessible to all those with a stake in official decisions (Obermeyer, 2002). It is a study of the uses and applications of geographic information and/or geographic information systems technology used by members of the public, both as individuals and grass-root groups, for participation in the public processes (collection, mapping, analysis and/or decision-making) affecting their lives (Centre for Remore Sensing and Spatial Analysis, 2008).

Malaria as a disease lends itself to the optimal use of this tool to identify disease distribution, clusters and risk areas. The environmental disease determinants are heterogeneous in space and ideal for analysis at a level where

malaria incidence can be overlaid geographically. This technology is becoming more feasible in all of Africa and proper documentation of GIS development initiatives and operational use will facilitate this process (Tanser & Le Sueur, 2002). The contemporary simplistic nature of geographical information system (GIS) software allowed basic spatial analysis of the malaria relational dataset.

1.5 Aim and objectives

The major aim of this work is the conceptualization, development and utilization of basic geographical and malaria information system tools for enhanced malaria control within an operational malaria control programme setting.

Specific objectives:

To analyse the epidemiological situation of malaria transmission in Mpumalanga using eight years of historical data to better understand the dynamics of the disease in the area (Chapter 2).

To describe the development, implementation and application of a unique intervention monitoring tool through an integrated data mining approach and provide examples of successful expansion implementation in five African countries (Chapter 3).

To explore the application of a simple outbreak detection and response system using an integrated three tier approach during two seasons of implementation (Chapter 4).

To describe the spatial and temporal heterogeneity of malaria occurrence at town/village level and explore the utility of local cluster detection for

prompting outbreak response using three years of cluster surveillance data (Chapter 5).

To better understand household and micro-economic factors associated with malaria (Chapter 6).

CHAPTER 2

2. Epidemiology of malaria in Mpumalanga province

2.1 Introduction

The South African Malaria Control Programme (SAMCP) was formally initiated following a World Health Organization advisory group visit to the National Institute of Tropical Diseases in Tzaneen, Limpopo Province, in 1978. The main control strategies at this time were indoor residual insecticide spraying with DDT, larviciding, epidemiological investigations, chemoprophylaxis and active surveillance (Strebel *et al.*, 1986). These approaches still form the basis of control. Morbidity and mortality data were historically captured manually in notification registers. However this process was cumbersome and analysis was limited to describing malaria occurrence by month, gender, age-group at provincial level.

The unstable nature of malaria in Mpumalanga province with a tendency for epidemics warranted a responsive surveillance system to facilitate timely targeted action. To limit malaria morbidity and mortality requires allocation of resources where these are most needed. Previous analysis of seasonal malaria case data in Mpumalanga has been restricted to basic description to provide background information to research papers (Durrheim *et al.*, 1998a; Durrheim *et al.*, 1999b; Govere *et al.*, 2002; Martin *et al.*, 2002).

A computerized malaria information system (MIS) designed in Microsoft Access for Windows 95 (version 7.0, Microsoft®, Redmond, Washington, United States) initiated and developed by the Mpumalanga Malaria Control Programme was introduced in 1997 to provide more accurate and timely data to assist

programme management. This information system replaced the outdated Dbase database management system. The runtime interpreter architecture allowed the user to execute commands by typing them in a command line "dot prompt", a tedious and laborious activity.

Extensive data cleaning activities before the migration process allowed for and prepared data repositories for comprehensive data analysis.

The most important motivation for this work was the lack of prior in-depth analyse of the epidemiological situation of malaria transmission in Mpumalanga over time to better understand the dynamics of the disease in the area and to pave the way for conceptualization and implementation of appropriate innovative surveillance and monitoring tools.

2.2 Methodology

Eight seasons of data from the Mpumalanga Malaria Control Programme MIS were available for this analysis; 1998/1999 to 2004/2005 malaria seasons. A malaria season refers to the period 1 July to 30 June the following year. The analysis of this data preceded all other analysis as presented in this thesis and formed the basis for further investigation, tools development and implementation.

Only malaria cases formally notified on malaria notification forms and definitively diagnosed, by either blood smear or rapid diagnostic test, are included in the MIS. Health facilities have an established procurement procedure for card tests and notification books are supplied by malaria case investigators during their weekly rounds to collect notification forms. A total of 118 individual health care facilities/providers reported malaria cases during the period.

Notifications are generated by clinicians and nurses working at public primary health care facilities, private general practice, and hospitals. In addition to case information, a travel history is collected to assist in determination of source of infection, which is classified either as local, referring to patients who most likely contracted the disease within Mpumalanga province, or imported.

Malaria control programme case investigators also contribute notifications to the reporting system following epidemiological surveys. Active case detection activities follow cases are passively reported from a specific locality (town/village) and traced to household level, with neighbours and immediate household members of the index case/s being tested, notified and referred to a health facility if positive.

During outbreaks active detection occurs using mass surveys, with screening of all people residing in the affected locality.

The smallest geographical unit that cases are assigned to is a locality, which is usually a town or village although other categories include farms, rural holiday resorts, manufacturing plants, game lodges and reserves. It was not possible to determine incidence rates for these latter localities due to uncertain and relatively small denominators.

Data were aggregated at locality, municipal, district and provincial levels. A uniform growth rate of 2 percent was used to project population figures forward and backward based on the national census of 2001 (Statistics South Africa, 2003).

Arc View GIS software was used (version 3.2, ESRI: Environmental Systems Research Institute, Inc. Redlands, California, USA 1999) to visually portray the study area and the geographical variability of malaria risk.

The relationship between rainfall as well as temperature compared to malaria case reporting was examined by using linear regression procedures.

The Kruskal-Wallis non-parametric test for independent samples was used to determine the overall difference of reported cases during four quarters, between districts and municipal areas. The Mann-Whitney U test for two independent groups tested the hypothesis that risk is not equal for all months of the transmission period.

Graphs and tables were used to visually display data when appropriate.

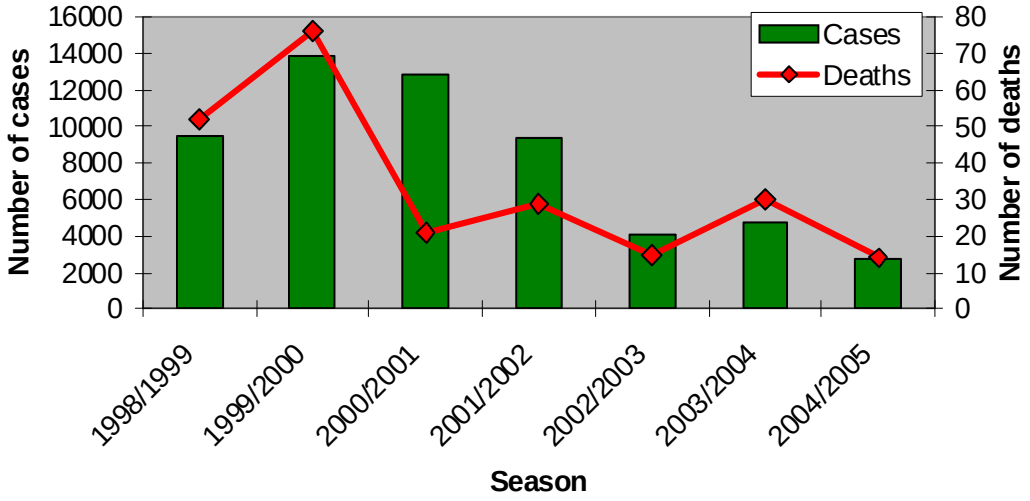
2.3 Results

2.3.1 Malaria cases and deaths, 1997/1998 to 2004/2005 season

A total of 63,537 cases and 256 deaths were reported during the period 1 July 1997 to 30 June 2005 with a peak in cases and deaths during the 1999/2000 season and an average of 7,942 cases and 32 deaths per season (Fig. 2.1). The majority of malaria cases (70%) resided in towns/villages, followed by farms (19%), neighbouring countries (4%), game lodges and reserves (3%). The remainder (4%) resided in other provinces, mine housing and commercial premises outside town boundaries.

Most cases (61,127, 96%) and deaths (248, 97%) were reported in the low-lying Ehlanzeni district, which borders Mozambique in the east and Swaziland in the south (Table 2.1).

Figure 2.1 Notified malaria cases and deaths, 1997/1998 to 2004/2005 seasons, Mpumalanga province



The Kruger National Park (KNP) is included in the Bohlabela Cross Boundary District. This portion is considered a tourist sensitive area and 1 835 cases and 3 deaths were notified during this period. Skukuza, the largest and major camp in the KNP contributed most of the case burden (n=1 100, 63%). All private game parks when combined contributed 625 cases (34%) for the same period when referring to source of infection area.

2.3.1.1 Cases by month

Differences in the number of notified cases per month is an indication of the seasonality of malaria in Mpumalanga (Fig. 2.2). Dry months (June to September) with rainfall over a period of eight years (1998 to 2005) averaging 7.3 mm had the least cases reported. For the same four month period over eight years temperatures averaged 19°C. Number of cases reported during the wet summer months differed from those in the dry months as the main vector of malaria in southern Africa (*Anopheles arabiensis*) has a larval habitat dependent on temporary water bodies, especially rain pools (Gilles & Coetzee, 1987).

Climate variation plays a major role in the development of the parasite and thus transmission, seasonality and incidence of the disease. The duration of the cycle from egg to adult varies according to temperature and at 31°C the approximate time of development is 7 days and 20 days at 20°C. Below 16°C parasite development within the mosquito stops. A high relative humidity prolongs the life of the mosquito and thus time to transmit the disease (Bruce-Chwatt, 1980).

Figures 2.3 and 2.4 illustrate the number of cases reported by month from July 1997 to June 2005 overlaid by average monthly rainfall and temperature (South African Weather Services, 2006). There was a significant association between average monthly rainfall and notified cases (R^2=0.79, P=0.003). When cases were considered by quarters, starting with quarter 1 in July over the eight-season (1997/1998 to 2004/2005) period, a significant difference between quarters was noted (χ^2=44.8, p<0.000).

The Guidelines for the prevention of malaria in South Africa state that the period from October to May is the highest risk period (National Department of Health, 2003). This recommendation is strongly supported by the statistical correlation between malaria notification and risk period (Mann-Whitney U test for two independent groups =263.5, p<0.000).

2.3.1.2 Case reporting

Passive case reporting over the period totalled 58,864 (93%) compared to 4,673 (7%) actively reported cases. Cases in both categories peaked in the 1999/2000 epidemic season (Fig. 2.5). Hospitals reported a greater percentage of

cases during the epidemic season than any other period. A reverse trend was noted for primary health care facilities (Figs. 2.6).

Figure 2.2 Number of malaria cases notified by month, 1997/1998 – 2004/2005 seasons, Mpumalanga province

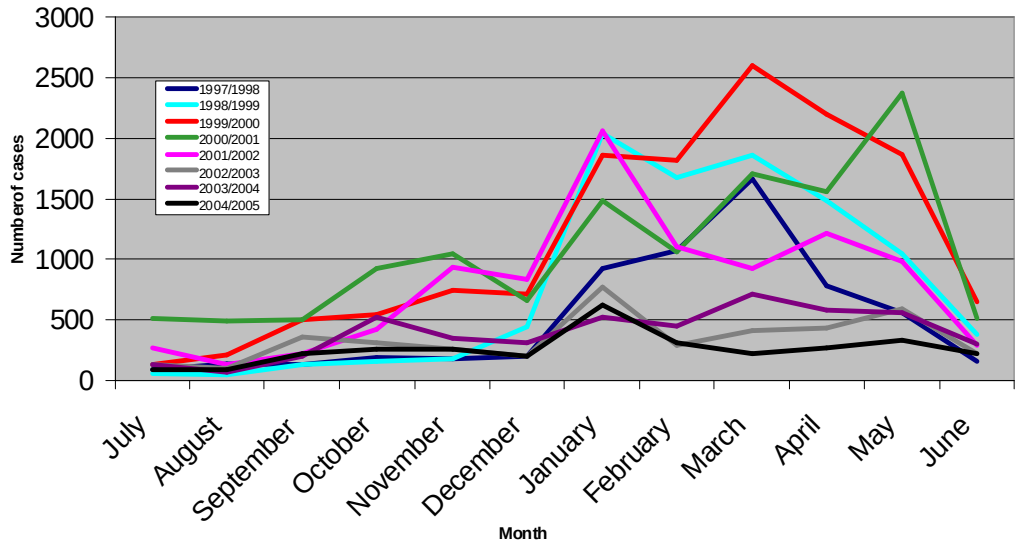
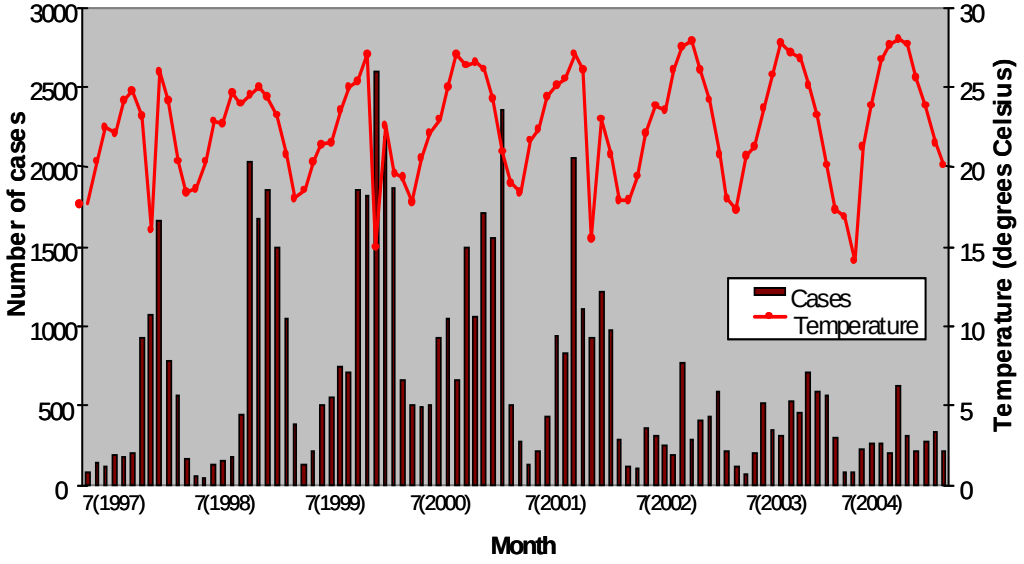


Figure 2.3 Notified malaria cases and average temperature by month, July 1997 to June 2005, inclusive, Mpumalanga province



Primary heath care facilities exclude all hospitals. A possible reason may have been the intensified health promotion campaigns and media reports that highlighted the serious nature of the disease and changed health treatment seeking behaviour. Hospitals are usually associated with serious illness. Provincial

primary health care clinics were responsible for notifying on average 47% of cases (n=29,675) over the 8 season period (Fig. 2.7). Most deaths were reported from provincial hospitals (n=218, 85%) followed by provincial (29, 11%) and municipal primary health care clinics (n=7, 3%) (Table 2.2).

Table 2.1 Notified malaria cases by district, 1997/1998 to 2004/2005 seasons, Mpumalanga province

	Season*							
District*	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
A								
n	219	507	366	290	254	181	107	105
(%)	(3.59)	(5.33)	(2.64)	(2.27)	(2.70)	(4.45)	(2.27)	(3.39)
B								
n	5 827	8 884	13 408	12 486	9 125	3 882	4 603	2 912
(%)	(95.42)	(93.45)	(96.77)	(97.57)	(97.17)	(95.45)	(97.65)	(93.97)
C								
n	20	27	52	10	7	2	1	60
(%)	(0.33)	(0.28)	(0.38)	(0.08)	(0.07)	(0.05)	(0.02)	(1.94)
D								
n	40	89	27	10	4	2	2	17
(%)	(0.65)	(0.94)	(0.19)	(0.08)	(0.04)	(0.05)	(0.04)	(0.55)
E								
n	1	0	2	1	1	0	1	5
(%)	(0.02)	(0)	(0.01)	(0.01)	(0.01)	(0)	(0.02)	(0.16)
Total								
n	**6 107**	**9 507**	**13 855**	**12 797**	**9 391**	**4 067**	**4 714**	**3 099**
(%)	**(100)**	**(100)**	**(100)**	**(100)**	**(100)**	**(100)**	**(100)**	**(100)**

***Districts:** A= Bohlabela Cross Boundary, B= Ehlanzeni, C= Gert Sibande, D= Nkangala, E= Sekukune Cross Boundary
***Season:** 1=1997/1998, 2=1998/1999, 3=1999/2000, 4=2000/2001, 5=2001/2002, 6=2002/2003, 7=2003/2004, 8=2004/2005

2.3.1.3 Source of infection

A malaria case is traditionally classified as acquired locally, i.e. infected within the province based on travel and exposure history captured on the notification form, or as imported. There were more cases classified as locally acquired (n=41,354, 65%) than imported (n=22,183, 35%), (1997/1998 to 2004/2005 season).The majority (n=38,935, 94%) of local cases contracted malaria in the Ehlanzeni district during this period. The proportional contribution

from the Ehlanzeni district between seasons ranged from 90% to 95%. Bohlabela was the only other district with percentages above 1%, (Table 2.3).

Figure 2.4 Notified malaria cases and average rainfall by month, July 1997 to June 2005, inclusive, Mpumalanga province

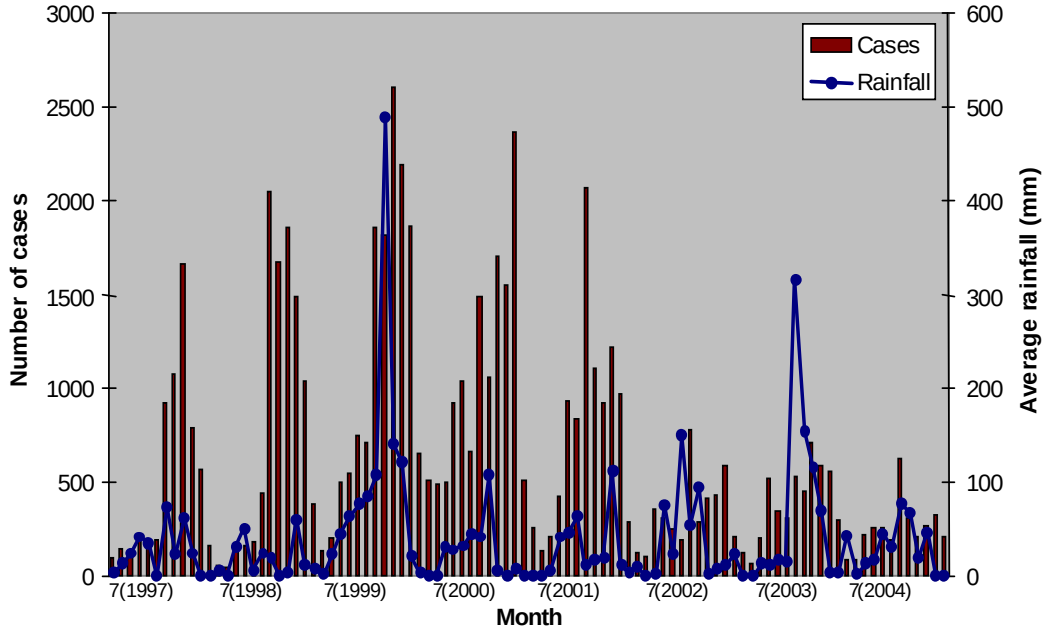


Figure 2.5 Number of malaria cases by reporting type, 1997/1998 – 2004/2005, Mpumalanga province

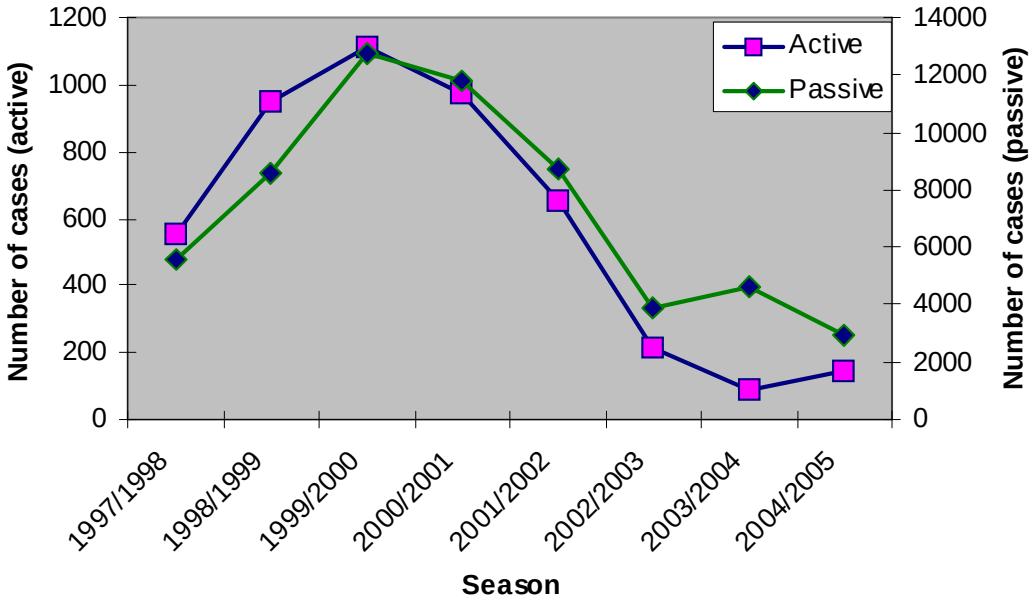


Figure 2.6 Malaria case reporting percentages by primary health care facilities and hospitals, 1997/1998 – 2004/2005, Mpumalanga province

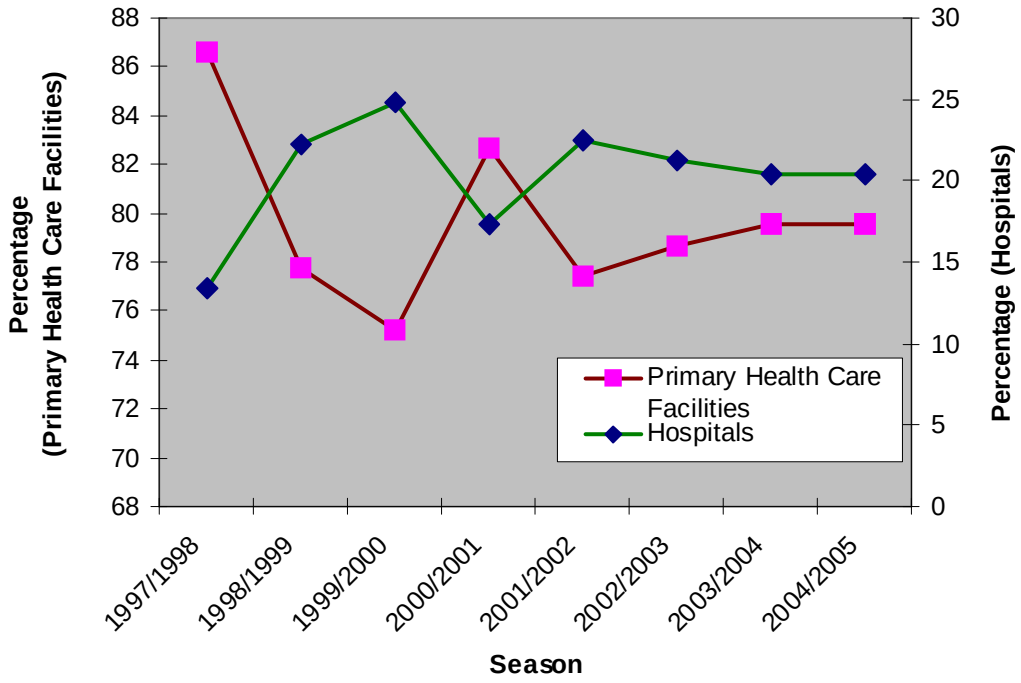


Figure 2.7 Seasonal proportion of cases notified by reporting category, 1997/1998 to 2004/2005 season, Mpumalanga province

