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Correlation between surrounding climatic or environmental conditons and malaria incidence in selected sub-districts of Mpumalanga Province, South Africa (2001-2010)

Khumalo, Mbhekiseni Phikelamangwe

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University of the Witwatersrand Johannesburg

SCHOOL OF PUBLIC HEALTH

Master of Science (Medicine) in the field of Epidemiology and Biostatistics

Research Report

Title: Correlation between surrounding climatic or environmental conditions and malaria incidence in selected sub-districts of Mpumalanga Province, South Africa (2001 – 2010)

By

Mbhekiseni Phikelamangwe Khumalo (Wits)

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

Supervised by:

Professor Maureen Coetzee (Wits University, School of Pathology)

Professor Benn Sartorius (University of KwaZulu-Natal, School of Nursing & Public Health)

Year 2014

Declaration

I, Mbhekiseni Phikelamangwe Khumalo, declare that this research report is my own work. It is being submitted for the degree of Master of Science in Medicine in the field of Epidemiology and Biostatistics at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

……

[Signature of candidate]

…….day of

…… [Month] 2014.

Dedication

I would like to dedicate this work to God of our ancestors, my mom (Mrs Sizakele Khumalo), my brothers (Mr Thabani and Siboniso Khumalo), my sisters (Ms Zama and Nqobile Khumalo), my two dear daughters (Ms Philile and Nokubongwa Khumalo) and my friend Dr Nomtha Manyisela who have been supporting me and made all this possible for me.

Abstract

Background

Malaria remains one of the most devastating vector-borne parasitic diseases in tropical and subtropical regions. Approximately 40% of the world's population lives in malaria endemic areas mostly in developing countries. The estimated global incidence is about 225 million cases and 80% of these cases occur in sub-Saharan Africa. The approximated global deaths due to malaria every year is about 700,000 people and 90% occur in Africa. In South Africa, parts of Mpumalanga, Limpopo and KwaZulu-Natal have endemic malaria. The incidence of malaria in South Africa by province is 56, 2 cases per 100,000 population at risk; 31,1 cases per 100,000 population at risk and 3,3 cases per 100,000 population at risk for Mpumalanga; Limpopo and KwaZulu-Natal, respectively. Approximately 80% of the cases are imported from malaria endemic countries and diagnosed in the South African health facilities. It is therefore important that these cases are disentangled from local cases using environmental or climatic conditions as proxy measures especially in light of South Africa eradication goal.

Methodology

Secondary data used in this study were obtained from Mpumalanga Department of Health, South African Weather Services, Statistics South Africa and Global Climatic Research Units. These data were analysed from 2001 to 2010 to determine the correlation between surrounding climatic or environmental conditions and malaria incidence in Mpumalanga Province. The Pearson correlation was used to assess for significant correlations between malaria incidence and environmental or climatic conditions. A negative binomial regression model was used to identify and quantify factors significantly association with

malaria risk. The Kulldorff spatial and space-time scan statistic was used to detect significant clustering of malaria cases in space and space-time.

Results

The incidence of malaria has decreased significantly since 2001 to 2010 in Mpumalanga Province. The decline has been observed from 1,304 cases per 100,000 population at risk in 2001 to less than 200 cases per 100,000 population at risk in 2010. About 96% of malaria cases were reported from Ehlanzeni District and less than 4% were reported from Gert Sibande and Nkangala Districts. The temperature, rainfall and humidity were statistically significant in all months from all years ($p<0.05$). The temperature, rainfall and humidity had a significant positive correlation with malaria cases. An excess of 1,752 and 104 malaria cases were detected in May and June over time when using weather stations data. When using remote sensed data, an excess of 1,131; 3,036; 4,009; 994 and 235 cases were observed from March, April, May, June and July, respectively.

Discussion and conclusion

The significant positive correlations between malaria cases and temperature, rainfall and humidity suggested that for an increase in each unit factor, malaria cases also increases. The excess number of cases observed especially during the winter season, suggested the likelihood of the importation of those cases. These results were in accordance with results from previous studies.