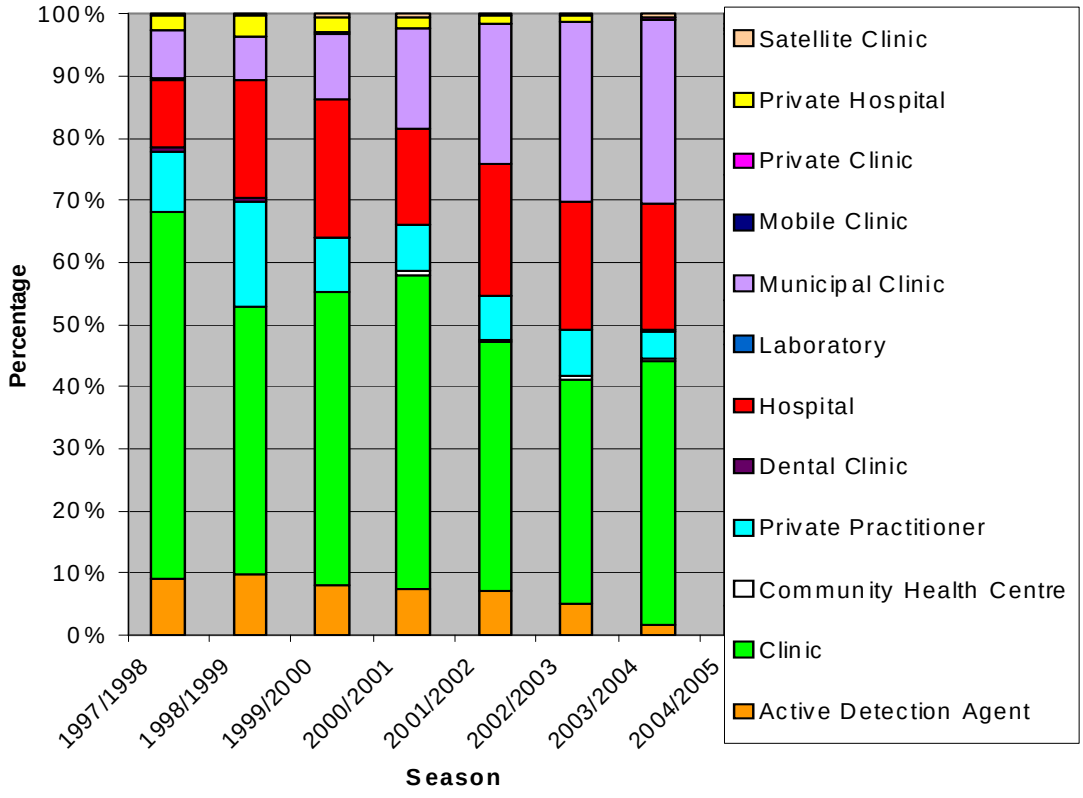


Table 2.2 Deaths notified by reporting category, 1997/1998 to 2004/2005 season, Mpumalanga province

	Season*							
Type	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Clinic n	4	8	11	5	0	0	1	18
Hospital n	1	43	62	15	27	15	27	0
Municipal Clinic n	0	1	1	1	2	0	2	0
Private Hospital n	0	0	1	0	0	0	0	0
Private Practitioner n	0	0	1	0	0	0	0	0
Total	**15**	**52**	**76**	**21**	**29**	**15**	**30**	**18**

***Season:** 1=1997/1998, 2=1998/1999, 3=1999/2000, 4=2000/2001, 5=2001/2002, 6=2002/2003, 7=2003/2004, 8=2004/2005

When local cases are compared to imported cases from travel and exposure history more people appeared to contract malaria within Mpumalanga than outside the borders of the province with the exception of the 2002/2003 and 2004/2005 seasons. The stacked bar graph in figure 2.8 provides a visual display of the increasing percentage of imported compared to local cases with specific reference to the 2002/2003 and 2004/2005 seasons. This trend was sustained beyond this period (Kok, 2007).

2.3.2 Population malaria incidence and case fatality ratios (CFR), 1997/1998 to 2004/2005 season

2.3.2.1 District incidence

The highest malaria incidence rates were recorded in the Ehlanzeni district with a peak in the 1999/2000 season of 1.2%. There was a significant difference in incidence between Mpumlanga districts (Kruskal-Wallis χ^2 =18.2, p<0.000)

(Table 2.4). These results necessitated further breakdown of case incidence to municipal level specifically for the Ehlanzeni district.

Figure 2.8 Local and imported malaria cases, 1997/1998 to 2004/2005 season, Mpumalanga province

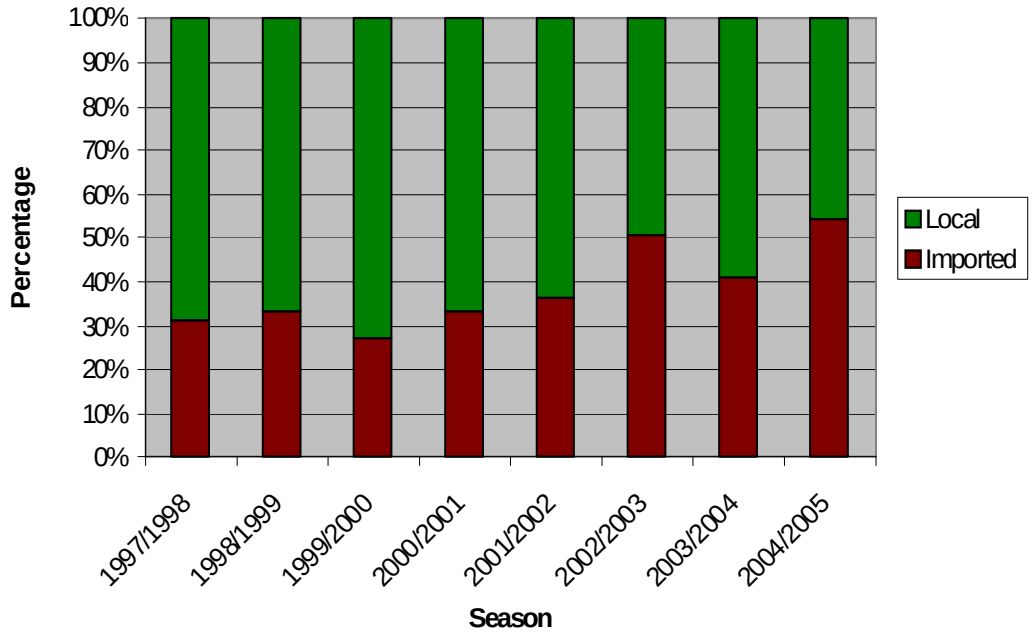


Table 2.3 Locally acquired cases by source district, 1997/1998 to 2004/2005 season, Mpumalanga province

	Season*							
District*	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
An	204	514	399	320	280	195	150	101
Bn	3 997	5 788	9 642	8 129	5 681	1 809	2 594	1295
Cn	5	9	18	11	2	1	0	2
Dn	1	5	0	3	1	0	1	2
En	0	10	40	73	21	3	26	22
Total	**4 207**	**6 326**	**10 099**	**8 536**	**5 985**	**2 008**	**2 771**	**1 422**

***Districts:** A= Bohlabela Cross Boundary, B= Ehlanzeni, C= Gert Sibande, D= Nkangala, E= Sekukune Cross Boundary

***Season:** 1=1997/1998, 2=1998/1999, 3=1999/2000, 4=2000/2001, 5=2001/2002, 6=2002/2003, 7=2003/2004, 8=2004/2005

Table 2.4 Malaria case incidence per 100,000 population by district, 1997/1998 – 2004/2005, Mpumalanga province

	Season*							
District	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Ehlanzeni	550.66	767.75	1222.76	989.65	663.30	202.05	285.22	137.17
Gert Sibande	0.99	1.22	2.48	1.88	0.36	0.11	0.22	0.32
Nkangala	0.11	0.56	0.10	0.31	0.09	0.00	0.09	0.17

***Season:** 1=1997/1998, 2=1998/1999, 3=1999/2000, 4=2000/2001, 5=2001/2002, 6=2002/2003, 7=2003/2004, 8=2004/2005

2.3.2.2 Municipal incidence within Ehlanzeni district

Within the Ehlanzeni district small-scale variation occurred during the period analyzed and between seasons. The average case incidence varied significantly between municipal areas during the study period ranging from 2 – 160 cases per 10,000 population (Kruskal-Wallis χ^2 =24.8, degrees of freedom=3, P=0.000) (Fig. 2.9).

Nkomazi municipality, bordering two neighbouring countries, Swaziland in the south and Mozambique in the east, had the highest rates in all seasons (Table 2.5).

Table 2.5 Malaria case incidence per 10,000 population by municipal area, 1997/1998 season, Ehlanzeni District

	Season*							
Municipality	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Mbombela	7.55	16.00	30.56	35.33	12.14	5.80	7.34	5.57
Nkomazi	153.22	208.53	326.32	248.01	184.96	53.34	74.70	31.84
Thaba Chweu	0.71	0.86	1.81	4.42	1.67	0.00	2.66	0.96
Umjindi	23.27	13.73	21.00	8.79	4.32	1.39	5.14	8.17

***Season:** 1=1997/1998, 2=1998/1999, 3=1999/2000, 4=2000/2001, 5=2001/2002, 6=2002/2003, 7=2003/2004, 8=2004/2005

Relative risk of malaria in Nkomazi varied from 9 to19 when compared to the remaining municipalities in Ehlanzeni District (Fig. 2.10).

Figure 2.9 Average case incidence by municipal area, 1997/1998 to 2004/2005 season, Ehlanzeni district

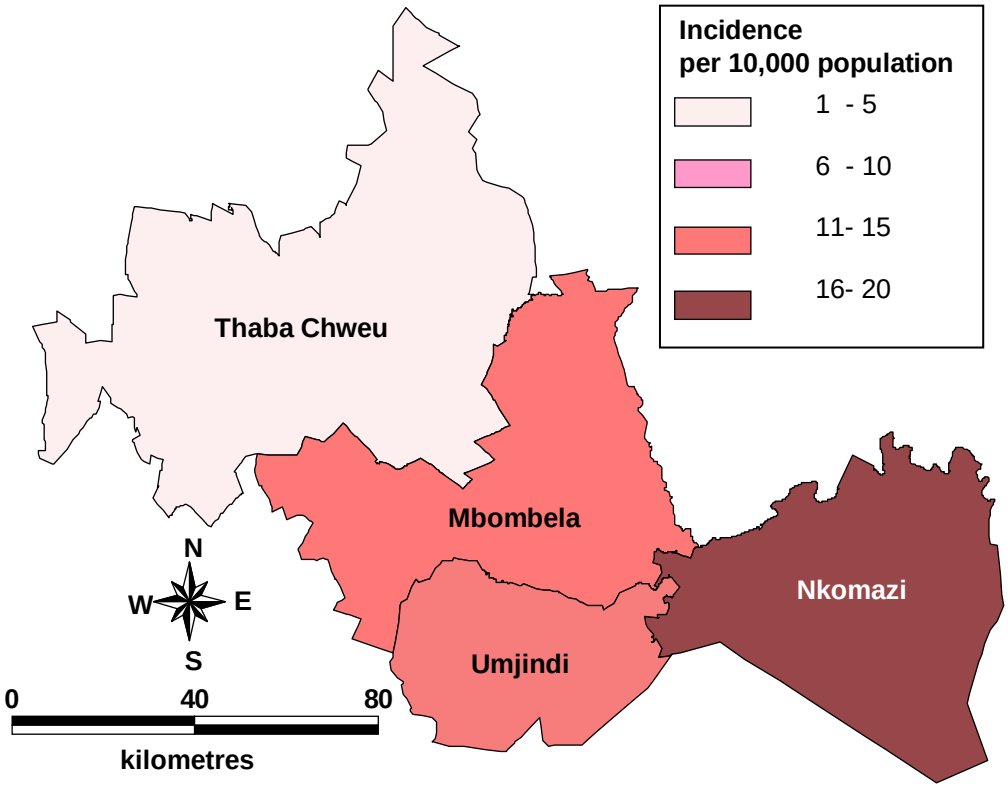
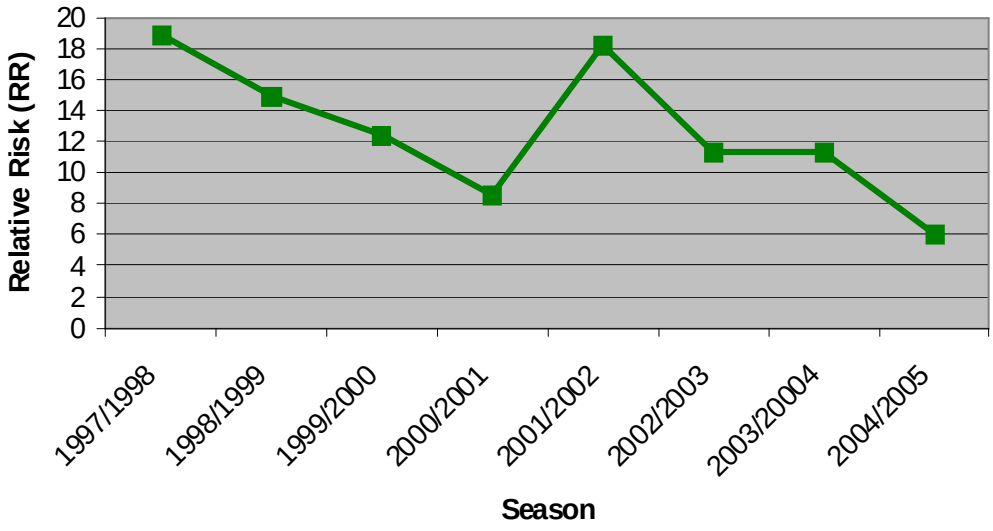


Figure 2.10 Relative risk ratios by season, Nkomazi municipality compared to Mbombela, Umjindi and Thaba Chweu municipalities combined, 1997/1998 – 2004/2005 season, Ehlanzeni District, Mpumalanga province



2.3.2.3 Town (locality) incidence

Malaria incidence rate analysis at town level confirms the marked heterogeneity in malaria risk even in the highest risk Nkomazi Municipality. In 2004/2005 populations ranged from 403 to 31,964 in the various towns. Fifty percent of the high-risk towns in Nkomazi are located within the 5 km buffer zone from the Mozambican border (Booman *et al.*, 2000).

The most stable season over the period was the 2004/2005 with incidence ranging from 1 to 30 per 1,000 population.

The five most affected towns during the time period are shown in figure 2.11. Clear fluctuations were visible by season and between towns. Only Komatipoort and Mbangwane had the highest peaks in incidence during the epidemic season of 1999/2000. Towns bordering Swaziland in the south experienced an average incidence rate of 21 per 1,000 population compared to 56 per 1,000 for towns bordering Mozambique in the east. The relative risk ratios show only a slight variation over the eight seasons except for the 2002/2003 season (Fig. 2.12).

2.3.2.4 Gender specific incidence

Malaria case incidence by gender showed consistently higher rates in males. Gender specific incidence as seen in Figure 2.13 peaked for both genders during the 1999/2000 season. Male to female ratios ranged from 1:1.28 to 1:1.72 over the 8 seasons (average 1:1.46). The ratio of deaths was similar being 1:1.31.

Figure 2.11 Average case incidence by town, 1997/1998 to 2004/2005 season, Nkomazi municipal area, Ehlanzeni district

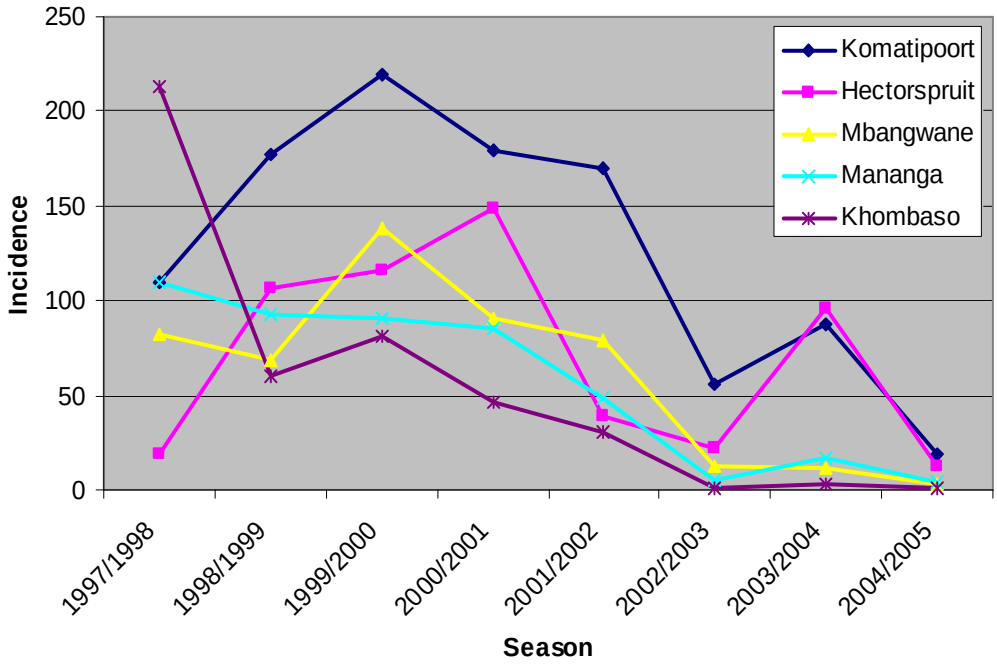


Figure 2.12 Relative risk ratios by season, comparing towns bordering Mozambique and towns bordering Swaziland, 1997/1998 – 2004/2005 season, Nkomazi municipality, Mpumalanga province

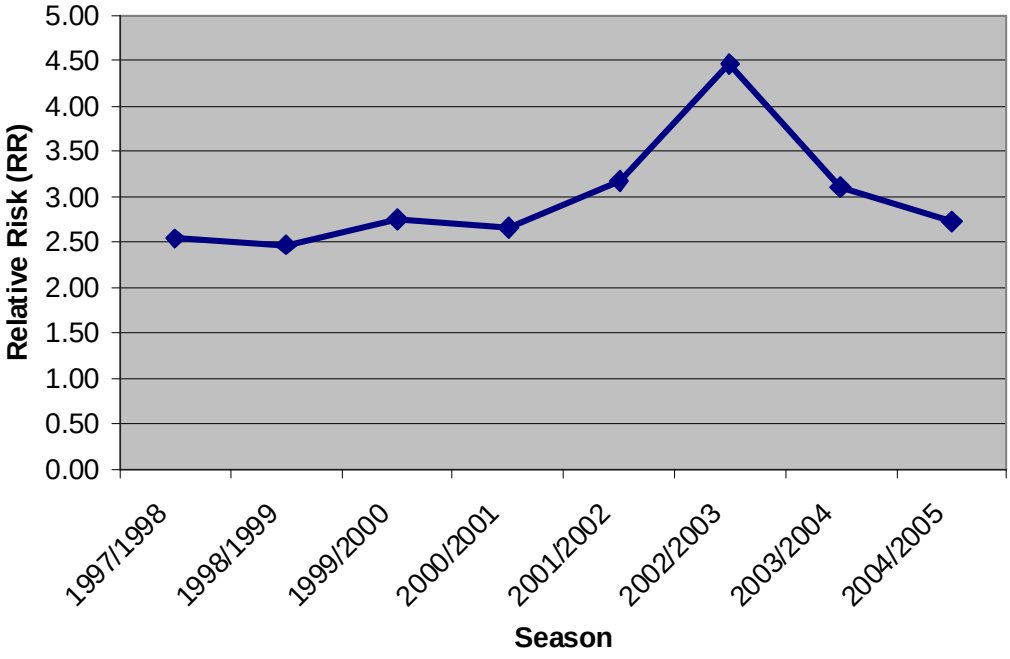
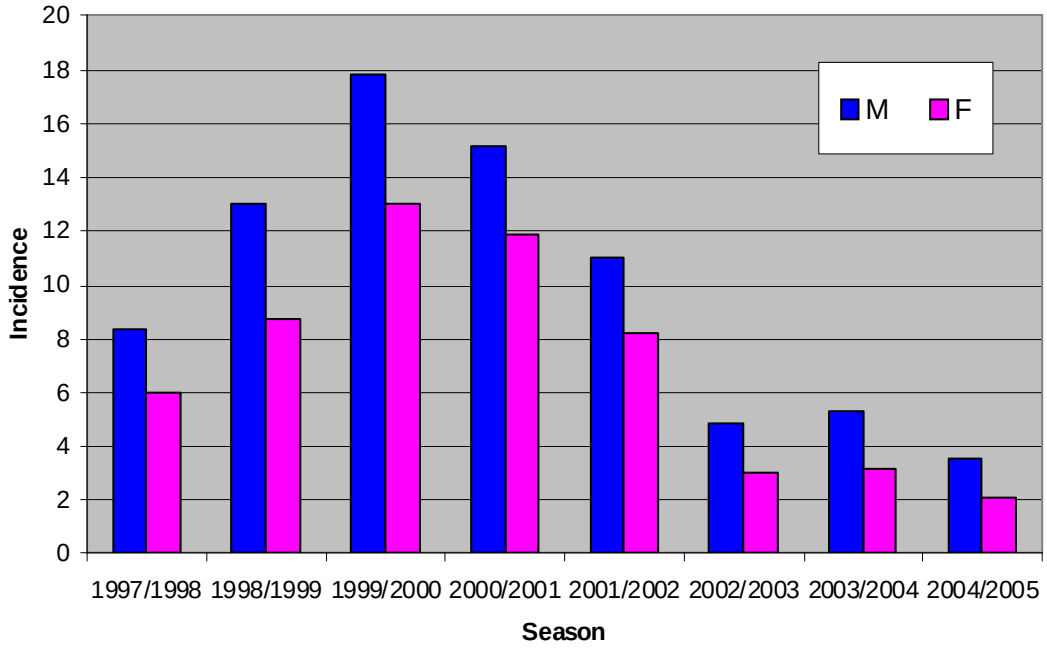


Figure 2.13 Gender specific incidence rate per 1 000 population, 1997/1998 – 2004/2005 season, Mpumalanga province



2.3.2.5 Age specific incidence

Age specific incidence was highest on average over the period in the age-group 10-19 years (Fig. 2.14). This can be explained by the high incidence recorded during the 1999/2000 and 20001/200s seasons for this group. Due to the seasonality of malaria and the lack of acquired immunity it is generally agreed that all age groups in low transmission areas are at equal risk of malaria. Lifestyle and outdoor activities can be contributing factors for increased risk of certain age groups.

2.3.3 Case fatality

One of the national and provincial targets for effective malaria management is to maintain a case fatality ratio of less than 0.5% of notified malaria cases. This was not achieved in 1998/1999, 1999/2000, 2003/2004 and 2004/2005 seasons (mean = 0.58, confidence interval = 0.51 – 0.65) (Fig. 2.15).

Figure 2.14 Age specific incidence per 10,000 population, 1997/1998 – 2004/2005 season, Mpumalanga province

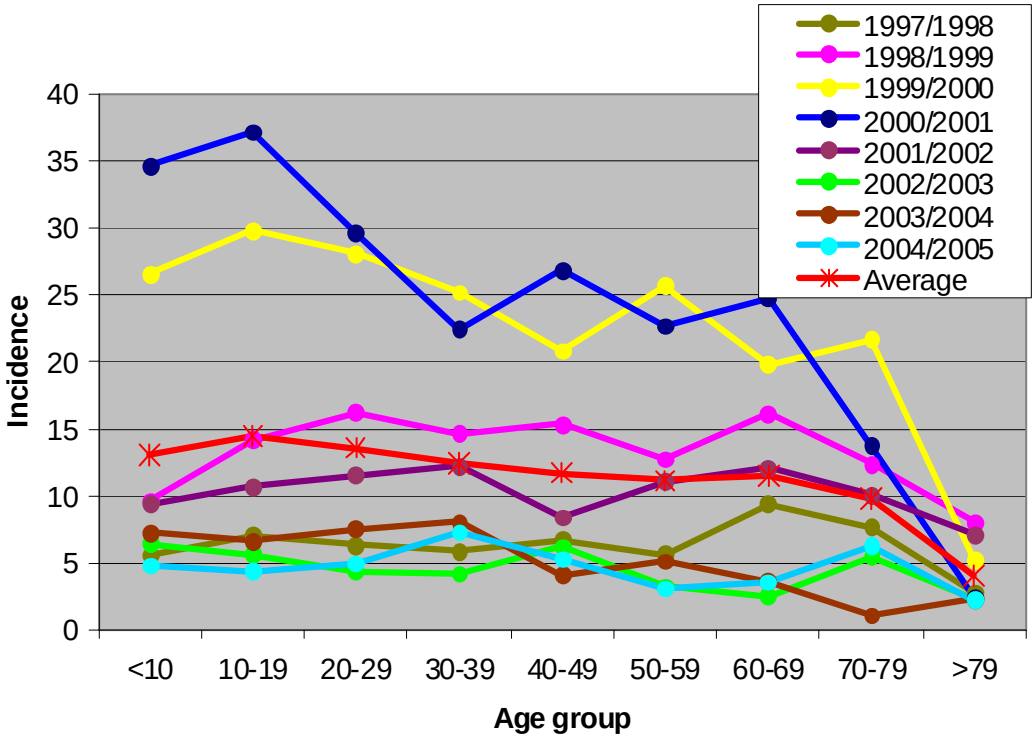
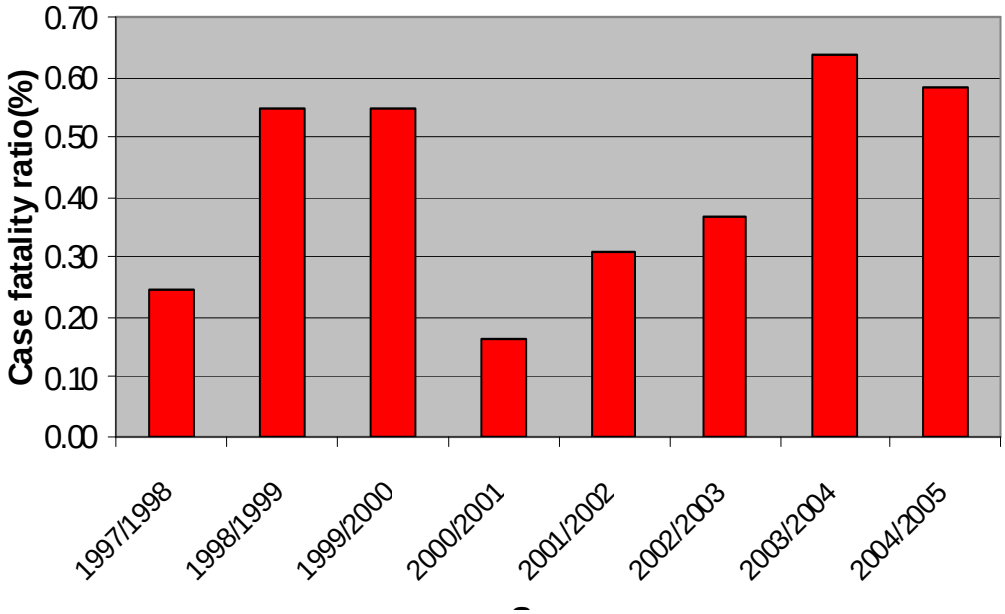


Figure 2.15 Malaria case fatality ratio (%), 1997/1998 to 2004/2005 season, Mpumalanga province



The highest case fatality ratios at district level was reported in the Gert Sibande area an area rarely affected by malaria (Table 2.6).

Table 2.6 Malaria case fatality ratio (%) by district, 1997/1998 to 2004/2005 season, Mpumalanga province

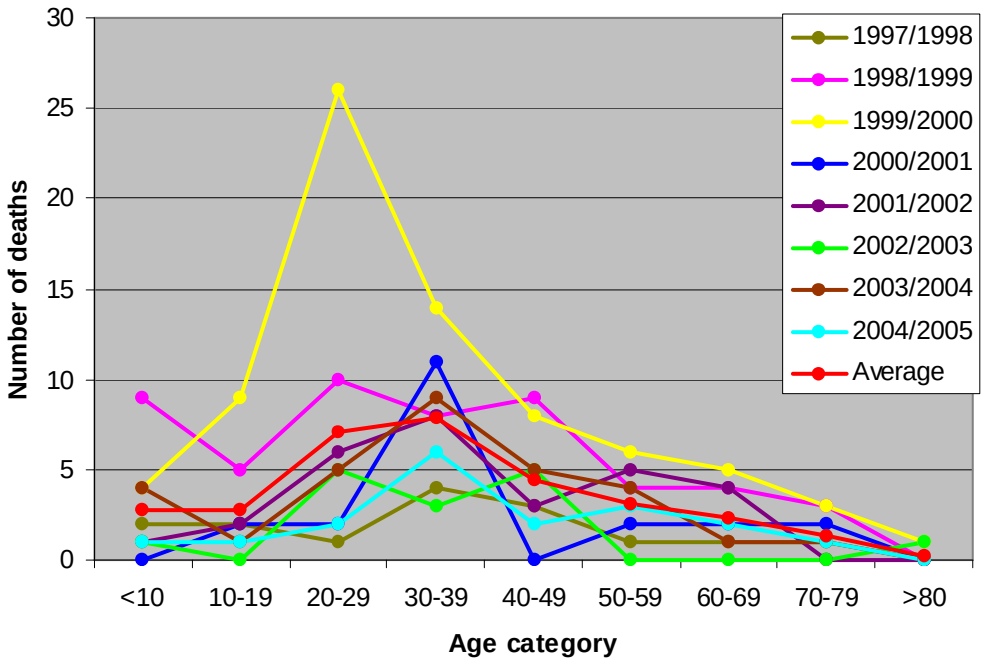
	Season*							
District	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Ehlanzeni	0.22	0.56	0.55	0.17	0.32	0.39	0.65	0.55
Gert Sibande	10.00	7.41	3.85	0.00	0.00	0.00	0.00	1.67
Nkangala	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.88
Total	0.25	0.58	0.56	0.17	0.32	0.39	0.65	0.60

***Season:** 1=1997/1998, 2=1998/1999, 3=1999/2000, 4=2000/2001, 5=2001/2002, 6=2002/2003, 7=2003/2004, 8=2004/2005

All malaria deaths from areas outside the boundaries of the highest risk Ehlanzeni district were reported from hospitals.

Deaths by age group over the eight-year period show a clear peak in the young adolescent group during the 1999/2000 epidemic season (Fig.2.16).

Figure 2.16 Number of malaria deaths by age group, 1997/1998 to 2004/2005 season, Mpumalanga province



2.4 Discussion

An in-depth analysis and discussion of eight seasons of malaria data was conducted to provide a deeper understanding of malaria epidemiology in Mpumalanga province. Malaria surveillance of cases and deaths is invaluable for malaria programme planning, resource allocation and monitoring of intervention success over time (Breman & Holloway, 2007; Teklehaimanot *et al.*, 2007).

Malaria case incidence in Mpumalanga showed a clear east/west gradient with greater risk in the low lying (<600m altitude) eastern areas. Malaria in the province is seasonal and prone to epidemics and focal outbreaks.

Heavy rains in the 1999/2000 season contributed to an epidemic situation in the eastern Ehlanzini district. More than 100mm of rain per week was reported at the Komatidraai weather station in this district from December 1999, peaking at 200mm in the second week of February (South African Weather Services, 2006). Cases followed a similar trend with a two-week delay on average. The following season commenced with high case reporting that transcended all other seasons. A warmer, wetter climate creates better conditions for breeding, continuous transmission and shorter sporogonic cycles, thus improves vector and parasite survival (Onori & Grab, 1980).

The proportion of cases reported at primary health care facilities compared to hospitals in the province decreased during the epidemic time. Media coverage and intense awareness campaigns heightened the fear of malaria and the possibility of death. Communities might have perceived hospitals as the most appropriate malaria management facilities.

Two focal outbreaks were reported during the eight season period. The Thaba Chweu district had an unexpected increase of cases during October 2003 to May 2004 with 77 cases and 6 deaths. The majority of cases (n=41,53%) and deaths (n=4,66%) were imported. All the cases were reported from farms where migrant workers resided. This area is not considered high risk and additional resources were mobilized to contain the outbreak.

The second outbreak occurred during the 2003/2004 season. Dindela, an informal rural town in the Ehlanzeni district of Nkomazi municipal area reported cases above the expected. The outbreak occurred between January and March with 281 cases and no deaths. A total of 47% (n=132) of cases were imported from Mozambique and Swaziland. No timely warning system was in place during this time to ensure pro-active control measures. The outbreaks were contained but the necessity for tools to sensitize malaria management and field staff in real time was recognized.

It appeared that CFRs were higher in districts where malaria occurrence was relatively uncommon. It is possible that facilities diagnosing and treating patients in low risk areas are not as informed and vigilant as those in the higher incident areas. Most education awareness and training efforts were directed at the highest risk Ehlanzeni district.

Case fatality ratios dropped after the 1999/2000 epidemic season but steadily increased to reach levels above the recommended national objective (<0.5%). The upward trend imitated that of HIV prevalence in South Africa (Health Systems Trust, 2004; National Department of Health, 2004) and it is speculated that HIV figures will continue to rise and double by 2010. In 2002 it

was estimated that AIDS accounted for 51% of deaths in Mpumalanga (Dorrington *et al.*, 2002). HIV co-infection increases the risk of severe disease and malaria deaths (Grimwad *et al.*, 2004).

Malaria cases occurred throughout the age spectrum but, compared to highly endemic regions in southern Africa, did not peak in children under the age of five years. This is explained by the non-immune status of the majority of the population in Mpumalanga. Repeated infections are needed for immunity to be achieved and the hypo endemic (prevalence less than 10%) nature of malaria in Mpumalanga does not allow development of immunity in the affected population. In endemic areas children surviving repeated episodes of malaria until the age of five or six years are likely to have developed sufficient partial immunity to withstand further lethal infections (Bell, 1995).

The highest risk months extend from October to May and this period corresponds with the national recommendations for chemoprophylaxis (National Department of Health, 2003). The low risk winter months are characterized by lower temperatures and rainfall. The vector mosquito populations are reduced to undetectable levels due to lower humidity, decreased longevity and fewer breeding sites.

Thirty years of malaria incidence data in KwaZulu-Natal demonstrated that spatial and temporal variability of malaria cannot only be explained by climatic factors alone. Human immunodeficiency virus (HIV) prevalence and drug resistance levels were significantly association with seasonality of malaria (Craig *et al.*, 2004a; Craig *et al.*, 2004b). However literature indicates that

climatic and environmental factors do contribute largely to the transmission of the disease in Sub-Saharan Africa (Craig *et al.*, 1999).

The implementation of a malaria control programme in southern Mozambique, as part of a three-country Lubombo Spatial Development Initiative, commenced in 2000. Structures were sprayed with a carbamate residual insecticide and sulphadoxine-pyrimethamine (SP) and artesunate (AS) combination therapy was later introduced as first line treatment. Case surveillance and intervention monitoring systems were step-wise implemented to compliment the malaria control activities (Medical Research Council, 2005).

The proportion of imported cases notified in Mpumalanga has increased while local cases decreased when the first season (1997/1998) is compared to the last (2004/2005). After the 2000/2001 season imported case numbers declined by 45% as did local cases after the 1999/2000 season. The decline for local cases was slightly less (39%) but both reached a low in the 2004/2005 season. No significant differences between the case numbers (P=0.16) and ratios (P=0.39) between the two groups were established.

The Lubombo Spatial Development Initiative focussed malaria control activities in the southern part of Mozambique since 2000 and continuous as well as effective intervention limited the introduction of imported infections (Sharp *et al.*, 2007a). The majority of imported cases derive from Mozambique. Introduction of additional parasites in an area with identified malaria vectors do impact on malaria transmission and malaria incidence. Health services face the additional load of diagnosis, treatment and notification.

Another noteworthy intervention to discuss was the introduction of effective chemotherapy namely sulphadoxine-pyrimethamine (SP) in 1997 and combination therapy commencing in 2003. The SP and artesunate (AS) combination was followed by artemether-lumefantrine as first line treatment of uncomplicated malaria. The startling resistance figures found in 1997 for chloroquine (48.4%, RI, RII, RIII) demanded the change to SP (Govere *et al.*, 1999). No alarming drug resistance has been found using SP (6%, 7%, 8% failure) but there were disturbing increases in gametocyte carriage which prompted SP and AS combination treatment being introduced (Mabuza *et al.*, 2001). Clinical trails in Africa have demonstrated improved cure rates and decreases gametocyte carriage with the use of combination therapy (Adjuik *et al.*, 2002; International Artemesinin Study Group, 2004).

The first official mass use of immunochromatographic card tests for malaria diagnosis in Mpumalanga commenced in 1997. An operational study performed just after introduction of rapid diagnostic tests (RDTs) revealed sensitivity and specificity percentages above 95%. Polymerase chain reaction (PCR) was used as the gold standard. Earlier, accurate diagnosis not only at health facility level but quick diagnosis during active case detection became possible and so followed timely treatment (la Grange *et al.*, 1999). Combination therapy currently used in several African countries are costly and the move away from clinical diagnosis to RDTs can be justified when the cost of misdiagnosis and unnecessary treatment of patients are compared to the cost of the tests themselves (Lona *et al.*, 2005).

Synthetic pyrethroids replaced DDT with the commencement of the 1996/1997 season. Initial evaluations promoted the use of synthetic pyrethroids above that of DDT due to its potential health risk (Bouwman *et al.*, 1994; Bouwman *et al.*, 1990a; Bouwman *et al.*, 1991; Bouwman *et al.*, 1990b; Bouwman *et al.*, 1990c). Reports later indicated the development of pyrethroids resistance (Brogdon & Mc Allister, 1998; Hargreaves *et al.*, 2000) and a drastic increase in cases during 1999 and 2000 necessitated the reintroduced of DDT in Mpumalanga in 2001. All traditional structures in high-risk areas were targeted for indoor residual spraying.

After the floods in 2000 the National Government made additional financial resources available to provinces. This enabled the planning and implementation of complimentary control interventions. A total of 17 626 insecticide treated nets (ITNs) in 8 high risk rural towns in Nkomazi municipal area were distributed from 2002 to 2003. Delays caused by administrative holdups resulted in procurement and delivery delays and ultimately distribution of the ITNs. The evaluation of acceptability within communities who were unfamiliar with the use of ITNs and effectiveness of this new intervention followed. The incidence reduction amongst towns where ITNs were distributed ranged from 11 – 34% pre-and post seasons.

Several other factors including climatic aberrations may have contributed to this decline. It has been suggested that the effect of ITNs varies with levels of endemicity, vector and human behaviour. However, as a vector control tool ITNs appear to be promising in their simplicity and cost-effectiveness (Misra *et al.*, 1999). ITNs show potential for preventing malaria mortality and morbidity, and

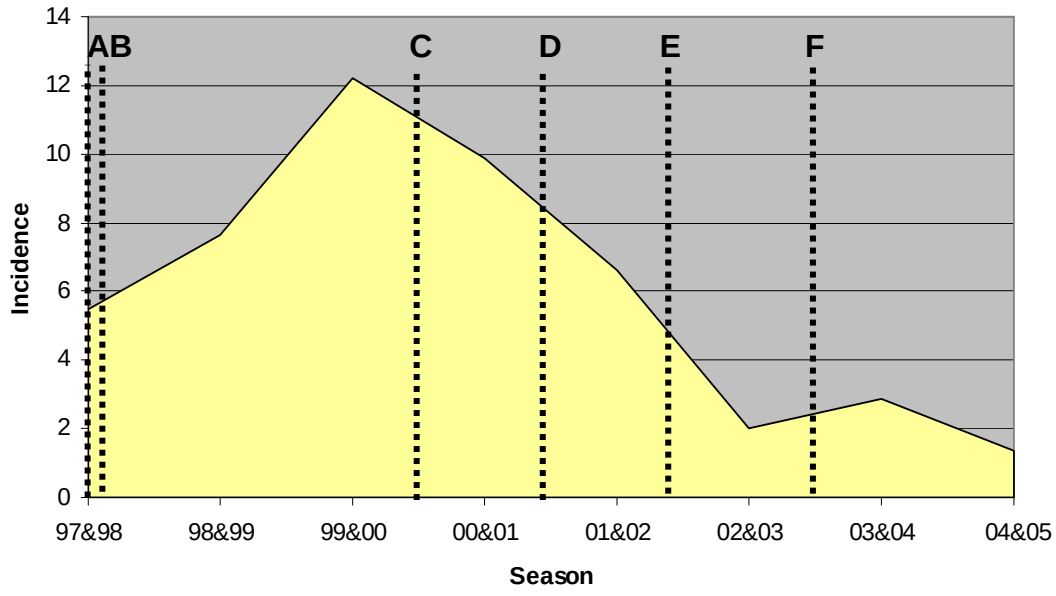
are making a significant contribution to the renaissance in control initiatives such as Roll Back Malaria (RBM) (Guyatt & Snow, 2002; Rowland *et al.*, 1999).

In Mpumalanga ITNs are only used as a supplementary intervention during epidemic situations. The distribution of ITNs followed the 1999/2000 epidemic season. A case control study conducted during 2005 shed light on the role of ITNs in an area traditionally not utilizing ITNs as a major personal protection measure (Govere *et al.*, 2000a).

Major interventions are overlaid by malaria incidence to visually illustrate the time of introduction and temporal trends of malaria incidence (Fig. 2.17).

The analysis of malaria mortality and morbidity data simplified the stratification of malaria in Mpumalanga province and understanding the temporal and spatial variation patterns prompted questions regarding significant contribution factors and will in future guide further intervention and initiatives. Financial and human resources for malaria are limited. Effective monitoring and evaluation as well as stratification of risk by utilizing malaria information systems, including GIS, can facilitate focused service delivery where most needed (Ceccato *et al.*, 2007). Advocacy mapping to management has made the decision making process easier and transformed data into visual and transparent information.

Figure 2.17 Malaria case incidence per 1,000 population, 1997/1998 to 2004/2005 season and malaria control intervention changes



A. Introduction of sulphadoxine-pyrimethamine as first line treatment; B. Use of rapid immunochromatographic card test for diagnosis C. Commencement of residual spray activities in southern Mozambique; D. Reintroduction of DDT in Mpumalanga; E. Introducing ITNs in high risk towns F. First use of combination therapy as first line treatment.

CHAPTER 3

3. Development and use of a computerized management system for malaria intervention monitoring

3.1 Introduction

A computerized management system is a tool to collect relevant data for analysing performance and guiding action.

Malaria control programmes utilising indoor residual spraying are only effective if a high coverage of targeted structures is achieved and an insecticide that is effective against the specific mosquito vector is correctly applied. Ongoing monitoring of spraying operations is essential to assure optimal programme performance and early corrective action, where indicated.

In 1946, South Africa introduced intradomiciliary spraying with residual insecticides, DDT (dichlorodiphenyltrichloroethane) and BHC (Benzene hexachloride), to kill indoor-resting vector mosquitoes and thereby control malaria (Sharp *et al.*, 1988). This resulted in a 75 percent reduction in the geographic extent of the malaria-affected area, with malaria occurrence limited to summer epidemics in the low-lying northern and eastern border areas with Botswana, Zimbabwe, Swaziland and Mozambique (Le Sueur *et al.*, 1996; Sharp *et al.*, 2001). Similar malaria control programmes were initiated in other southern African countries. In Mozambique, spraying operations for malaria control collapsed during the 1970s due to a protracted civil war with a resulting high burden of endemic malaria throughout the country (Scahwalbach & de la Maza, 1985). During the last decade of the 20th century there was a resurgence of malaria

in southern Africa, attributed to a number of factors, including parasite drug-resistance, mosquito insecticide-resistance, climate changes and large-scale population migration (Durrheim *et al.*, 1999b; Sharp *et al.*, 2001). The HIV/AIDS epidemic resulted in a simultaneous dwindling of resources available for other public health programmes, thus placing an onus on programme managers to ensure optimal efficiency of their activities.