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Abbreviations

ACT	Artemisinin-based combination therapy
ACD4	Clusters of Differentiation
AIDS	Acquired Immune Deficiency Syndrome
CDC	Centre for Disease Prevention and Control
DDT	Dichlorodiphenyltrichloroethane
DHIS	District Health Information System
E8	Elimination eight
EPR	Epidemic Preparedness Response
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
IEC	Information, education and communication
IRS	Indoor Residual Spraying
IRR	Incidence Risk Ratio
ITN	Insecticide treated-nets
KZN	KwaZulu-Natal
LLIN	Long Lasting Insecticide Treated Nets

LSDI	Lubombo Spatial Development Initiative
NDoH	National Department of Health
RDTs	Rapid Diagnostic Tests
SA	South Africa
SADOH	South African Department of Health
Stats SA	Statistics South Africa
WHO	World Health Organization

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

Overview of the Chapter

This Chapter will provide the background information about malaria in South Africa with special emphasis on the epidemiological aspects. These epidemiological aspects will focus on the distribution of malaria globally, in sub-Saharan Africa, in South Africa and in Mpumalanga province. The concept of infectious disease epidemiology and determinants of malaria transmission particularly in South Africa will be dealt with. The issue of imported cases from other malaria endemic countries will be highlighted. The biology and control intervention strategies for malaria as recommended by WHO and SADOH will be explained. The published current literature on the effects of climatic or environmental conditions on malaria prevalence will be reviewed. At the end of this Chapter, the research question, objectives and hypothesis of the study are given.

1.1 Background information

According to WHO (2012), malaria remains one of the most devastating vector-borne parasitic diseases in the tropical and subtropical regions of the world. This disease is one of the primary public health problems in sub-Saharan Africa (Mabaso *et al*., 2007). Approximately 40% of the world population lives in malaria endemic areas mostly in developing countries (Suh *et al*., 2004; RBM/WHO/UNICEF, 2005). Reports by WHO

(2009, 2010, 2011, 2012) indicate that in developing countries malaria is the fourth leading cause of childhood mortality resulting in 8% of deaths worldwide.

Kim *et al*. (2012) reported that the estimated global incidence of malaria in 2009 was 225 million cases. In 2010, there were an estimated 216 million cases of malaria and approximately 81% were estimated to occur in African region (WHO, 2011). The reports from the World Malaria Reports indicate that approximately 700,000 people die every year from malaria infection (WHO, 2012). In 2010, an estimated 655,000 malaria deaths were reported and 91% occurred in Africa (WHO, 2012). About three-quarters of all malaria related deaths are affecting African children (Breman, 2001). However, since 2000, the global malaria incidence has declined by 17% and malaria-specific mortality rates by 26% (WHO, 2012).

The incidence of malaria as reported to the South African National Department of Health in 2012 was: Mpumalanga Province, 56.2 cases per 100,000 population at risk; Limpopo Province 31.1 cases per 100,000 population at risk; and KwaZulu-Natal Province 3.3 cases per 100,000 population at risk (source: Heath System Trust website http://www.hst.org.za/content/health-indicators accessed 12 October 2013). Nevertheless, these are subject to increase due to the issue of imported cases from malaria endemic African countries.

Malaria is a parasitic vector-borne disease caused by the parasite species *Plasmodium falciparum, P. vivax, P. ovale* and *P. malariae* (Jackson *et al*., 2010). However, *P. falciparum* is the one that leads to severe cases and malaria deaths and is the most common species in Africa (Jackson *et al*., 2010). The species *P. vivax* is primarily the cause of

malaria in densely populated areas of Asia (Jackson *et al*., 2010). The species of *P. ovale* and *P. malariae* are less common and cause less severe malaria (RBM/WHO/UNICEF, 2005).

Malaria parasites are transmitted by female mosquito vectors of the genus *Anopheles*. In Africa, there are approximately 140 species of anopheline mosquitoes but only four are major vector species. These species are *Anopheles funestus, An. arabiensis, An. coluzzii* and *An. gambiae* (Gillies & Coetzee, 1987; Coetzee *et al*., 2013).

In countries where malaria has been reported to be endemic, climatic factors (temperature, rainfall and humidity) have been reported to contribute to the high number of mosquito populations (Jackson *et al*., 2010). This makes the transmission more favourable for the malaria parasites. Mabaso *et al*. (2006) conducted a study that quantified and predicted the effect of rainfall, vapour pressure and temperature on the incidence of malaria in Zimbabwe. The findings indicated that rainfall and vapour pressure coincided with increased malaria incidence (Mabaso *et al*., 2006).

1.2 The life cycle of malaria

The life cycle of malaria involves the human host and mosquito vector. The mosquito vector injects parasite sporozoites into the blood stream of a human host during feeding. The sporozoites invade the liver (hepatocytes) and this is where they develop into preerythrocytic schizonts. The preerythrocytic schizonts contain 10,000 to 30,000 merozoites which get released into the blood circulation and invade erythrocytes. The merozoites within the erythrocytes develop through the process of erythrocytic schizogony

to ring, trophozoite and schizont stages. The erythrocyte harbouring schizonts (containing newly formed merozoites) ruptures and release more merozoites that invade more new erythrocytes.