An efficient spraying programme is characterized by application of the correct volumes of insecticide on surfaces suitable for mosquito resting (Pampana, 1969). This should be achieved before the onset of peak malaria transmission with a high coverage of targeted structures. A formal spraying management system was introduced in South Africa for the first time in 1973, with activity forms being completed by the field officials responsible for each spraying team and a "hut-card" left under the eave of each sprayed dwelling. This was expanded to a set of seven different spraying record forms in 1975 under the auspices of the World Health Organization (Fig. 3.1). The spray operator record was completed by the individual spray operator after completion of spray activities at each targeted household. The number of structures/rooms sprayed, insecticide used, number of can refills, and number of structures left unsprayed were recorded with simple marking with crosses. Locality/village/town name, operator name and date of spray activity were also captured on the card. The cards were submitted to team leaders after the completion of daily spray activities. The team leader aggregated daily spray data to produce a daily spray-team report, a weekly report, a monthly report and a locality completion report. These reports were collected by the respective field manager who subsequently produced summarized weekly,

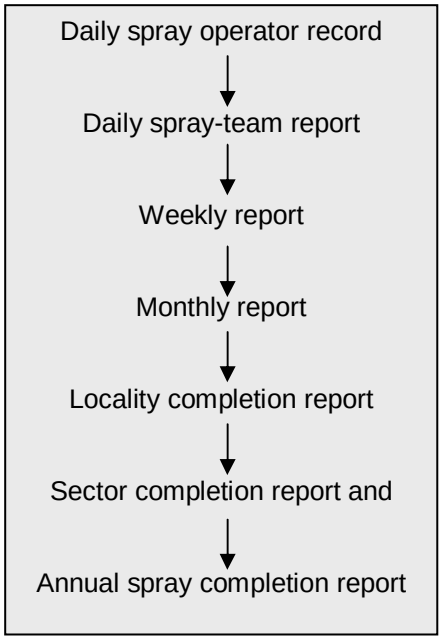
monthly as well as sector reports. Programme managers then collated data to produce annual spray completion reports. Although this manual system was cumbersome it became entrenched, and remained essentially unaltered in South Africa for more than 20 years. A major flaw of this data system was that field staff did not use the data for programme monitoring. Data was merely collected for statistical purposes. Thus serious programme deficiencies usually only became apparent at the end of the spraying season when the data were centrally analyzed. This resulted in missed opportunities for immediate corrective action.

In response to financial pressures, an ageing workforce and the seasonal nature of most malaria programme activities, during 1998, Mpumalanga province began to replace permanently employed spray personnel with temporary spray personnel recruited from each malaria-affected community. One hundred community based spray personnel were appointed, each accountable to their local community, and the provincial spray team was responsible for spraying almost 170,000 structures during each annual spraying round. With supervisory support limited to one field manager and six field officers, it was postulated that unless an improved spraying management system was introduced, programme performance and efficiency might deteriorate.

A novel computerised management system was developed in Mpumalanga province to enable provincial malaria programme management and local field supervisors to monitor, even on a daily basis when required, spraying coverage, individual spray operator's performance, and insecticide consumption and application rates. Use of the computerized management system commenced during 2000 during the first round of spraying (Booman *et al.*, 2000). Bioko island

(Sharp *et al.*, 2007a) and Ghana in west Africa soon followed suit and implemented a similar system (Coetzee *et al.*, 2006; Sharp *et al.*, 2007b). This chapter describes the structure and components of the computerised management system and provides operational evidence of its value in Mpumalanga province where it was first developed and implemented and refer to it's subsequent use in southern Mozambique malaria control programme as part of a trilateral agreement to control malaria across borders. Indoor residual spraying remains the mainstay of control interventions in Mpumalanga and the management of other complimentary interventions such as the use of impregnated treated nets and focal larviciding is not discussed here.

Figure 3.1. List of paper based spray data capture forms, 1975 to 1998



3.2 Methods

3.2.1 Spray cards and forms

Two of the original hard copy data collection forms, the SP1 spray operator card (Appendix A) and SP2 daily summary spray record (Appendix B),

were revised and edited to form the basis of the computerized management and monitoring system for spray activities. The SP2 form were compiled by the team leaders from the SP1 cards and submitted weekly to the district office where field managers scrutinized forms for data quality and submitted the records for data capture. The SP1 card and SP2 form were translated into local languages for individual country use in the new millennium.

3.2.2 Database design and data capture

Access 97 (version 9.0.2, Microsoft®, Redmond, Washington, United States) was the original front-end data entry, storage and retrieval software selected. The data entry screen mirrored the manually completed daily spray form (SP2), that collated data from the daily spray cards (SP1), submitted each week by team leaders to their field managers and after data verification this was entered into the computerized spray system. Additional functionality for event procedures was achieved by adding visual basic script.

The stand alone computerized management system was replaced by Microsoft SQL Server 2000 software (Microsoft® SQL Server™, Redmond, Washington, United States), a relational database management solution during the 2005/2006 malaria season in Mpumalanga province. The main reasons for this change were improved data storage, retrieval, a server based sharing platform and a web interface. This system was the first of its kind in an African public health programme to monitor and evaluate malaria vector control. As it integrated with defined intervention methods it serves as a good model of the integrated approach. A database switchboard was designed to navigate the user to the appropriate database window (Fig 3.2). Three primary functions are available: data entry;

view, print or export reports as table summaries, graphs or maps and maintain the database tables. Data entry is the front end application of the system to add spray data. Static reports with user defined functions such as dates, specific seasons, areas of spraying or spray operator names are included for reporting purposes. The maintenance function allows for restricted access to change fields within the look-up tables e.g. insecticide formulation, locality/town name and sector names.

The switch board form opened in a maximized mode as the spray database application was requested.

A customised digital form was designed for data entry. The form mimicked the SP2 hard copy daily spray form (Fig. 3.3). Auto generated fields and drop down menus limited data entry mistakes. Month, year and season was generated from spray date and locality name, sector and spray area were generated from the locality/village/town ID selected. The entry date and record number were auto generated ensuring no human error during entry. Each record had a unique reference number. The unique locality, sector and area codes facilitated a relational design allowing for a vector based spatial platform to be added.

Data entry commenced after intensive training on all spray activities, data verification, accurate data entry and archiving of forms. A supervised data entry clerk was responsible to enter all SP2 forms and produce reports when required.

3.2.3 Data retrieval and query tools

Data retrieval tools were developed using customised Access queries. For queries to function optimally, relationships amongst tables were created (see schema of all table interactions - Fig 3.4). Lookup tables had a one to many relationship as defined by primary keys in the table design view.

Preset queries, to generate standardized management reports, were designed in partnership with field supervisors and programme management staff to meet their specific needs. However, the system was designed to allow user-friendly production of customized additional reports where required.

Figure 3.2 Spray database navigation switchboard window

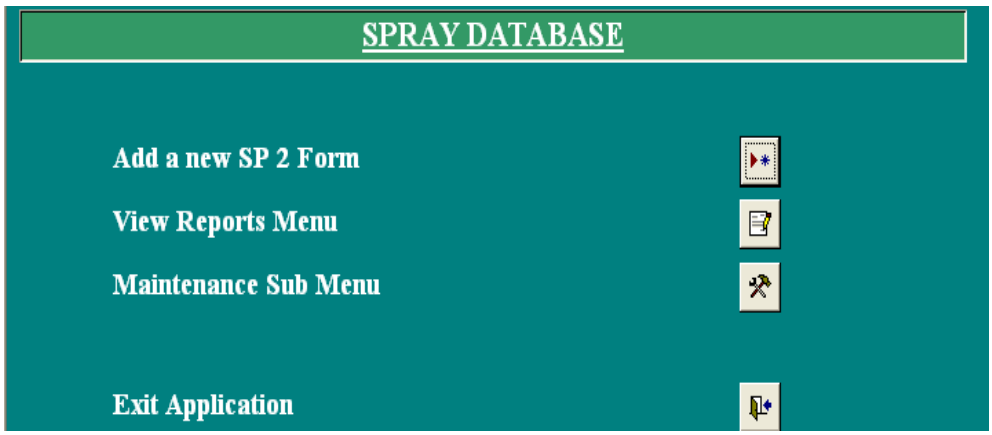
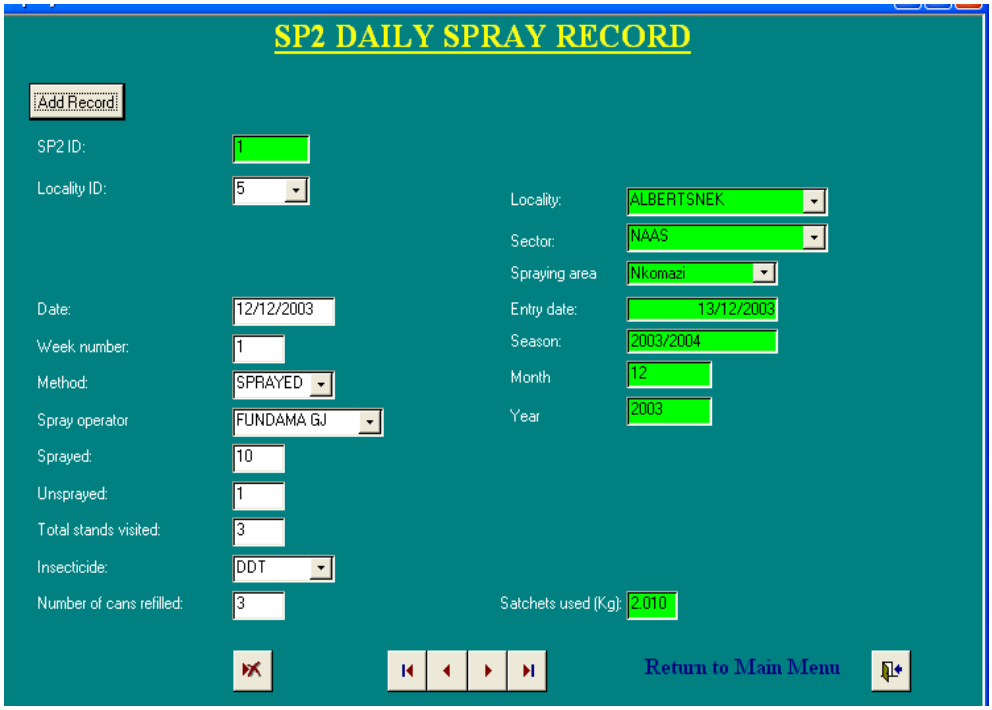


Figure 3.3 SP2 data entry window



Specific training was provided for programme supervisors on making sense of data and interpreting reports. A major emphasis during training was on identifying operational problems and implementing timely remedial action. As field managers entered the summary data on a weekly basis, necessary remedial action was taken within a week.

Static reports were developed and a selection list made available for the user (Fig. 3.5). Criteria for the report range included (Fig. 3.6): start and end dates; week number; locality name; sector name; insecticide name; malaria season and spray operator name.

Table 3.1 SP2 table, field names and descriptions

SP2 Table	Description
SP2ID	Unique record number
Locality ID	Unique locality/town/village code
Locality	Locality/town/village name
Sector	Unique spray area (locality areas combined)*
Spraying area	Municipal spray areas*
Date	Date of spray activities
Month	Month of spray activities
Year	Year of spray activities
Entry date	Data of data entry
Season	Malaria season of spray activities
Week number	Progressive week of spaying in a locality
Method	First spray attempt method = “sprayed” or return after unsprayed status due to locked structures method = “mop-up”
Spray operator	Name of spray operator
Sprayed	Total number of structures sprayed
Unsprayed	The number of structures unsprayed
Total stands visited	Total number of stands visited
Insecticide	Name of insecticide used for spraying
Number of cans refilled	Total amount of times the spray can was refilled
Sachets used	Total amount of insecticide used in kilograms according to number of cans refilled

***Sector – combination of localities/towns/villages to constitute an operational spray sector with a spray team allocated to each sector and a field team supervisor appointed.**
Spraying area – the specific municipal area where the locality/town/village is situated.
A locality/town/village targeted for spray activities can be part of a spray sector and spray area for reporting purposes

Figure 3.4 Entity relationship diagram

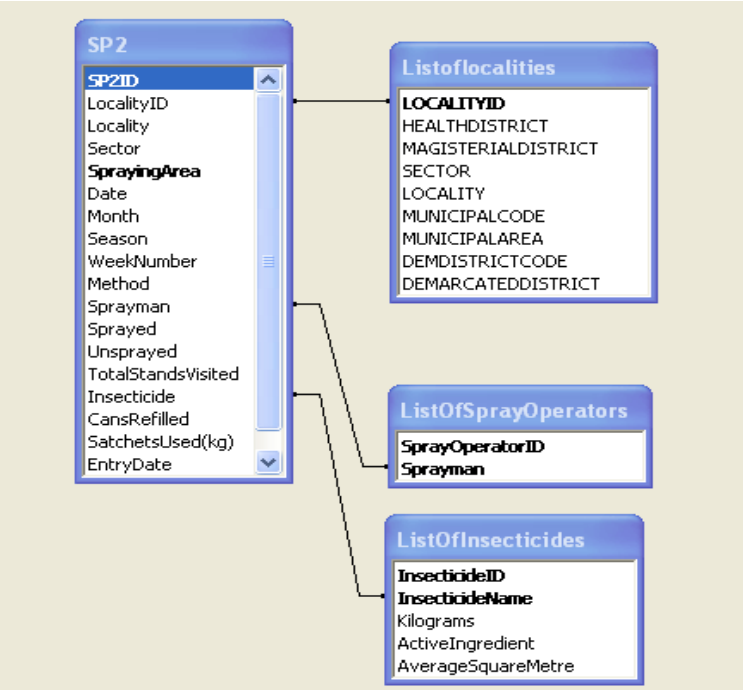


Figure 3.5 Reports list database window

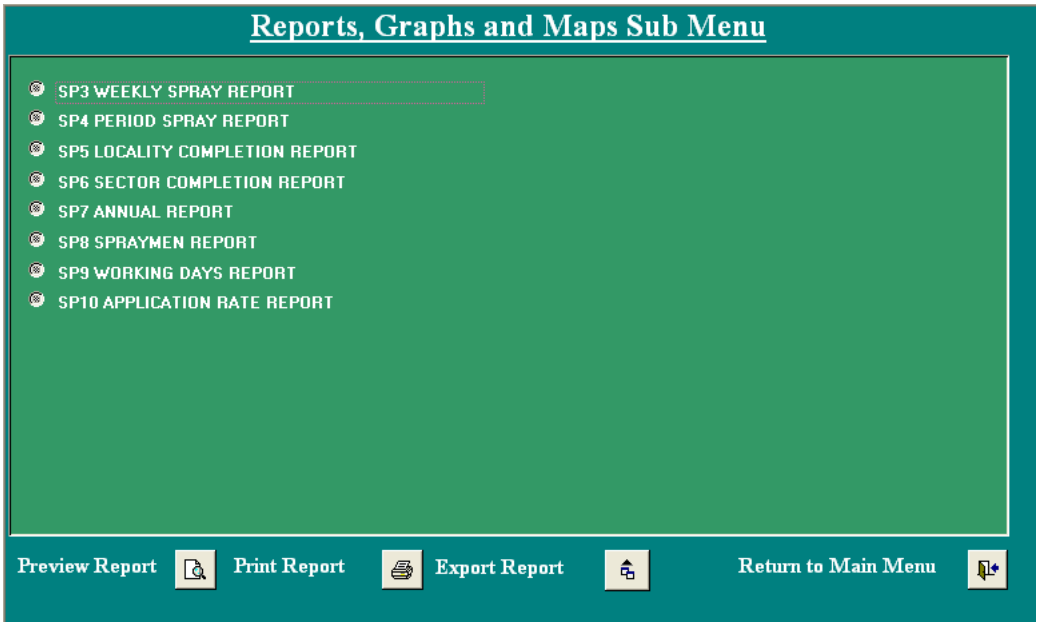
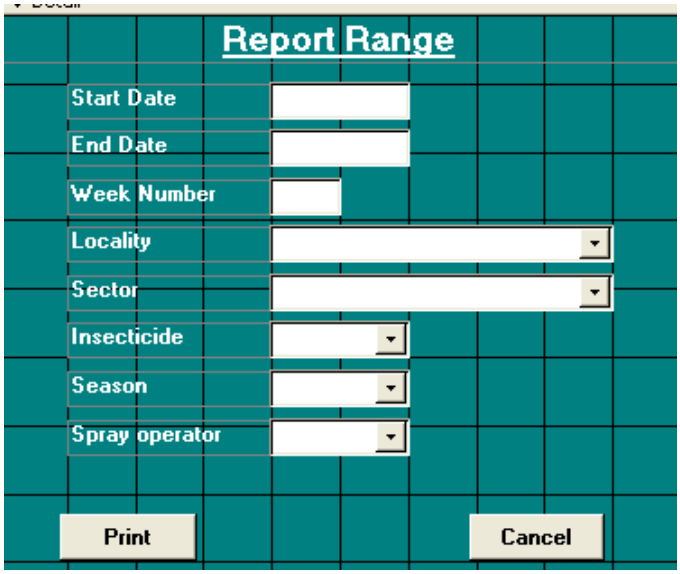


Figure 3.6 Report range database window



3.2.3 Spatial platform

Demarcated spatial maps at a scale of 1:250 000 were acquired from a private cartography company, NetGroup, Pty (Ltd) South Africa. The maps included all demarcated boundaries of municipal as well as locality/town/village boundaries. Maps were originally produced by digitizing aerial photographs of the area in 1998. Geomedia software (Symmetry Systems Inc., New York, USA) was used to convert the images to MapInfo (version 6.4, MapInfo Corporation, New York, USA) format. Map updates were supplied every two years. Unique sector boundaries were digitized on screen and locality positions used as spatial references. The spray sectors were saved as a separate geo-referenced layer for mapping spray activities and tracking progress. Each sector was an operational working boundary for spray teams and field supervisors to better manage the workload.

Maps of southern Mozambique at a scale of scale 1:250 000 were obtained from the Direcção Nacional de Geografia eCadastro in Maputo. The South African Medical Research Council digitally captured relevant geographical and

cadastral features, including roads, rivers, towns and different administrative level boundaries. The smallest administrative unit boundaries at which data was captured (localities) were drawn onto local maps by the staff of the Mozambican Ministry of Health involved in the project and then digitally captured for inclusion in the GIS display.

The relational database allowed the production of spraying progress maps at all administrative as well as sector levels. The GIS software package MapInfo Professional® (version 6.4, MapInfo Corporation, New York, USA) was the mapping software selected and maps were produced as an option product from static reports.

3.2.4 Security and data backup

User password restricted access was assured to the computer housing the database. Additional passwords were allocated for data capture, data modification and system design changes.

In addition to data storage on the hard disk drive, data was automatically backed up after each day of data entry onto an external Zip drive and locked up in a steel cupboard in a separate building.

3.2.5 Data analysis

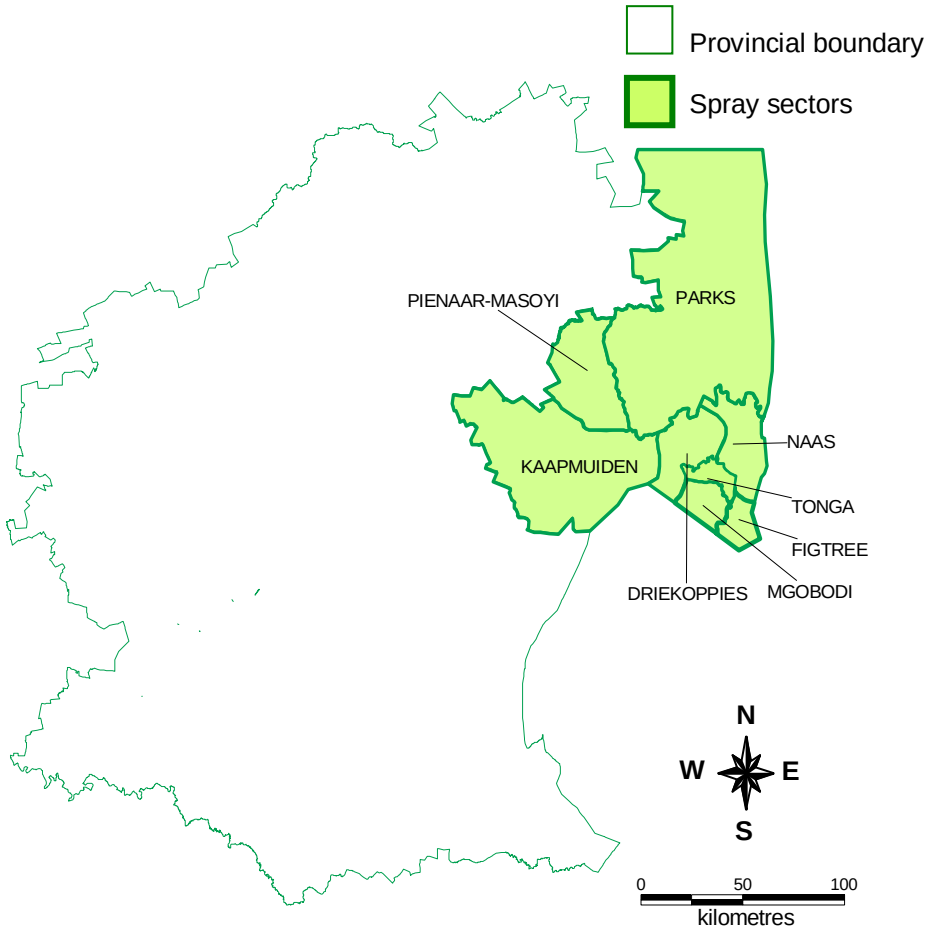
Descriptive data for spray activities from the 1999/2000 to 2005/2006 seasons were included in the analysis and presented as graphs, tables and maps. The Kruskal-Wallis Chi-square test was used to perform one-way analysis of variance. Regression analysis was used to investigate the relationship between coverage rates and incidence for the three spray areas as well as productivity measures and the actual number of spray operators utilized.

Operational use of the system is described with examples from Mpumalanga province and when specifically mentioned, southern Mozambique.

3.2.6 Intervention area

Residual indoor spraying is mainly confined to the north eastern part of Mpumalanga province and includes eight spray sectors (Fig.3.7). Each sector has a spray team allocated to the area and a field team supervisor. Teams differ in size ranging from 17 for Kaapmuiden sector to 81 spray operators for Naas sector. Spray sectors are operational spray boundaries and do not follow municipal demarcation.

Figure 3.7 Mpumalanga provincial boundary including spray sector boundaries



The area targeted for spraying in southern Mozambique during the initial deployment of interventions included the rural districts of Namaacha and Matutuine, and sections of the peri-urban districts of Matola and Boane in Maputo Province, covering an area of 7,962 square kilometres with an estimated 200,000 homes.

3.3 Results and use of the management information system

3.3.1 Comparing spray activity data from the 1999/2000 to 2005/2006 seasons for Mpumalanga province and where indicated southern Mozambique

There was variation in number of structures sprayed, unsprayed, spray coverage and total number of structures targeted by year (Table 3.2).

The targeted and sprayed structures for the 2000/2001 season were the highest of all seasons. This season followed the epidemic in 1999/2000 and increased intervention resulted from intense advocacy for improved control and renewed efforts for accurate recordkeeping. Number of sprayed structured fluctuated over the following years.

Table 3.2 Spray data for structures sprayed, 1999/2000 – 2005/2006 seasons

Season	Number of structures sprayed	Number of structures unsprayed	Number of structures targeted	Coverage rate (%)
1999/2000	107 988	31 980	139 968	77
2000/2001	197 606	42 537	240 143	82
2001/2002	168 400	31 016	199 416	84
2002/2003	154 070	24 415	178 485	86
2003/2004	170 262	46 026	216 288	79
2004/2005	155 644	49 318	204 962	76
2005/2006	167420	64 813	232 233	72

Coverage rates ranged from 72 % during the 2005/2006 season to 86% for 2002/2003 but no significant change in coverage was found over seasons (Kruskal-Wallis, χ^2 =9.66, degrees of freedom=6, P=0.139) and by municipal area (Kruskal-Wallis, χ^2 =5.43, degrees of freedom=2, P=0.06).

Recurrent coverage rates lower than 80% prompted the introduction of a monitoring system to determine possible reasons for low coverage. Reasons could include refusal or locked structures. This coverage monitoring system was formally incorporated in the computerized system during the 2005/2006 season and addressed the concerns raised. Unpublished data showed 98% of unsprayed structures being locked and unoccupied for most of the season (Coleman, 2006).

Coverage and incidence for the three municipal spray areas were poorly correlated. A regression line to show the best representation of data for incidence and coverage revealed poor linearity for all municipal areas (Fig 3.8). Coverage alone could not predict variability of incidence. It can be hypothesized that in low endemicity areas fluctuation in coverage below that of 80% but not lower than 70% is alone not the driving predictor for variation of malaria incidence and this deserves further specific study.

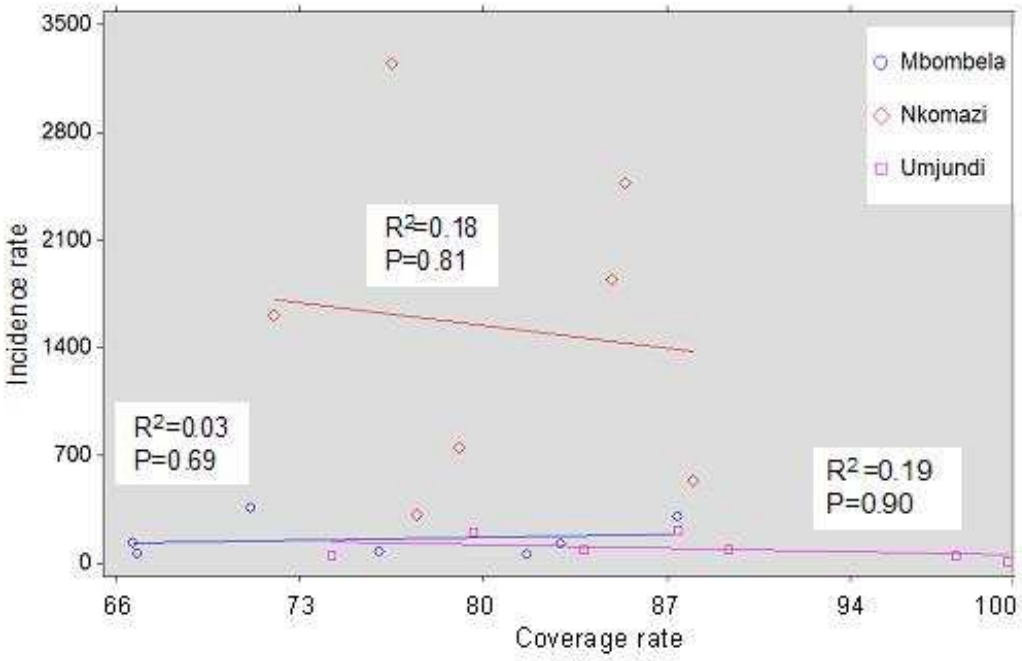
Over the seven seasons 44% (n=498 398) of all structures were sprayed with DDT and 66% (n=622 992) with deltamethrin insecticide. DDT was not in use during the 1999/2000 season.

In southern Mozambique, spray coverage during the first round of spraying in 2000 exceeded 90% of 222,000 structures, a level that is considered more than adequate (World Health Organization 1996). In areas where the management system repeatedly identified lower coverage than expected (80%),

investigations were conducted to determine whether this was the result of diminished community support, absenteeism of people in the household or poor motivation of the specific spray operator.

Human resources to spray targeted structures ranged from 72 operators (1999/2000 season) to 158 (2004/2005) (Table 3.3). Appointment of temporary staff was dependant on financial resource allocation for malaria programme activities.

Figure 3.8 Scatter plot to show linear association between incidence rate per 10 000 population and coverage rate (%) per municipal area, 1999-2000 to 2005/2006 seasons



Number of days utilized to complete spray activities over the seven season period ranged from 112 days (1999/2000 season) to 164 days (2001/2002 season) and structures sprayed per day from 964 (1999/2000) to 1185 (2002/2003) (Table 3.3). When structures per day for each season were divided by the actual

manpower the structures per day sprayed per operator ranged from 7 to 13 structures (CI = 6.90 – 11.78).

Maps depicting the progress achieved by each team provided useful information to malaria control programme management for tracking teams' progress, providing ongoing updates to senior health management and encouraging spray personnel to attain their target (Figs. 3.9, 3.10). The focus of spray activities in the highest risk areas bordering Mozambique is depicted (Fig.3.9)

Figure 3.9 Spraying progress map by sector, 2005/2006 season, Mpumalanga province

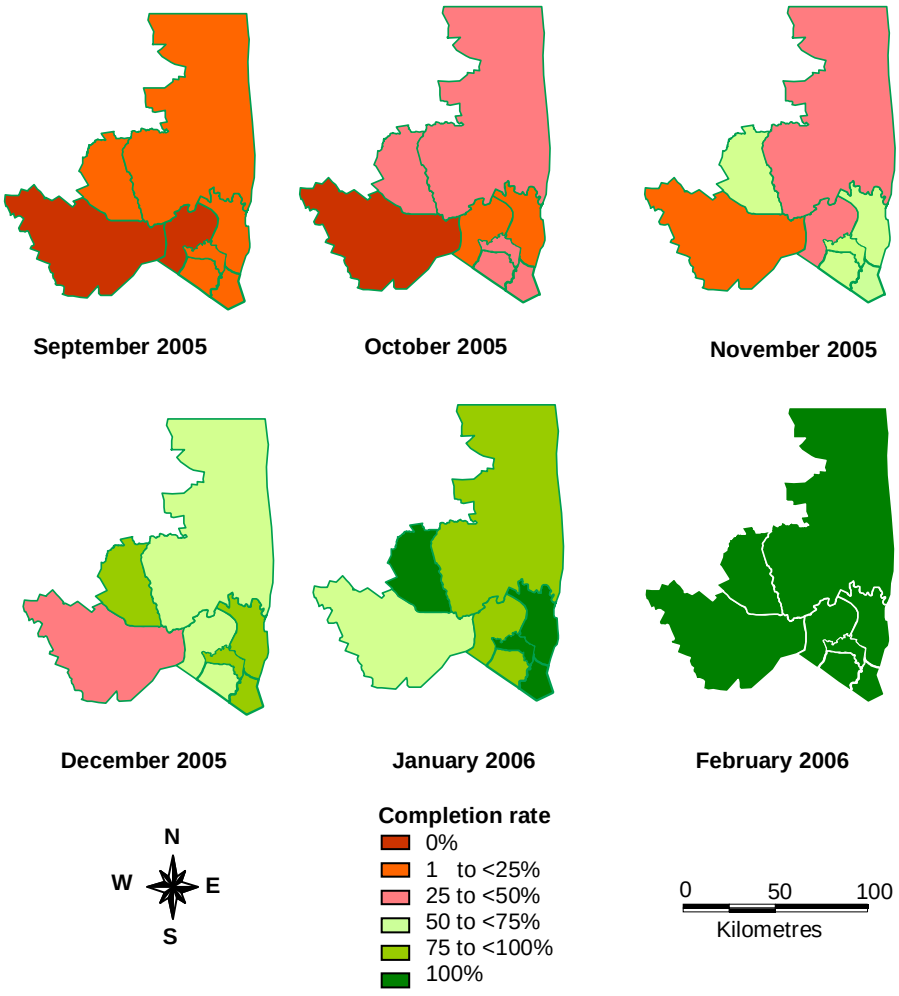


Table 3.3 Productivity results for spray activities, 1999/2000 – 2005/2006 seasons

Season	Number of spray operators utilized	Number of days utilized to spray structures	Number of structures sprayed	Structures sprayed per day (number of structures / days)
1999/2000	72	112	107 988	964
2000/2001	107	143	197 606	1 381
2001/2002	131	164	168 400	1 026
2002/2003	138	130	154 070	1 185
2003/2004	146	148	170 262	1 150
2004/2005	158	137	155 644	1 136
2005/2006	150	147	167 420	1 138

An additional benefit was that data captured during the first spray round in southern Mozambique during 2000 was used to verify official data sources and provide actual household figures to replace official government estimates. This provided more precise information for malaria control planning and demographic data needed by other government agencies for planning.

Insecticide application rates (grams per square meter) are constantly monitored for under- and over-application. The recommended rate for DDT application for indoor house spraying on walls at a formulation of 75% is $2g/m^2$ (grams per square metre) and deltamethrin at a formulation of 25% is 20 mg/m^2 (milligrams per square metre). An application rate ranging between 1 and 2 for DDT and 20 to 25 for deltamethrin is considered acceptable (Schofield, 2001; World Health Organization, 1996, 2006).

Under-application reduces insecticide residual activity and thus effectiveness, while over-application is wasteful. Where sub-optimal application rates were detected, investigations included scrutiny of insecticide preparation,

nozzle condition, application pressure, distance of nozzle tip from sprayed surface, and spraying rhythm.

The type of insecticide used had a significant association with the compliance to acceptable application rates (Kruskal-Wallis, χ^2 =31.12, degrees of freedom=1, P=0.000). The use of DDT insecticide yielded rates far better than the application of deltamethrin. Only the Parks sector had under application (lower than 1g/m^2) for DDT and this practice was noticed in the 2005/2006 season.

Figtree sector demonstrated the most consistent ideal application rate over time when including both insecticides (Fig. 3.11, 3.12).

Under-application becoming more common and more widespread by time with the use of deltamethrin and only the Kaapmuiden sector showed over-application (2004/2005). Application rates as categorized as over application, under application or recommended application was significantly different over seasons (Kruskal-Wallis, χ^2 =15.98 , degrees of freedom=6, P=0.01) and between the two insecticides (Kruskal-Wallis, χ^2 =16.39, degrees of freedom=1, P=0.0001).

The success of this computerised management system resulted in it being extended to neighbouring Swaziland and southern Mozambique where a malaria vector control programme was re-introduced and strengthened through the multilateral Lubombo Spatial Development Initiative (LSDI), a partnership between the governments of Mozambique, Swaziland and South Africa.

Figure 3.10 Example of a spraying progress map by town, Zone 1, first round spraying, southern Mozambique, 2000

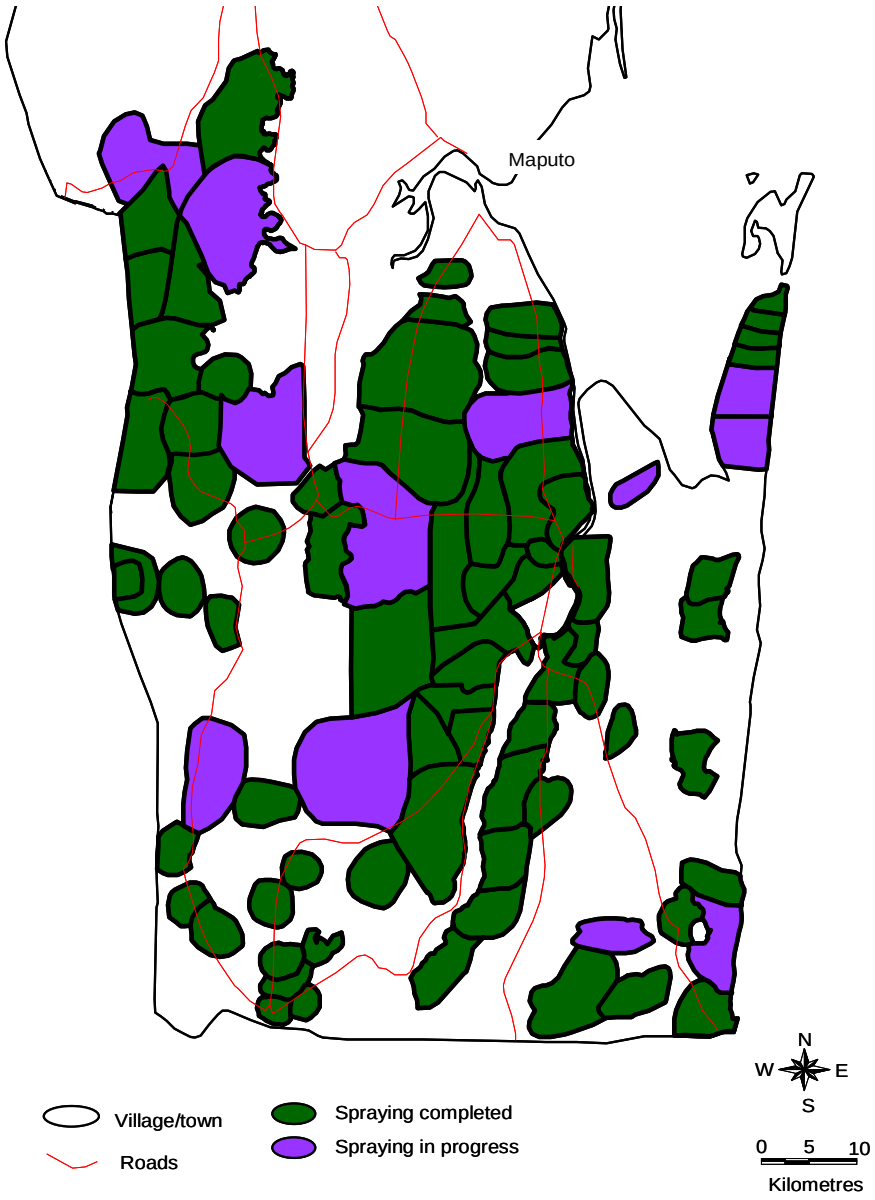


Figure 3.11 DDT insecticide application rate by season, 2000/2001_2005/2006 seasons

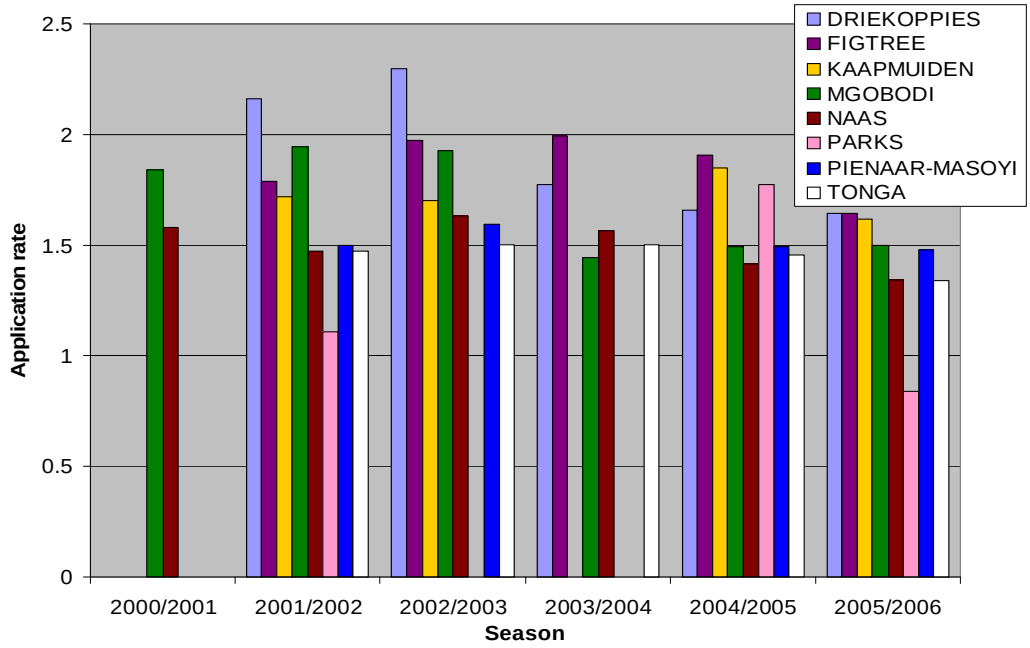
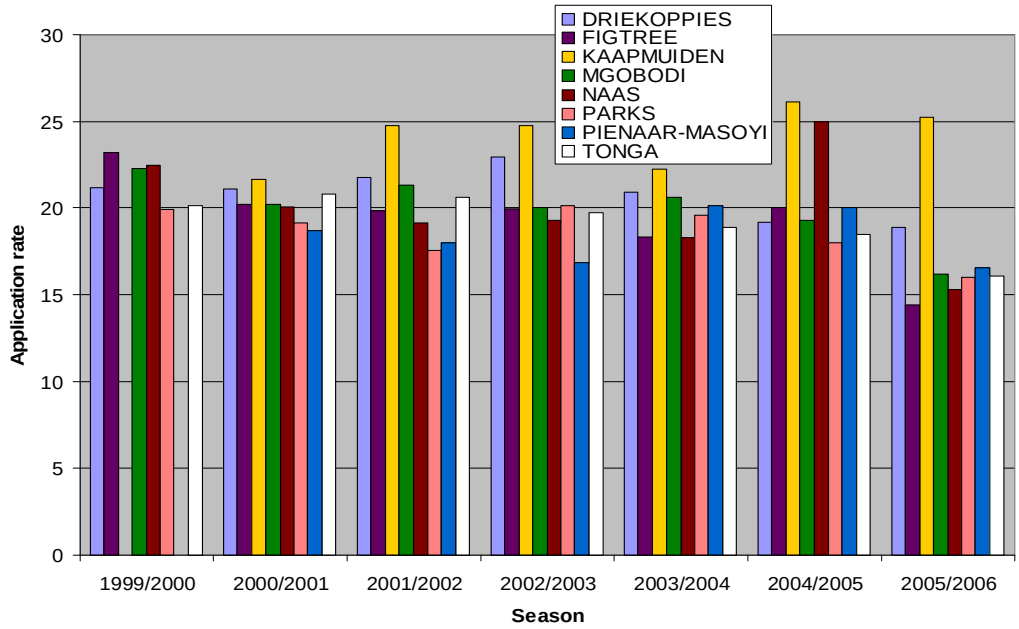


Figure 3.12 Deltamethrin insecticide application rate by season, 1999-2000 – 2005/2006 seasons



3.4 Discussion

The computerized management system to monitor residual indoor spraying in Mpumalanga province was unique in its design and application and the first to

be operationally adopted within a malaria surveillance system . The system has been adapted for other malaria programmes in South Africa and became an integral part of the success of the Lubombo Spatial Development Initiative and in addition covered Swaziland and Mozambique malaria control programmes (Sharp *et al.*, 2007a).

Bioko Island, Equatorial Guinea commenced spray operations in February 2004 in a quest to lessen the burden of disease in the area. The system developed and piloted in Mpumalanga province was implemented with minor adaptations to cater for country specific needs. The monitoring of indoor residual spraying coupled with entomological surveillance highlighted the efficacy and resistance challenges of the insecticide used prompting the change to a more efficient chemical for control of malaria vectors (Sharp *et al.*, 2007b). Continuous use of insecticides without monitoring may lead to wasteful application and no impact on disease incidence.

Private sector companies have accepted the challenge of improving community health in areas of mining operations and reaping the benefits of a healthier workforce. As IRS is recognised as an expensive intervention that warrants continuous monitoring to ensure cost effective application and timely progress the MIS has been adopted in a number of these initiatives (Teklehaimanot *et al.*, 2007). AngloGold Ashanti commenced vector control interventions during January 2006 in the Obuasi municipality, mine and surrounding villages in Ghana, west Africa. Monitoring of all spray activities was possible through the use of the computerized management system. During the first round 134 000 structures were sprayed. By November the same year a 50%

reduction in malaria cases were noted (AngloGold Ashanti, 2006; Coetzee *et al.*, 2006).

Competition for ever-dwindling public health resources is a major challenge for malaria control programmes in sub-Saharan Africa (Marsh, 1998; Nchinda, 1998). Constant monitoring and evaluation of spraying activities is obligatory where indoor residual spraying is an important component of malaria control, to ensure effective application and prevent wastage (Goodman *et al.*, 1999).

Not only has it supported a successful and cost-effective transition to a community-based spraying approach in several settings, but ensured that spraying is completed to schedule (Harvard *et al.*, 2003). The system equipped management and field supervisors to monitor spraying coverage, insecticide consumption and application rates on an ongoing basis. The system supports the transition to community-based spraying, while monitoring insecticide application and spray completion according to schedule.

CHAPTER 4

4. Outbreak identification and response

This chapter has been accepted for publication in the *Malaria Journal.*

4.1 Introduction

It is estimated that 100 million people are at risk from malaria epidemics and the potential value of predicting malaria outbreaks and epidemics has been recognized (World Health Organization, 2000; World Health Organization and UNICEF, 2005). Epidemics generally refer to increases in disease in relatively large populations, while outbreaks are considered to be more focal in occurrence and often precede an epidemic by a number of weeks (Dirckx, 2006). Improved detection and response to malaria epidemics was included in the Abuja targets for rolling back malaria in Africa (World Health Organization, 2000). The implementation of malaria early warning systems are advocated by WHO with the goal of detecting and responding to outbreaks within two weeks (DaSilva *et al.*, 2004). Effective outbreak containment demands prompt recognition and reporting of an unexpected increase in malaria cases to those responsible for control activities (Teutsch, 1994). This is a challenge in under-resourced malaria-affected African regions where limited public health information systems exist (Hay *et al.*, 2003a). It is critical in these areas that tools to assist programmes and responses are successfully deployed at operational level (Tarekegn *et al.*, 2004).

Stable endemic malaria characterizes much of Africa, however the fringes of the malaria affected area and highland areas (e.g. in Kenya and Uganda) are prone to epidemics. Climatic variation, including El Niño events, have been associated with the occurrence of malaria epidemics in these fringe areas (Bouma

& van der Kaay, 1996; Mabaso *et al.*, 2007). Thus, the WHO malaria early warning system, which is climate based, is useful at regional level for alerting countries to a possible increased risk of malaria epidemics, although this has not been universally successful (Hay *et al.*, 2003a).

Malaria endemicity is not homogenous at country level. Complementary local systems are required to allow rapid redistribution of local resources to areas experiencing outbreaks. A number of complex models have been proposed to provide a local level warning based on climate, remote sensing models, syndromic surveillance and incidence patterns, (Faye *et al.*, 1998; Hay *et al.*, 2002; Najera, 1999; Pavlin, 2003; Tarekegn *et al.*, 2004) but their complexity suggests that successful and sustained programme level adoption will be challenging.