Concurrently, some of the merozoites within the newly invaded erythrocyte differentiate into sexual macrogametocyte (females) and microgametocyte (males) forms. During the blood feeding by *Anopheles* mosquitoes, the mature macrogametocytes leave the erythrocytes (taken into the gut) to form macrogametes. Microgametocytes on the other hand develop flagella and migrate quickly to fertilize the macrogamete forming a zygote. The zygotes then transform into ookinetes that move to reach the extracellular space in the midgut epithelium of the mosquito. This is where the ookinetes transform into oocysts that contain sporozoites which migrate to the salivary gland and the transmission goes on (Hisashi & Masamichi, 2002).

1.3. Description of the malaria epidemiology in South Africa

According to Blumberg & Frean (2007), approximately 4.3 million people are at risk of contracting malaria in South Africa. From the year 2000 to 2009, there was a drastic reduction in malaria case notifications from 61,934 to 6040 due to good malaria control initiatives (Kift *et al*., 2011). The KwaZulu-Natal province was noted to have the largest decline in the number of malaria cases in 2010 (Maharaj *et al*., 2012). The malaria-associated mortality was also observed to have declined from 247 deaths in 2009 to 72 deaths in 2010 (Maharaj *et al*., 2012). However, Limpopo Province is still the largest contributor of high malaria incidence and mortality among the three endemic provinces

(Maharaj *et al*., 2012). The malaria cases were reported to have decreased by 82.3% (12390 versus 2187) from 2000 to 2010 in Mpumalanga Province (Moonasar *et al*., 2012).

When these figures were studied at the level of the sub-district of each province, considerable reduction in malaria cases were also observed (Moonasar *et al*., 2012). The Umkhanyakude, Utungulu and Zululand sub-districts of KwaZulu-Natal were recorded to, have a 99% reduction of malaria cases (Moonasar *et al*., 2012). The percentage of deaths was also seen to dramatically decrease by a range of 75% to 96.4% (Moonasar *et al*., 2012).

While malaria cases in the Bushbuckridge sub-district of Mpumalanga was seen declining, deaths were reported to increase (Moonasar *et al*., 2012). This was mainly attributed to late reporting to health facilities by patients. Nevertheless, Nkomazi sub-district in this province was reported to have 89.1% reduction in malaria cases from 2000 to 2010 (Moonasar *et al*., 2012). The lowest declines in malaria cases of 53.1% and 48% were also reported for Vhembe and Mopani sub-districts of Limpopo Province, respectively (Moonasar *et al*., 2012).

The incidence of malaria in South Africa currently is 0.71 cases per 1,000 population at risk (Kift *et al*., 2011). This has allowed South Africa to successfully move from control to the elimination stage of malaria (Kift *et al*., 2011). Nevertheless, the case fatality rate still remains at 0.76% for over a decade now and this is above the 0.5% WHO target for elimination (Weber *et al*., 2010).

1.3.1 Determinants of malaria transmission

Since malaria is a vector-borne infectious disease, environmental factors affecting mosquitoes remain the major determinant of transmission (Texier *et al*., 2013). The combination of three factors is required for malaria transmission: the presence of female mosquito vectors, human host and the plasmodial parasites (Lawpoolsri, 2009). This triangular relationship demonstrates the contribution of each stage to the transmission of the diseases. In other words, there are factors that relate to each organism individually in order for the transmission to occur (Ehrlich *et al*., 2007). At the level of the human host, the intrinsic factors that could lead to high malaria transmission involve host susceptibility, immune system or socio-economic status (Lawpoolsri, 2009). The parasites always need to be present to cause the malaria disease. The factors that could increase its existence include genetic modification and resistance to medication (Lawpoolsri, 2009).

The mosquito vector is favoured by climatic or environmental factors which speed up its reproduction and growth. These could be factors like rainfall, temperature, humidity, vegetation, soil quality, altitude, surface water pooling (irrigation) and hydrology (Lawpoolsri, 2009). All these factors favour the increase in mosquito density, longevity and vectorial capacity. For example, rainfall and temperature determines humidity which increases mosquito survival (Craig *et al*., 2004).