Malaria risk in Mpumalanga is relatively low compared to other hyper- and holoendemic areas of sub-Saharan Africa and thus immunity does not develop in the population at risk. This area has historically experienced malaria outbreaks and epidemics with attendant relatively high mortality (Durrheim *et al.*, 1998b; Govere *et al.*, 2000b). The introduction of definitive diagnosis using rapid diagnostic tests and mandatory reporting of cases made the development of a malaria incidence based outbreak identification system feasible (Durrheim *et al.*, 1998b; Durrheim *et al.*).

Successful local implementation of a health facility-based syndromic outbreak detection and response system suggested that a simple clinic based malaria outbreak detection and reporting system might be feasible if clinic staff were adequately trained, supported and appreciated the value of their contribution (Durrheim *et al.*, 2001).

This chapter describes the conceptualization and implementation of a three-tier malaria outbreak identification system using binomial thresholds to prompt early outbreak response and direct focal malaria control interventions. Retrospective data were used to compare the performance of the binomial threshold method to other currently recommended statistical approaches.

4.2 Methodology

4.2.1 Study region

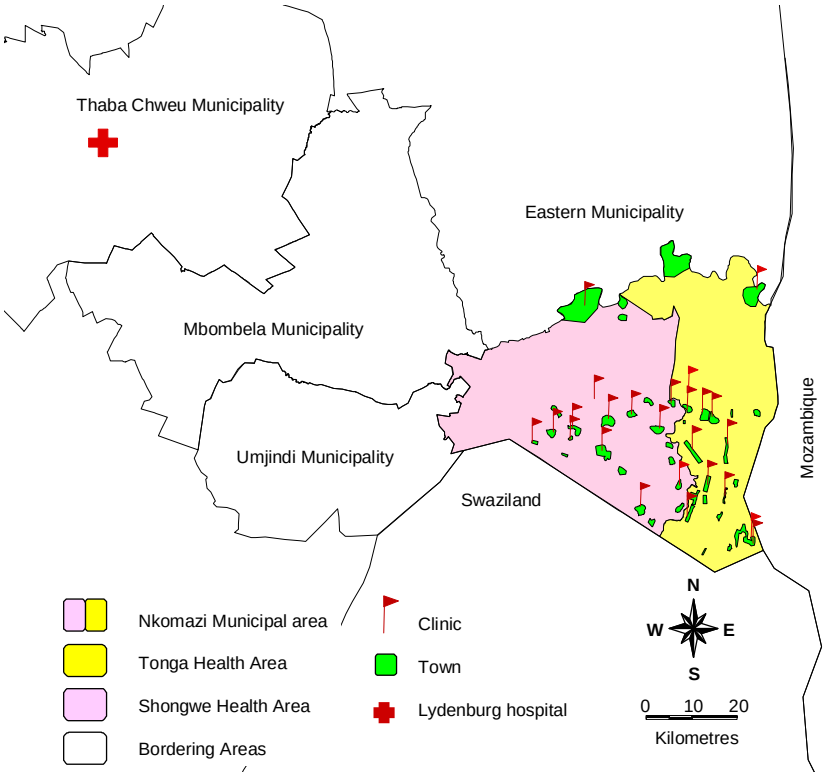
Twenty five health facilities and 42 town/villages in the highest risk Nkomazi municipal area in Mpumalanga province fully implemented the outbreak identification system in July 2005 (Fig. 4.1). Malaria is seasonal in this area with the high-risk period occurring from September to April, during the period of high humidity and rainfall. Estimated population at risk in this area is 380,000 (Statistics South Africa 2005).

4.2.2 Threshold calculation

The binomial exact calculation was used to determine individual thresholds for each health facility and town/villages by week (Sheynin, 1970). Exact confidence intervals (95% and 99%) were used to calculate level 1 and level 2 outbreak thresholds respectively. Town/village populations and catchments populations for each health facility were used to determine the denominator populations at risk of malaria (Mpumalanga Department of Health and Social Services, 2002). Expected cases were calculated from malaria notifications by facility and source of infection at town/village level by week for the previous five malaria seasons (July to June) using weightings derived during a nominal group

exercise. During a three round e-mail Delphi survey, eleven malaria experts from the South African Medical Research Council, World Health Organization, South African National Department of Health and Mpumalanga Provincial Department of Health provided their weighting and rationale for the differential proportional contribution of previous seasons in predicting the next season's total malaria notifications.

Figure 4.1 Clinics/hospital and towns/villages under outbreak surveillance in the Nkomazi and Thaba Chweu municipal areas, 2004/2005 –2005/2006, Ehlanzeni District, Mpumalanga province



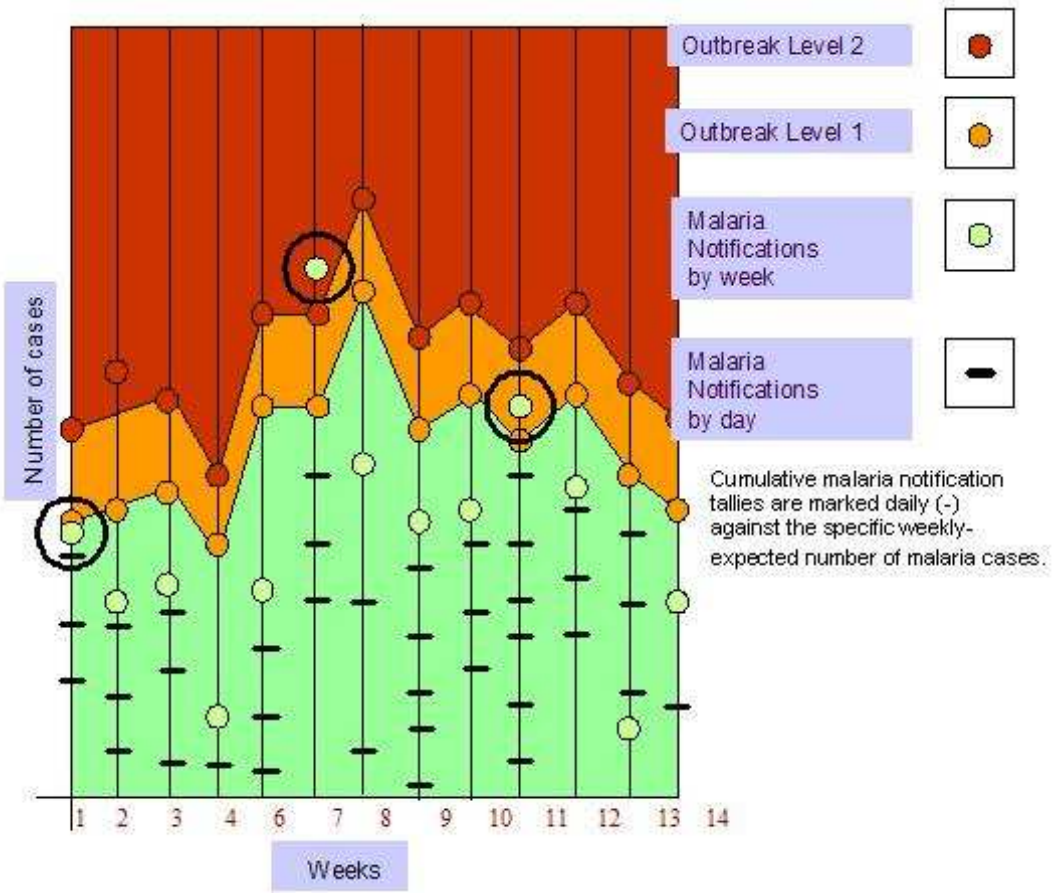
4.2.3 Description of the outbreak identification and response system

4.2.3.1 Tier 1

Charts with weekly bi-level outbreak thresholds were developed for each health facility allowing daily tallies of confirmed cases to be cumulatively charted against the weekly threshold (Fig.4.2). The mandatory paper notification forms

were also completed for each case. When outbreak level 1 or 2 thresholds were exceeded the malaria control programme (MCP) was notified by clinic staff and stock levels of malaria treatments and rapid diagnostic tests (RDTs) verified to ensure that adequate supplies were available for outbreak case management.

Figure 4.2 Example of the outbreak detection chart



4.2.3.2 Tier 2

MCP field staff received tables with the weekly thresholds pre-entered for each town/village within their area of responsibility (Table 4.1). Tallies were based on the most likely source of infection town/village as completed on each notification form from health facilities. Notified weekly town/village cases were compared to weekly thresholds.

Where thresholds were exceeded, field staff conducted home visits to confirm the likely source of infection and performed screening amongst individuals in the case household and neighbouring households. If a person was symptomatic, a RDT was performed and all individuals with positive RDTs were referred to the nearest health facility. Blood slides were taken from remaining household members and screened at the provincial malaria laboratory. All positive individuals were contacted and referred to health facilities for treatment within 48 hours. If level 1 or 2 outbreak thresholds were exceeded at town/village level, environmental assessment was conducted to identify local mosquito breeding sites (Braack *et al.*, 1994). Larviciding was performed as required and local coverage with indoor residual spraying (IRS) confirmed. If a level 2 outbreak threshold was exceeded for more than one successive week, additional IRS was considered in the town/village.

Table 4.1 Example of outbreak identification threshold table for field use

Kamhlushwa					
Week	**Date**	**Outbreak Level 1**	**Outbreak Level 2**	**Cases**	**Total weekly cases**
27	3/7/2006 - 9/7/2006	3	5	*I*	1
28	10/7/2006 - 16/7/2006	2	4	0	0
29	17/7/2006 - 23/7/2006	3	5	*II*	2

4.2.3.3 Tier 3

All malaria case information was entered into the malaria surveillance system within a week of notification and outbreak detection algorithms by source location (town/village) were automatically run as each case was entered. If either threshold was exceeded an email alert was automatically sent to the relevant MCP

staff members and their managers. This allowed performance monitoring of tier 2 responses.

4.2.4 Comparison

The binomial exact thresholds used in this identification system were retrospectively compared to the WHO recommended threshold mean +2 standard deviation (Najera, 1999; World Health Organization, 2001b) and the Centres for Disease Control and Prevention recommended cumulative sum (Hay *et al.*, 2002) during the 2003/2004 season when a local malaria outbreak was experienced.

Uptake and usefulness of the system was evaluated by administering a structured questionnaire after each implementation season (2004/2005 and 2005/2006) at all primary health care facilities. A season refers to the period July to June.

4.3 Results

In July 2004, the outbreak identification and response system was implemented in 12 primary health care facilities, 20 town/villages and then expanded in July 2005 to include 13 more health facilities and 22 town/villages in the Nkomazi municipal area (Figure 4.1).

During the 2004/2005 season a total of six outbreaks were reported from three (25%) health facilities. Only one (8.3%) level 2 outbreak was reported. All outbreaks were reported within 48 hours and occurred between August 2004 and January 2005 (Table 4.2).

Table 4.2 Malaria outbreaks by month, 2004/2005 season

	Level 1		Level 2	
Month	**Health facility**	**Locality/Town/Village**	**Health facility**	**Locality/Town/Village**
July	0	0	0	0
August	4	1	1	0
September	0	1	0	0
October	0	2	0	1
November	0	0	0	0
December	0	0	0	0
January	1	1	0	0
February	0	0	0	0
March	0	0	0	0
April	0	0	0	0
May	0	0	0	0
June	0	0	0	0
Total	**5**	**5**	**1**	**1**

Response by the malaria field staff occurred within 24 hours of reporting. No stock-outs of drugs or RDTs were experienced. In the same season five (22%) town/villages reported level 1 outbreaks, and one a level 2 outbreak, all between August 2004 and January 2005 (Table 4.2). Only one town/village experienced a level 1 outbreak at both health facility and town/village level simultaneously. All cases were followed up and epidemiological field investigations conducted by field staff identified four additional patients by testing neighbours of index cases. Fifteen breeding sites were identified and larviciding performed with an organophosphate.

During the 2005/2006 season, 107 outbreaks were identified from health facilities. Twenty (80%) and 11 (44%) health facilities reported level 1 and level 2 outbreaks respectively. This differed significantly when compared to the first season (P=0.0005; P=0.0163 respectively). All outbreaks were reported within 72 hours and the majority (n=91, 85%) within 24 hours. They occurred throughout the season (Table 4.3). Of the 77, level 1 outbreaks identified 30 (39%) became

level 2 outbreaks. Review of stock inventories and routine ordering indicated that health facilities would have exhausted malaria treatment and RDT stocks if there had been no warning and additional orders placed.

Table 4.3 Malaria outbreaks by month, 2005/2006 season

2005/2006				
	Level 1		Level 2	
Month	Health Facility	Town/village/Village	Health Facility	Town/village/Village
July	3	0	1	0
August	1	1	0	0
September	1	2	0	0
October	3	3	1	1
November	2	1	0	0
December	9	4	5	0
January	22	5	14	3
February	13	4	5	2
March	13	5	3	3
April	4	3	0	1
May	4	2	1	0
June	2	0	0	0
Total	**77**	**30**	**30**	**10**

In the same season 40 outbreaks were identified at town level between the months of August 2005 and May 2006 (Table 4.3). Nineteen (45%) town/villages reported outbreaks at level 1 and eight (19%) reported level 2 outbreaks. Focal larviciding was carried out in 27 town/villages where breeding sites were identified. Testing of neighbours of index cases identified 19 additional malaria cases. New cases were notified and referred to a primary health care facility for treatment.

The rapid response at tier 2 was verified by finding that 100% of email outbreak alerts (tier 3) were received after a response to an identified outbreak had already been initiated.

Outbreaks and response activities were verified by field managers and malaria information managers during weekly operational meetings and by provincial management at monthly MCP meetings.

The use and acceptance of the charts at health facilities was assessed using a structured questionnaire during site visits to all participating health facilities. Charts were available for viewing at all health facilities and all respondents indicated that the chart was useful, with the majority satisfied with the design (n=32, 86%). A total of 25 (68%) respondents claimed that the charts gave an awareness of malaria risk and 6 (16%) used the chart for regular stock orders of malaria treatment and RDT's (Table 4.4).

Table 4.4 Summary of health facility survey responses regarding the outbreak identification chart, 2004/2005 and 2005/2006 seasons, Tonga health area

Season	Question	Yes n (%)	No n (%)
2004/2005	**Chart available?**	13 (100)	0 (0)
2005/2006		26 (100)	0 (0)
2004/2005	**Chart complete?**	10 (77)	3 (23)
2005/2006		22 (85)	4 (15)
2004/2005	**Chart need to change?**	1 (8)	12 (92)
2005/2006		4 (15)	22 (85)
2004/2005	**Chart useful?**	13 (100)	0 (0)
2005/2006		26 (100)	0 (0)
2004/2005	**Rather prefer to use formulas to determine own thresholds?**	0 (0)	13 (100)
2005/2006		1 (4)	25 (96)

The outbreak identification thresholds were compared using retrospective case data from the 2003/2004 outbreak in Dindela town/village, Nkomazi municipal area. Comparisons were made between the WHO recommended mean +2 standard deviation (Najera, 1999; World Health Organization, 2001b), the

CDC recommended cumulative sum thresholds (Hay *et al.*, 2002) and the binomial thresholds method described above.

This particular period was selected as the seasonal malaria incidence rate for Dindela town was 25%, being the worst outbreak season recorded for a town in Mpumalanga Province (Mpumalanga Malaria Control Programme, 2005). No outbreak identification system was in existence at that time. The number of outbreak identifications for the specific season varied according to threshold tested: C-sum (n=32), mean +2 standard deviation (n=29), binomial outbreak level 1 (n=18) and level 2 (n=12). The number of false outbreaks (this being outside the 20 week outbreak period) detected by the different thresholds also varied. The binomial exact thresholds detected 1, C-sum 12 and the mean + 2 SD points 9. All except the binomial level 2 threshold identified the actual outbreak four weeks before occurrence.

The level 2 outbreak thresholds only detected the actual outbreak when it commenced.

4.4 Discussion

The binomial outbreak identification and response system provided rapid alerts to focal malaria increases that prompted targeted public health action in the high-risk malaria area of Mpumalanga province during the two seasons following introduction. The need for ensuring adequate diagnosis and prompt treatment is essential as the local population has no acquired immunity following five decades of malaria control that has limited malaria transmission to the summer months (Govere *et al.*, 2002; Mabuza *et al.*, 2001).

In southern Africa a number of countries have acknowledged their inability to implement the WHO recommended malaria early warning system despite its stated aim that it provides a simple and practical outbreak alert system (Hay *et al.,* 2003a). The primary goal of an outbreak surveillance system is to ensure timely recognition of abnormal levels of disease (Reingold, 1998). However, surveillance must be followed with a timely response or it becomes an academic exercise of limited value (Satcher, 1995). The Mpumalanga malaria control programme, in recognising the need for a malaria outbreak alert system, developed the tools described in this paper for supporting programme operations.

A climatic early warning system (Hay *et al.*, 2003b; Thomson *et al.*, 2000a; Thomson *et al.*, 2000b) with long lead times add limited value to Mpumalanga malaria control as extensive IRS is implemented annually. Simple models have been demonstrated to perform well in other areas (Abeku *et al.*, 2002). Reliable focal outbreak detection is possible in Mpumalanga because timely and good quality malaria notification data is available (Hay *et al.*, 2002).

In many malaria epidemic fringe areas the three tier binomial alert system could provide valuable intelligence to guide rapid public health action that could limit the extent and duration of outbreaks. It could ensure that there are adequate diagnostic and treatment supplies, provide ongoing monitoring of the performance of programme staff and guide focussed control activities.

It was encouraging to find that primary health care facilities embraced the system and recognized the additional benefit of utilising the charts for routine stock orders of malaria treatment and RDT's. This may ensure its sustainability.

Epidemiological methods including the WHO mean + 2 SD (Cullen *et al.*, 1984) and CDC's cumulative sum (Hay *et al.*, 2002) have previously been used for outbreak identification and response. Historical comparisons using data from a known epidemic period indicated limited concordance between the binomial thresholds and the C-sum [15] and mean + 2SD thresholds (Najera, 1999; World Health Organization, 2001b). The large number of false weekly outbreaks identified by the C-sum and mean + 2 SD thresholds during this retrospective analysis would likely make them impractical in the Mpumalanga situation as unnecessary and costly responses would be required by the MCP staff. Our findings compare to similar findings from an evaluation project in Kenya that questioned the operational validity of WHO thresholds (Hay *et al.*, 2002).

The computerized system, implemented as the third tier automatically calculated outbreak thresholds at the beginning of a malaria season. It also provided a timely quality monitoring mechanism for supervisors and managers to verify field operations.

The outbreak system described here was developed for a low malaria transmission setting and has direct application in other regions with a similar transmission pattern. These are expected to increase as a larger number of countries invest in enhanced malaria control and elimination. Current initiatives to control malaria with support from the Global Fund and President's Malaria Initiative are delivering success stories in malaria control including the Lubombo Spatial Development Initiative (Sharp *et al.*, 2007a) and Bioko programme in

Equatorial Guinea (Kleinschmidt *et al.*, 2006; Sharp *et al.*, 2007b). These will result in expansion of the zones where malaria endemicity is unstable with

increased need to identify and rapidly contain focal outbreaks. The binomial outbreak identification and response system piloted in Mpumalanga should be tested in these areas as it appears to provide early identification of malaria outbreaks that facilitate timely response to ensure that control gains are sustained.

CHAPTER 5

5. Using the SaTScan method to detect local malaria clusters for guiding malaria control

This chapter has been submitted for publication to the *Tropical Medicine and International Health* journal.

5.1 Introduction

In common with most infectious diseases, malaria is heterogeneous in its distribution in both time and space (Carter *et al.*, 2000; Gamage-Mendis *et al.*, 1991; Greenwood, 1989), and incidence can vary greatly between districts, villages and towns. The heterogeneity of malaria is affected by patterns of malaria vector distribution, human-vector contact, human host behavioural factors, house construction, and malaria prevention methods used (Gamage-Mendis *et al.*, 1991; Snow *et al.*, 1998a; Thomas & Lindsay, 2000; Thompson *et al.*, 1997; Trape et al., 1992).

Characterization of malaria heterogeneity may allow prioritization of risk areas to permit focusing of malaria control interventions at an operational level. The ability to identify localized malaria clusters in remote highland areas of east Africa facilitated early intervention in the absence of early warning systems, as these malaria "hotspots" remained constant in epidemic and non epidemic years (Ernst *et al.*, 2006).

A number of models have been developed for describing malaria spatial distribution and seasonality (Craig *et al.*, 1999; Hay *et al.*, 1998; Omumbo *et al.*, 1998; Tanser *et al.*, 2003a), transmission (Kleinschmidt *et al.*, 2000; Snow *et al.*, 1998b; Thomas & Lindsay, 2000; Yang *et al.*, 2002), mosquito distribution

(Kitron *et al.,* 1994; Linthicum *et al.*, 2003; Sithiprasasna *et al.*, 2003) and risk factors associated with malaria (Brooker *et al.*, 2004; Gemperli *et al.*, 2004; Hu *et al.*, 1998). However many malaria endemic environments are resource limited (Hay *et al.,* 2003a) and tools to assist decision support need to take account of these limitations.

The burden of malaria in Mpumalanga is relatively well described as definitive diagnosis using rapid diagnostic tests and mandatory reporting of malaria cases (Durrheim *et al.,* 1998b; Durrheim *et al.,* 2001) is universally practised in the public health system, which manages the vast majority of malaria cases. All confirmed malaria cases are entered into a malaria surveillance system.

SaTScan freeware was used to analyse malaria notification data from 2002-2005 to determine whether local clustering occurred that could direct local control efforts (Kulldorff & Information Management Services Inc, 2005)

5.2 Methodology

5.2.1 Study area

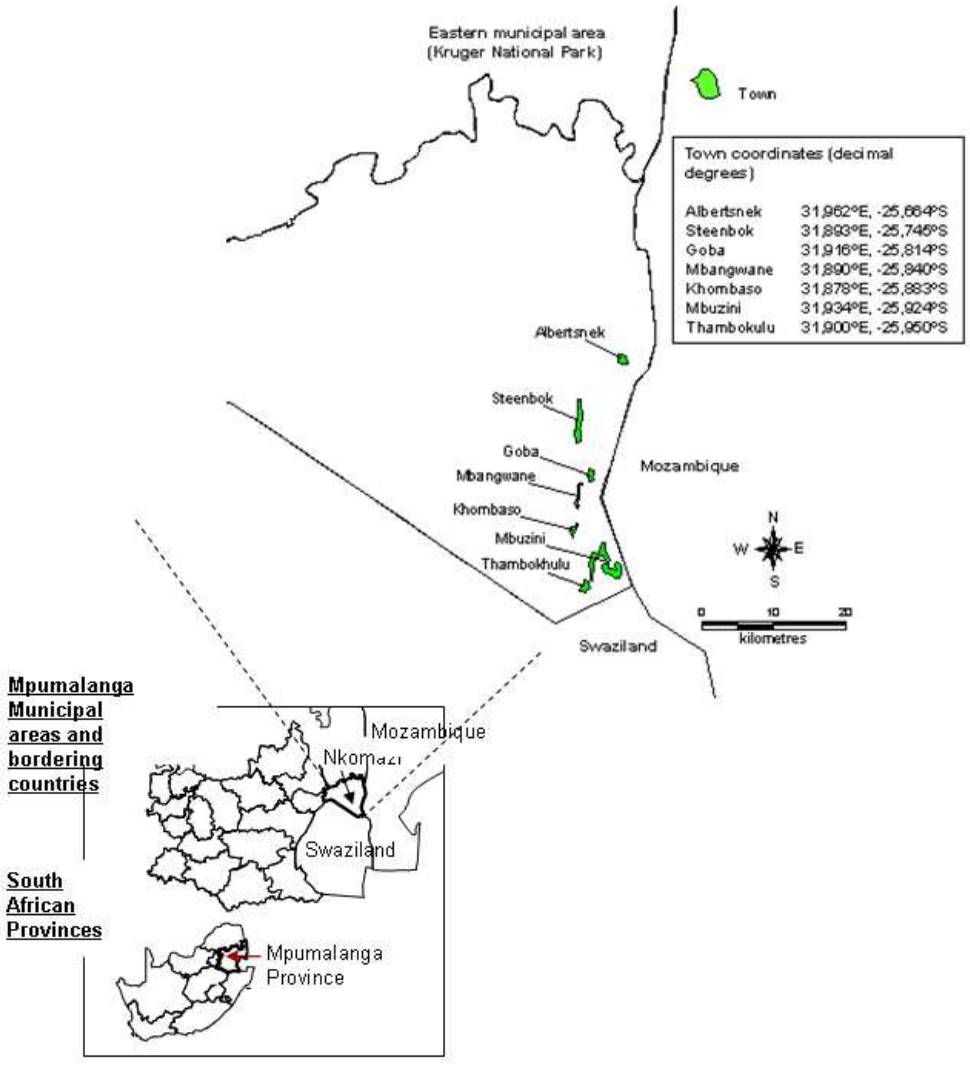
The area included the seven rural towns in Mpumalanga province South Africa close to the Mozambique and Swaziland borders (Figure 5.1), that are at relatively high malaria risk in a South African context (Booman *et al.*, 2000), with malaria incidence ranging from 30 to 61 per 1 000 persons between 1997 and 2005. Malaria is seasonal in South Africa, with almost all cases occurring between October and May.

Anopheles arabiensis is the main vector in the region. Vector control in the province is mainly by indoor residual spraying (IRS) with DDT on traditional

mud, unplastered and water based painted surfaces and a synthetic pyrethroid for enamel painted wall surfaces (Kager, 2002; Kapp, 2004; Manga *et al.*, 2004).

Original town maps produced in 2000 were upgraded from digitized aerial photographs produced in 2002 and updates converted into MapInfo version 6.4 files (MapInfo Corporation, New York, USA) with Geomedia software (Symmetry Systems Inc., New York, USA). Unique stand (household) numbers were allocated during the digitizing process. A stand may include one or many number of structures belonging to a family unit on a designated piece of land.

Figure 5.1. Location of the seven towns selected for detailed GIS surveillance, Nkomazi municipal area, Mpumalanga.



5.2.2 Active malaria case investigation

Malaria case investigators followed up all malaria cases in the specified towns as part of malaria control programme activities for the 2002/2003, 2003/2004 and 2004/2005 seasons. Following a definitive diagnosis of malaria at a health care facility, an investigator would identify the probable source of infection by confirming the travel history of the patient indicated on the notification.

5.2.3 Spatial and temporal clusters

SaTScan^{TM} software, version 5.1.3 using the Kulldorf method of retrospective space-time permutation and the Bernoulli purely spatial model (Kulldorf *et al.*, 1998; Kulldorff *et al.*, 2004) was used to identify malaria clusters in individual towns for the three seasons under investigation and over the combined time period. This method has previously been validated for plotting and understanding local malaria time-space cluster analysis (Boscoe *et al.*, 2003; Brooker *et al.*, 2004; Kulldorf, 1997; Nkhoma *et al.*, 2004; Odoi *et al.*, 2004). The circular scan statistic is isotropic with respect to the rotation of the geographical area (Kulldorf, 2005).

Observed cases in a cluster were compared to the distribution of expected cases if spatial and temporal locations of all cases were independent. The model adjusts for entirely spatial or entirely temporal clusters. With spatial adjustment time remained dormant and during the temporal analysis seasons were considered. The distribution and statistical significance of the clusters were identified by means of Monte Carlo replication of data sets under the null hypothesis. Replications were not less than 999 to ensure “excellent” power for defining

clusters (Kulldorf, 2005). Clusters were prioritized according to their statistical significance.

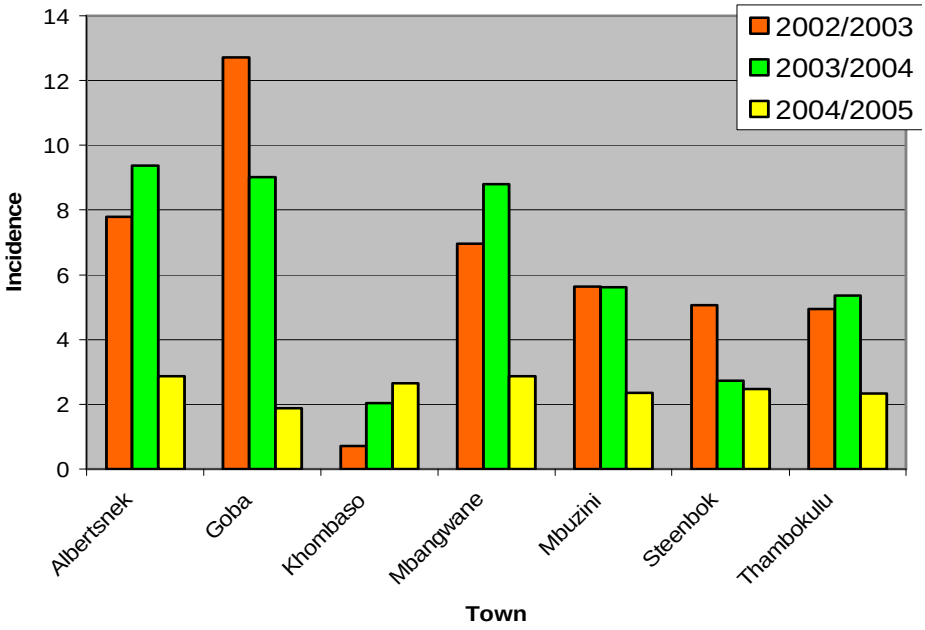
5.3 Results

5.3.1 Malaria incidence

Four hundred and twenty two malaria cases were notified during the three seasons from 341 stands (households) across the seven towns. No significant association was found between multiple case reporting at household level and season (χ^2 =0.435, degrees of freedom=2, P=0.805).

Malaria incidence differed significantly between the towns during the three seasons (χ^2 =6.442, degrees of freedom=6, P=0.040) (Fig. 5.2).

Figure 5.2. Malaria case incidence per 1,000 population by town, 2002/2003 – 2004/2005 seasons, Nkomazi municipal area



5.3.2 Case clustering

SaTScan analysis detected a number of clusters during the study period (Table 5.1).

Table 5.1. Cluster and outbreak profile by town, 2002/2003 – 2004/2005 season

Town	Number of space time clusters n (season)	Number of space clusters
Albertsnek	1 (2004/2005)	2
Goba	0	1
Khombaso	0	0
Mbangwane	0	0
Mbuzini	0	1
Steenbok	0	0
Thambokulu	1 (2004/2005)	1

Albertsnek produced two space clusters over the three season period using the Bernoulli model, one in the northern (log likelihood ratio = 12.308, p = 0.003) and one in the south eastern part of town (log likelihood ratio = 12.187, p = 0.003). Three additional space clusters were observed; in Goba (log likelihood ratio = 12.226, p = 0.001), Mbuzini (log likelihood ratio = 22.372, p = 0.001) and Thambokulu (log likelihood ratio = 22.372, p = 0.001). Only two towns, Albertsnek (test statistic = 5.548, p = 0.007) and Thambokulu (test statistic = 3.668, p = 0.004), had space time clusters and both were during the 2004/2005 season (Figs. 5.3, 5.4, 5.5, 5.6).

5.3.3 Cluster detection to guide control activities

The third season for case cluster identification, 2004/2005 overlapped with the first season of implementation of an outbreak identification and response system in the Tonga area. Thambokulu and Albertsnek triggered outbreak declarations during this season (Coleman *et al.*, 2008).

Figure 5.3 Spatial malaria case clusters, 2002/2003 - 2004/2005 seasons, Albertsnek town

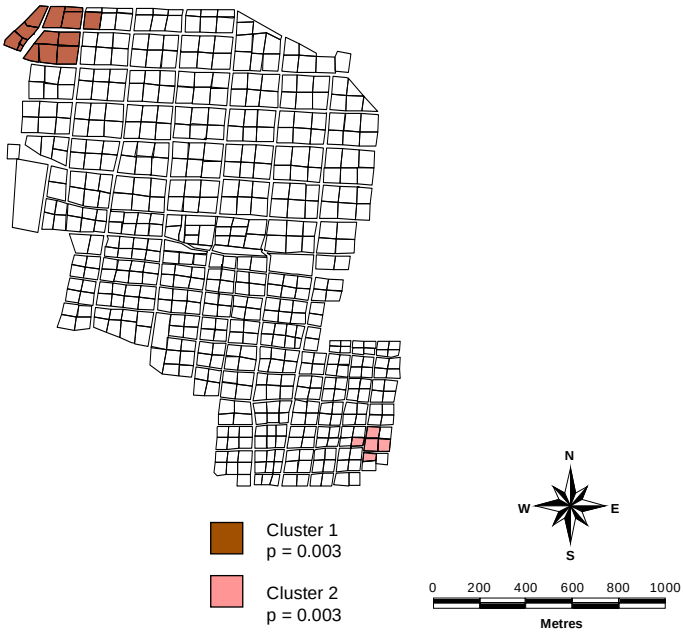
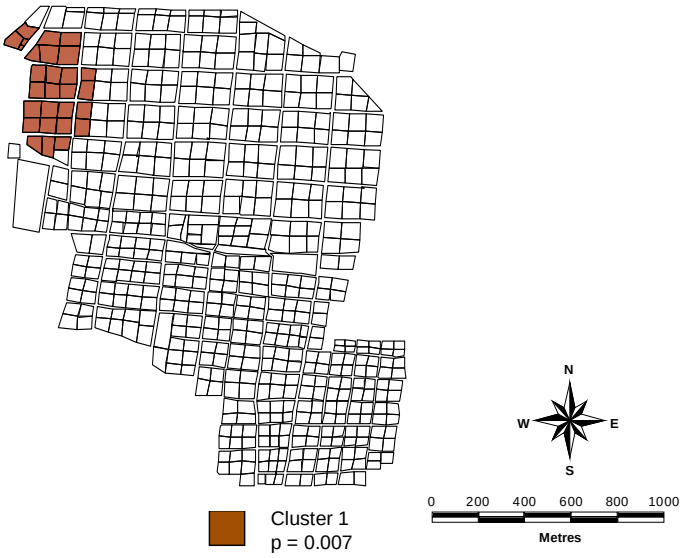


Figure 5.4 Space time malaria case cluster, 2004/2005 season, Albertsnek town



Retrospective analysis showed clusters in both towns for the season. The physical plotting of cases by household during this season (2004/2005) as part of the cluster identification activities provided a visual distribution of risk in the towns and assisted with the planning of interventions in areas most needed. Activities for consideration included verification of stocks at health facilities for diagnosis and treatment, active case detection and diagnosis, additional indoor residual spraying, focal larviciding and health promotion.

Figure 5.5 Space time malaria case cluster, 2004/2005 season, Thambokulu town

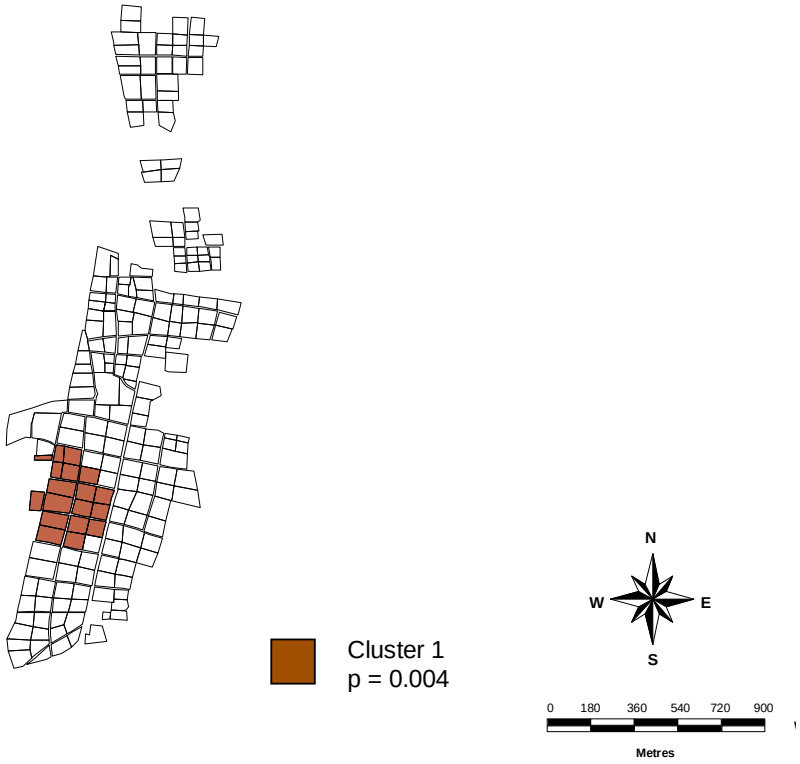
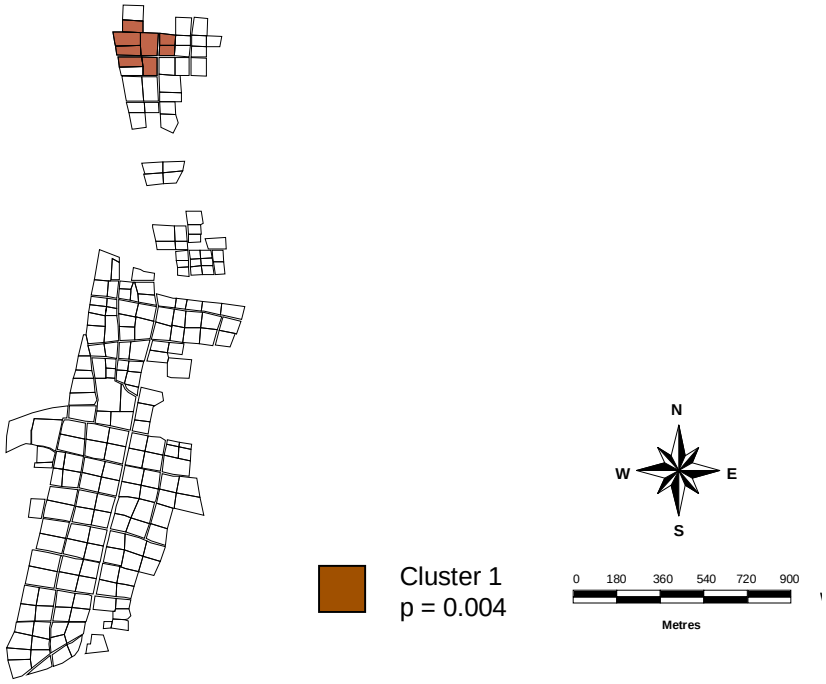


Figure 5.6 Space malaria case cluster, 2002/2003 - 2004/2005 seasons, Thambokulu town



5.4 Discussion

Application of the SaTScan method successfully identified malaria case clusters and clearly demonstrated malaria risk heterogeneity at local level. Four towns in this study experienced spatial clusters and two produced space time clusters in the 2004/2005 malaria season, the latter resulting in targeted local control efforts.

Spatial clustering of infectious disease is facing renewed interest allowing for the quantification of the degree of clustering infections. Such approaches have been used to investigate the spatial clustering in dengue (Morrison *et al.*, 1998) encephalitis (Kitron *et al.*, 1994) and sleeping sickness (fever) (Abdelrahman *et al.*, 2006) but the application to malaria has been limited (Chadee & Kitron, 1999).

Gaudart *et al.* (2005) compared the oblique decision tree model, a complex statistical technique with Kulldorff's SaTScan™ cluster technique used here. Their study in a village in West Africa to identify malaria risk clusters produced similar results from both methods. The Mpumalanga investigation confirmed the usefulness of the Kulldorff's scan statistic that has been documented in other settings (Hjalmars *et al.*, 2006; Kulldorf *et al.*, 1997; Shaheen *et al.*, 1987). In the Mpumalanga setting, high rates of treatment seeking behaviour at primary health care level (Govere *et al.*, 2000a) and the use of passive notification and active case detection, strengthens disease surveillance to provide relatively complete data for cluster identification.

SaTScan cluster identification has also proven valuable for targeting control strategies in the Kenyan highlands (Brooker *et al.*, 2004) . Over a ten week period during a 2002 epidemic spatial targeting of vector control reduced the abundance of *Anopheles* mosquitoes.

It is important to identify this circular isotopic technique to detect clusters as valuable but acknowledge of its limitation to detect irregular shaped clusters due to its fixed scan window is mentioned in literature (Aamodt *et al.*, 2006; Patil & Taillie, 2003).

The same Mpumalanga towns under cluster surveillance were included in a malaria outbreak identification and response system based on formal case reporting (Coleman *et al.*, 2008). The incorporation of cluster identification as a complimentary measure for the outbreak system was identified. Results indicated that clusters areas corresponded with outbreaks. The towns of Albertsnek and Thambokulu both reported malaria outbreaks in the same season as the time space

clusters. The synergy of being able to locate high risk clusters in towns identified as experiencing outbreaks, allows limited resources to be maximised when an outbreak is identified.

CHAPTER 6

6. Household and micro-economic factors associated with malaria

This chapter has been submitted for publication to the *International Health and Geography* journal.

6.1 Introduction

Variation in malaria incidence in small geographical areas can be explained by a variation of exposure to risk factors (Casman & Dowlatabadi, 2002). Common risk factors described in literature associated with malaria are climate, altitude, distance from breeding site, house construction, crowding index and personal protection measures (Abeku *et al.*, 2004; Adiamah *et al.*, 1993; Clarke *et al.*, 2002; Ghebreyesus *et al.*, 1999; Koram *et al.*, 1995; Snow *et al.*, 1998b; Tanser *et al.*, 2003b; Thomas & Lindsay, 2000). Many of these factors are directly or indirectly linked to socio economic status of a household.

Globally, disease burden in impoverished rural settlements is higher and poverty has been directly associated with increased disease risk (Blakely *et al.*, 2005). A downward spiral of income due to illness contributes to less available finances for improvement of house location, structure, design as well as personal protection measures. House construction and design may affect the risk of mosquito bite exposure. The main activities employed to lessen contact between malaria vectors and humans include the use of insecticide treated nets (ITNs) and reliance on indoor residual spraying with insecticides (IRS).

The renewed drive to scale up these interventions in Africa requires reliable evidence based knowledge to direct allocation of resources to those who are at greatest risk to ensure cost effectiveness of interventions (Breman *et al.*,

2004; Johns & Tan Torres, 2005). Identifying household risk factors that contribute to malaria transmission is therefore important for reducing the burden of disease (Brooker *et al.*, 2004).

Furthermore, the role of such factors in areas that have successfully reduced malaria but where transmission persists has not been well elucidated. This study aimed to investigate socio economic variables and household characteristics amongst cases and controls in seven towns within the hypo endemic Nkomazi municipal area characterized by seasonal malaria transmission.

6.2 Methodology

6.2.1 Study area

The seven rural Mpumalanga towns closest to the international border with Mozambique in the east and Swaziland in the south at highest malaria risk are Goba, Albertsnek, Steenbok, Mbuzini, Khombaso, Thambokulu and Mbangwane (Figure 5.1). Almost a quarter (23%) of the households in Nkomazi are traditional mud structures or informal shelters (Statistics South Africa, 2005). Official unemployment is reported to be 41% of adults > 17 yrs and 21% of all households in this area have an income of less than R4 801 per annum (Statistics South Africa, 2005).

The area is sub-tropical and the altitude of towns ranges from 300 (Albertsnek, Khombaso, Steenbok) to 700 metres (Mbuzini) above sea level. *An.arabiensis* is the main vector in the area. The average annual malaria incidence per 1 000 population from 1997/1998 to 2005/2006 ranged from a minimum of 26

(Thambokhulu town) to 54 (Mbangwane town) (Mpumalanga Malaria Control Programme, 2006).

Spatial analysis in the seven towns in Tonga over the three seasons showed four towns experienced significant space clusters and two space time clusters using the Kulldorff method (Table 5.2).

6.2.2 Study design

A household matched case-control design was used to explore associations between household risk factors and malaria, with case households having at least one confirmed malaria case in the household during the period under review.

6.2.3 Case household enrolment

All households that reported malaria cases since the beginning of the 2005/2006 malaria season (1 July 2005 to 31 June 2006) were offered enrolment in the study. A control household was the nearest neighbouring household without malaria patient (s) during the period under review. Three control households were selected for every case household.

6.2.4 Data collection

A pre-tested structured questionnaire translated into the local language was used to collect information on potential risk factors that included household structure, household behaviour, protective activities and measures as well as household assets to determine wealth status.

Two experienced malaria case investigators were specifically trained to conduct field data collection. An adult over the age of 18 that resided in the household was eligible to participate, with preference given to the head of the household.

Data was captured and double entered in a Microsoft Access 2000 database (version 9.0.2, Microsoft®, Redmond, Washington, United States) designed specifically for this purpose. All dichotomous and categorical variables were coded for data analysis. Ownership of household assets to represent household's economic status used validated tools published in literature (Bonnila-Chagin & Hammer, 1999; Kakwani *et al.*, 1997; Schellenberg *et al.*, 2003). These included household income, radio, television set, car, live stock, electricity, flush toilet, lounge suit and number of bedrooms.

6.2.5 Data analysis

Principle components analysis (PCA) was used as this is the preferred economic analytical approach to calculate the wealth index as a composite of all socio-economic variables for each household (Brooker *et al.*, 2004; Ceccato *et al.*, 2007). A wealth index based on asset ownership has been shown to be a good measure of economic status (David & Haberlen, 2005; Filmer & Pritchett, 2001). The first principal component explained 29% of the variance and gave greatest weight respectively to ownership of a television, house with more than two bedrooms, and ownership of a lounge suit. The resultant scores were divided into quartiles to ensure that each household could be classified in terms of relative socio-economic status (Malik *et al.*, 2006).

Conditional univariate logistic regression analysis was used to assess the association of case and control households with potential risk factors and selected protective activities. All variables with P-values less than 0.1 were entered into conditional multivariate logistic models. Owing to the co-linearity between house structure type, wall structure and wall covering, the effect of each of these factors

on malaria risk was evaluated in three separate multivariate models and tested using the Akaike Information Criterion (Hamparsum, 2000). The model with the smallest AIC value was considered the best fit model. All analysis were performed using STATA (version 9, STATA Corporation, College Station, Texas)

6.2.6 Ethics

The study protocol and relevant forms were submitted to the Witwatersrand University Research Ethics Committee for ethical clearance and approval. (Appendix E). The Malaria Control Programme management team agreed to the study and formal approval from the Mpumalanga Department of Health Research Ethics Committee were obtained before commencement of the study (Appendix F).

A written consent form translated into the local language (Siswati), was developed. The purpose of the study, a guarantee of freedom of choice to participate, the withdrawal of consent at any stage and assurance of the anonymous nature of any data gathered during the study was discussed prior to signing of the consent form in local language.

6.3 Results

A total of 53 case households and 159 control household were enrolled. All household characteristics used in the analysis are listed (Table 6.1). Traditional/informal structures were more common for case households n=32, 60%) and western structure counts higher amongst control households (n=129, 81%). Traditional/informal structures were defined as any structure constructed

from any material except bricks and included mud, plastic, and corrugated iron. The odds ratio was the preferred measure of association used for analysis.

Results showed living in a traditional/informal household with mud walls (OR=5, P=0.000) and inner mud wall covering (OR=5, P=0.005) were significantly associated with increased risk of malaria. With regards to household behaviour re-opening the windows at night after the household members have gone to sleep was the only statistically significant variable that was associated with increased risk of malaria (OR=4, P=0.003). Households within the third (OR=0.34, P=0.015) and fourth wealth quartiles (OR=0.31, P=0.011) were associated with reduced risk of malaria. The use of repellent sprays were borderline protective (OR=2, P=0.052) but suggest superiority when compared to other personal protection activities. Multivariate analysis showed that of the selected household variables in the model the most important risk factor for increased risk of malaria was walls constructed from mud followed by re-opening of windows at night (Table 6.2). Households falling within a higher wealth quartile, according to the wealth index were consistently associated with reduced risk of malaria.

Table 6.1. Univariate analysis showing the frequency of potential risk factors and protective factors among cases and controls, odds ratios (OR) and confidence intervals (CI) for the association with malaria.

VARIABLES	**CASES**		**CONTROLS**		**OR**	**95 % CI**		**p-value**
	n	%	n	%				
	53	25	159	75				
HOUSEHOLD STRUCTURE								
House construction								
Western	32	19.9	129	80.1	1.00	.	.	.
Traditional/informal	21	41.2	30	58.8	4.04	1.73	9.45	0.001

VARIABLES	CASES		CONTROLS		OR	95 % CI		p-value
	n	%	n	%				
	53	25	159	75				
Wall structure								
Brick		19.9	129	80.1	1.00	.	.	.
Corrugated iron	0	0.0	4	100.0	0.00	.	.	0.316
Mud	20	43.5	26	56.5	5.10	2.03	12.80	0.000
Plastic	1	100.0	0	0.0	.	.	.	0.014
	53	25	159	75				
Wall covering								
None Brick	13	25.0	39	75.0	1.00	.	.	.
Non Corrugated iron	0	0.0	4	100.0	0.00	.	.	0.371
Mud	20	43.5	26	56.5	5.24	1.42	19.30	0.005
Plastic	1	100	0	0.0	.	.	.	0.317
Painted PVA	1	6.7	14	93.3	0.20	0.02	2.10	0.139
Painted enamel	2	13.3	13	86.7	0.28	0.01	6.04	0.383
Plastered	16	20.3	63	79.8	0.93	0.40	2.16	0.858
Roof structure								
Corrugated iron	45	25.1	134	74.9	1.00	.	.	.
Grass	8	24.2	25	75.8	0.96	0.44	2.07	0.911
Any visible openings								
No	12	27.9	31	72.1	1.00	.	.	.
Yes	41	24.3	128	75.7	0.80	0.34	1.86	0.600
Tap water inside								
No	51	25.6	148	74.4	1.00	.	.	.
Yes	2	15.4	11	84.6	0.44	0.07	2.76	0.372
HOUSEHOLD BEHAVIOUR								
Plaster walls								
<1 year before	7	35.0	13	65.0	1.00	.	.	.
>=1 year ago or never	46	24.0	146	76.0	0.51	0.16	1.59	0.236
Wash walls								
<1 year before	1	8.3	11	91.7	1.00	.	.	.
>=1 year ago or never	52	26.0	148	74.0	4.29	0.46	40.49	0.165
Re-open windows after sleeping								
No	42	22.1	148	77.9	1.00	.	.	.
Yes	11	50.0	11	50.0	3.78	1.45	9.84	0.003
PROTECTIVE ACTIVITIES								
Use mosquito coils								
No	37	22.6	127	77.4	1.00	.	.	.
Yes	16	33.3	32	66.7	1.83	0.85	3.91	0.114
Use repellent sprays								
No	27	31.8	58	68.2	1.00	.	.	.
Yes	26	20.5	101	79.5	1.90	0.98	3.68	0.052
Apply lotion sticks								
No	52	25.9	149	74.1	1.00	.	.	.
Yes	1	9.1	10	90.9	0.30	0.04	2.19	0.207

VARIABLES	CASES		CONTROLS		OR	95 % CI		p-value
	n	%	n	%				
	53	25	159	75				
Burn plant or animal dung								
No	47	24.4	146	75.7	1.00	.	.	.
Yes	6	31.6	13	68.4	1.45	0.51	4.11	0.481
Wear long sleeve clothing								
No	52	24.8	158	75.2	1.00	.	.	.
Yes	1	50.0	1	50.0	3.33	0.16	67.66	0.405
Have net								
No	26	26.5	72	73.5	1.00	.	.	.
Yes	27	23.7	87	76.3	0.87	0.47	1.58	0.637
Sleep under net								
No	45	25.4	132	74.6	1.00	.	.	.
Yes	8	22.9	27	77.1	0.86	0.34	2.15	0.742
Spray card								
No	22	32.4	46	67.7	1.00	.	.	.
Yes	31	21.5	113	78.5	0.56	0.30	1.07	0.078
WEALTH INDEX								
Quartile								
First (poorest)	19	38.0	31	62.0	1.00	.	.	.
Second	18	31.6	39	68.4	0.58	0.23	1.46	0.237
Third	8	15.1	45	84.9	0.34	0.14	0.85	0.015
Fourth (least poor)	8	15.4	44	84.6	0.31	0.12	0.80	0.011

Table 6.2. Multivariate analysis showing selected variables with their odds ratios (OR) and confidence intervals (CI) for the association with malaria.

VARIABLES	OR	95% CI		p-value
HOUSEHOLD STRUCTURE				
Mud wall	6.12	2.26	16.59	0.000
HOUSEHOLD BEHAVIOUR				
Re-open windows at night	4.01	1.32	12.18	0.014
PROTECTIVE ACTIVITIES				
WEALTH INDEX				
Third quartile	0.24	0.09	0.65	0.005
Fourth quartile (least poor)	0.27	0.10	0.79	0.016

6.4 Discussion

Identifying differences between households in small geographical areas has proven useful. The question remains how does risk for individual households

differ in areas where most important risk factors are alike. Malaria risk is defined as “the probability of contracting malaria” (Casman & Dowlatabadi, 2002).

The case control study identified that people living in traditional mud structures (OR=5, P=0.000) and households that re-opened their windows at night after bedtime (OR=4, P=0.003) have a greater risk of contracting malaria than those who live in western structures and do not re-open windows. These factors remained highly statistically significant after inclusion in the multivariate model.

The climate in the area often leads to opening windows as summer temperatures can cause discomfort at night. . In this area the peak biting time of the main vector *An. arabiensis* is between 21h00 and 03h00 this corresponds with risk behaviour of re-opening windows late at night (Mendis *et al.*, 2000).

The upper two wealth categories clearly showed protective associations. Improved housing can be hypothesized as possible reasons for the protective result. Traditional structures on the other hand are associated with sub-standard housing and have the potential due to structural defects to be more likely to provide opportunity for vectors to enter the house. This in turn increases the likelihood of vector human contact, exposure to the parasite and disease (Lindsay *et al.*, 2003).

The variation of malaria incidence in small geographical areas where transmission is low and immunity is not established is still not well understood. Transmission potential as an index using mainly climatic factors is often deployed to delineate areas of potential malaria risk (Casman & Dowlatabadi, 2002). A study conducted in Malawi estimated the costs of malaria prevention, treatment and loss of income due to morbidity for low-income households as around 20% of

annual income (Malaney *et al.*, 2004). Globally, disease burden in impoverished rural settlements is higher and poverty has been directly associated with an increased disease risk (Blakely *et al.*, 2005). A study in Bangladesh highlighted treatment health seeking behaviour, house structure, use of anti-malarial measures, the physical environment and poverty to be associated with an increased risk of morbidity and mortality of malaria (Ahmed *et al.*, 2005; Gallup & Sachs, 2001; Hu *et al.*, 1998).

The use of barriers to prevent mosquitoes from entering houses has proven a valuable intervention and contributed to elimination in some parts of the world (Celli, 1901; Lindsay *et al.*, 2003; Ross, 1913). The concept of elimination now, once again a topical issue of discussion, necessitates the investigation of current feasibility of all possible strategies. The renewed optimism in Africa is mostly due to focused operational research efforts to identify the most successful and cost effective control interventions. The drive to scale up intervention efforts requires reliable evidence based knowledge to direct location of financial resources to those who are at greatest risk (Breman *et al.*, 2004; Johns & Tan Torres, 2005).

A case control study investigating malaria risk factors in the highlands of western Kenya reiterated the importance and lack of epidemiological studies investigating household risk factors and socio economic status at micro level (Brooker *et al.*, 2004).

Our study suggests that the drive to improve housing in rural areas and the possible intervention of installing screens for windows to allow air flow during night time without increased risk of vectors entering the household can be a

positive contribution toward lowering risk of malaria in highest risk areas of Mpumalanga.

CHAPTER 7

7. General discussion and conclusion

Information is one of the most powerful weapons we have available to aid us to effectively control infectious diseases. It allows program managers to make informed decisions regarding disease intervention options, where activities should be focused and what the extent of resource investment should be.

Current initiatives to control malaria with support from the Global Fund and President's Malaria Initiative are delivering success stories in malaria control in Africa including the Lubombo Spatial Development Initiative (Sharp *et al.*, 2007a) and Bioko programme in Equatorial Guinea (Kleinschmidt *et al.*, 2007; Sharp *et al.*, 2007a). These programmes have included components of the information system and relevant tools described in this thesis to aid disease surveillance and programme planning.

Monitoring and evaluation are key components of the Southern Africa Development Community (SADC) Malaria Control Strategy (Durrheim *et al.*) as well as the Abuja Declaration (2000) that proposed countries introduce evidence based interventions for malaria control (World Health Organization, 2004).

The monitoring and evaluating of malaria control interventions in any transmission area is thus invaluable and necessary to maintain the continuation of financial support from either ministries or external funders and to sustain good practices through evidence based strategies (Booman *et al.*, 2003).

All three South African provinces have maintained IRS vector control activities since 1946 (Sharp *et al.*, 1988). Malaria control programmes utilising indoor residual spraying are most effective if a high coverage of targeted

structures is achieved, insecticides application is as recommended and spray operations are complete before the peak of the transmission season. This requires an efficient and timely intervention monitoring system. In 1973 South Africa introduced a manual system to monitor spray activities. Tardy data and the lack of tools for rapid analysis during a spray season made identification of operational problems difficult and appropriate adjustments challenging.

A unique computerised management system was developed and implemented as part of this study to enable malaria programme management and field supervisors to monitor, on a daily basis when required, spray coverage, individual spray operators' performance, insecticide usage and application rates (Booman *et al.*, 2003). This monitoring system has been adapted and implemented as part of malaria control in the Lubombo Spatial Development Initiative (LSDI) (Sharp *et al.*, 2007a), in Bioko, Equatorial Guinea (Kleinschmidt *et al.*, 2007; Sharp *et al.*, 2007b) and by AngloGold Ashanti, Obuasi, Ghana(Coetzee *et al.*, 2006).

Suggested future improvement of this tool includes the identification of individual households targeted for spraying. This is a resource intensive exercise as most rural town have no formal street names or house numbers. Provinces are currently in the process of addressing this issue and as soon as relevant data are available it should be incorporated and spray data entered separately for each individual household. This is a very feasible option as an initial objective when small intervention areas are targeted.

In addition it is also proposed that the impact of low spray coverage rates on case incidence rates in low malaria transmission areas be thoroughly investigated.

Previous analysis of seasonal malaria case data in Mpumalanga has been restricted to basic description (Durrheim *et al.*, 1999a; Durrheim *et al.*, 1998b; Govere *et al.*, 2000a; Martin *et al.*, 2002). The comprehensive analysis of malaria epidemiology in Mpumalanga for an eight season period (1997/1998 to 2004/2005) in this thesis produced valuable information to assist our understanding of the complexity of malaria in the province.

Retrospective analysis showed clear heterogeneity of disease risk at district, municipality and town levels in space and time. High case fatality ratios in low risk areas were identified as a concern and resulted in continuous community support and education campaigns as well as case management training at health facility level. The impact of change in treatment and intervention policy was clearly demonstrated although no single factor appeared to account for the decrease. The use of combination therapy and the reintroduction of DDT as well as cross border collaboration through the LSDI has clearly been factors influencing the decline in the disease incidence in Mpumalanga (Sharp *et al.*, 2007a).

The advancement in and improvement of surveillance systems now lends itself to accommodate outbreak identification components to ensure rapid detection and response. In low transmission regions all age groups are at equal risk for malaria disease due to the non-immune status of the population and serious disease outbreaks are expected (Bell, 1995). Mpumalanga communities

are vulnerable to malaria outbreaks and epidemics because of the seasonal dynamics of local malaria transmission with large-scale migration from neighbouring malaria-endemic areas, climate aberrations and low levels of acquired immunity in the human population (DaSilva *et al.*, 2004; Govere *et al.*, 2000a; Govere *et al.*, 2000b; Mabuza *et al.*, 2001; Martin *et al.*, 2002; Sharp *et al.*, 2007a). The majority of malaria cases (95%) in Mpumalanga are due to *Plasmodium falciparum* infection (Durrheim *et al.*, 1998b; Sharp *et al.*, 1988). Non-immune patients if untreated, misdiagnosed or presenting too late at health facilities may have fatal consequences.

Good quality data in a timely fashion and treatment seeking behaviour of communities at health care facilities for febrile disease provides an opportunity for developing and implementing an outbreak identification and response system in Mpumalanga province (Govere *et al.*, 2000a). The present system was developed using a binomial distribution model and compared to other recommended thresholds. However, the availability of accurate catchment population data for facilities is a challenge in many African countries (Hay *et al.*, 2002; Teklehaimanot *et al.*, 2004) and limits the use of binomial models as these data are important for the model. The binomial model appeared to out-perform the CDC (Teklehaimanot *et al.*, 2004) and WHO (DaSilva *et al.*, 2004) thresholds in this specific low transmission setting.

The unique three tier system involving primary health care facilities, malaria case detection teams and an automated computerized identification system provided rapid identification of focal malaria increases and prompted targeted intervention in the highest risk malaria area during the two seasons following

introduction. The effective implementation of the system ensured all outbreaks were responded to in a timely fashion and no epidemics resulted. Response activities included treatment and diagnostic tests stock control, larviciding of potential breeding sites, active case detection as well as community mobilization and education activities. It could have application in other low malaria transmission settings.

Areas with significantly higher endemicity have less temporal and spatial variation of disease and outbreaks do not characterise the transmission zones due to the high level of acquired immunity within the population (Bell, 1995). The outbreak identification and response system will be of minimal use in such an area. It has to be noted that many regions face the reality of a combination of transmission zone with borders in close proximity, where introduction of parasites into low risk areas where vectors are already present, is very likely.

The spatial and temporal micro variation of disease, as reflected by clusters, was clearly demonstrated in this thesis and this lead to further investigation into risk factors within the affected communities (Ceccato *et al.*, 2007). The utilization of real time cluster surveillance may prove a feasible complimentary activity to outbreak identification to guide response. It is one concept to identify outbreaks but timely visualization of cluster areas that correspond to outbreaks has proved valuable. Further exploration of other available freeware with a less restrictive scan window as part of the cluster analysis is suggested to improve the power of detecting clusters in areas with abnormal shapes. Cluster analysis requires significant resources to collect data at household level especially when household identification is not possible at the

notification stage. Resource poor countries will find it difficult to justify cluster analysis.

The case control study found that living in traditional mud structures (OR=5, P=0.000) or households that re-opened their windows at night after retiring to bed (OR=4, P=0.003) increased household risk of contracting malaria. Households in the 3rd (OR=0.34, P=0.015) and 4th (OR=0.31, P=0.011) wealth indexes quartiles were protected against malaria. The use of repellent sprays performed best of all personal protection methods (OR=2, P=0.052).

The incidence of malaria has a profound impact on the economic growth of an area (Teklehaimanot *et al.*, 2007). As a long term goal, improvement of the economic status of communities to facilitate better housing appears important for reducing malaria disease risk in rural Africa (Lindsay *et al.*, 2003). Integrated vector management projects should consider the screening of windows or use of insecticide treated curtains to prevent vectors entering the household.

The completion of this work is timely as there has been a recent resurgence in interest in global malaria elimination (Guerra *et al.*, 2008) and the scaling-up of malaria interventions (Teklehaimanot *et al.*, 2007). If elimination is to succeed it will require continuous effective monitoring and surveillance activities. Adequate tools at operational level, managed by operational staff to produce quality information for timely decision-making are critical. Understanding disease transmission risk at micro level will be an essential component to sustain any successful elimination campaign.

The cognizance of malaria disease dynamics including spatial and temporal characteristics of local malaria transmission combined with a functional

outbreak identification and response system, cluster detection capacity and the ability to monitor control interventions as part of an integrated surveillance and monitoring approach are valuable for any malaria control programme operating within a low transmission area.

The total or partial adoption and implementation of the outbreak, cluster and intervention monitoring tools and principles can in concept be duplicated as part of an existing or new malaria information system, either in a small or large transmission area. Tweaking of components can allow for resource constraints.

Consideration, stepwise implementation and evaluation of surveillance and monitoring tools conceptualized, developed and implemented in Mpumalanga province, has immense potential for other malaria areas especially when targeted for malaria elimination with the aim of saving lives.

APPENDICES

Appendix A: SP1 daily spray operator data collection card

SP1 Spray Card

INSECTICIDE:

STAND	SPRAYED	UNSPRAYED
Tot:	Tot:	Tot:
Can refills		
Locality:	Spray operator:	
Date:	Team leader:	

Appendix B: SP2 daily spray team summary form

MPUMALANGA DEPARTMENT OF HEALTH AND SOCIAL SERVICES

MALARIA CONTROL PROGRAMME

TO BE COMPLETED BY SPRAY TEAM LEADERS

SP2 v.2

Daily Spray Team Record

Team Leader: ..... Locality: .....

Date of spraying: ……/……/200…..

MAIN SPRAY

MOP_UP

SPRAY OPERATOR	STANDS	SPRAYED	UNSPRAYED	DDT	OTHER	CAN REFILLS

Appendix C: Expert questionnaire participation acknowledgement

This work was made possible by the Mpumalanga Department of Health and Social Services staff and the following specific participants: AM Mabuza, G Kok, A Zitha, F Mbokazi (Mpumalanga Provincial Malaria Control Programme); P Moonasar (National Malaria Control Programme, Department of Health); JB da Silva, J Govere (World Health Organization, Southern Africa); R Maharaj (South African Medical Research Council, Durban)

Appendix D: Case cluster questionnaire



MPUMALANGA DEPARTMENT OF HEALTH AND SOCIAL SERVICES

MALARIA CONTROL PROGRAMME

MALARIA CASE INVESTIGATION REPORT FOR CLUSTER DETECTION

Cluster form

CASE NO: _____

SECTION 1 **Status**

Case Investigator: ..... Date Investigated: dd/mm/yyyy

Source of infection: **A.** Correct Stand Number: | | | | | | | Locality Name: .....

Locality Code: .....

Complete sections 3

B. Incorrect **If incorrect investigate and complete all sections below**

C. Untraceable

Comments: .....

.....

SECTION 2 **Correct Source of Infection**

Locality Name: ..... Locality Code: ..... Stand Number: | | | | | | |

Address: .....

Comments: .....

SECTION 4 **Other Information**

Did you receive a bednet? YES | NO

If yes, did you or any of the household members sleep under a bednet/s last night? YES | NO

Appendix E: Ethics approval – University of the Witwatersrand

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/69 Booman

CLEARANCE CERTIFICATE	PROTOCOL NUMBER M060363
PROJECT	Household and Micro Economic Factors Associated with Malaria in the High risk Villages in Nkomazi Municipal Area,...
INVESTIGATORS	Ms M Booman
DEPARTMENT	APES
DATE CONSIDERED	06.03.31
DECISION OF THE COMMITTEE*	APPROVED UNCONDITIONALLY

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

DATE 06.09.06 CHAIRPERSON _____
(Professor M Vorster)

*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 10005, 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 F: Ethics approval – Mpumalanga Department of Health and Social Services

MPUMALANGA PROVINCIAL GOVERNMENT

Number 7
Government Boulevard
Riverside Park
Extension 2
Nelspruit
1200
South Africa

Private Bag X11288
Nelspruit, 1200
Tel: (013) 766 3429/30
Int: +27 13 766 3429/30
Fax: (013) 766 3459
Fax: +27 13 766 3458

Department of Health and Social Services

Litiko Letemphilo Nemiseberi Yenhlalakahle Yesive | Umnyango Weze Pilo neZehlalakuhle | Departement van Gesondheid en Maatskaplike Dienste

Enquiries: Nkhumiseni Mphathele (013) 766 3235

Ms. M. Booman
P.O. Box 12356
Nelspruit
1200
30 August 2006

APPLICATION FOR RESEARCH ETHICS APPROVAL: HOUSEHOLD AND MICRO-ECONOMIC FACTORS ASSOCIATED WITH MALARIA IN THE HIGHEST RISK VILLAGES IN NKOMAZI MUNICIPALITY, MPUMALANGA PROVINCE

The Provincial Research and Ethics Committee has approved your research proposal in the current format. No issues of ethical consideration were identified.

Kindly ensure that you provide us with the research report after the completion of the study.

Kind regards,

30/08/2006

Miss N.A. Mphathele: Research—coordinator — Date

Research—coordinator
Pp: Mpumalanga PHREC
Acting-Chairperson: Prof. J.P. Shongwe

1

We care. Do you?

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