Rainfall and agricultural irrigation provide surface water pools which are very good breeding sites for mosquitoes (Craig *et al*., 2004). The vegetation provides suitable habitats for mosquitoes thus increasing their life span/survival (Craig *et al*., 2004). The warmer temperatures increase the development of both the *Anopheles* mosquito and *Plasmodium* parasites (Jackson *et al*., 2010). The fast development of the *Plasmodium* parasites

harboured by infected *Anopheles* reduces the duration of the extrinsic cycle of malaria (www.cdc.gov cited in Jackson *et al*., 2010). Thus, in essence, all these factors affect the mosquito vectorial capacity (i.e. the number of new infections produced by a mosquito per person per day). This, therefore, determines the high transmission of malaria and an increased malaria incidence.

1.3.2 Malaria distribution

The transmission of malaria differs greatly with time (Craig *et al*., 2004). The malaria incidence rates are strongly affected by environmental factors that tend to differ from time to time through the year (Zacarias & Andersson, 2011). The changing seasons with their concomitant changes in rainfall and temperature lead to the change in vector populations, development of the parasites and thus malaria transmission. The transmission also differs with respect to spatial scales (Craig *et al*., 2004) and is not the same across all geographical regions showing variation in malaria incidence (Zhou *et al*., 2007).

The epidemiology of malaria could be described according to person exposed, place and time of high occurrence.

(i) Place

Malaria is endemic in low-altitude areas of eastern and northern parts of South Africa along borders of Mozambique and Zimbabwe (Blumberg & Frean, 2007). Therefore, the transmission occurs mainly in Limpopo, Mpumalanga and north-eastern KwaZulu-Natal Provinces (Blumberg & Frean, 2007). There are occasional cases that have been reported in the North West Province along the Molopo River (SADOH, 2010). Mpumalanga

Province alone has been reported to contribute about 44% of malaria notifications in the whole country (Ngomane & de Jager, 2012).

(ii) Time

The transmission of malaria is seasonal in South Africa with transmission occurring during the summer season (between September to May) and the greatest transmission peak observed around March of every year (SADOH, 2010).

(iii) Person at risk

About 4.9 million of the South African population live in malaria risk areas (SADOH, 2010). South African residents are not immune to malaria and therefore at high risk of developing severe malaria (SADOH, 2010). In malaria occurring areas in South Africa, all age groups, travellers and immigrants are susceptible to malaria (Blumberg & Frean, 2007). It has been indicated that children under five years of age and pregnant women are more at risk of getting complications from malaria (SADOH, 2010). The increased prevalence of severe malaria has been documented among HIV-positive patients with CD4 counts less than 200 x 10^6 cells/l in South Africa (Cohen *et al*., 2005; Grimwade *et al*., 2004). This suggests that HIV/AIDS patients are also a high risk group of getting severe malaria.

1.4. The control of malaria in South Africa

The important control intervention strategies in South Africa include vector control, case management, disease surveillance, epidemic preparedness and response, malaria advocacy and information, education and communication (Blumberg & Frean, 2007). Cross-border

initiatives are also very important for the control of malaria in South Africa, for example the Lubombo Spatial Development Initiative (LSDI).

1.4.1 Vector control

This intervention strategy involves the indoor spraying of houses (IRS) with residual insecticide such as DDT, long lasting insecticide treated nets (LLINs) and larval control in malaria affected areas (WHO, 2012). According to WHO (2012), vector control remains one of the most efficient strategies for decreasing malaria and interrupting transmission.

(i) IRS

The success of indoor residual spraying strongly depends on mosquitoes biting humans when resting/asleep indoors (Blumberg & Frean, 2007). After taking a blood meal, some of these vectors settle and rest on the inner walls of the house. This is particularly true for *An. funestus* and *An. gambiae* (Coetzee, 2005; Blumberg & Frean, 2007). *Anopheles arabiensis* however, has a wide range of behaviours that does not necessarily include indoor resting (Blumberg & Frean, 2007). This species feeds on humans and rests indoors but will also feed on cattle and rest outdoors making it far hard to control using conventional means (Coetzee, 2005). The IRS reduces the survival time of mosquitoes and reducing the number of infectious mosquito bites each person received per unit time (WHO, 2008). This results in a decrease of the number of malaria transmitting mosquitoes and therefore reduces transmission.

(ii) LLINs

Long-lasting insecticide treated nets (LLINs) cover resting or sleeping people and as such provide personal protection so that they don't get bitten by mosquitoes (WHO, 2008). This

reduces the rate at which humans are bitten by infective mosquitoes (WHO, 2008) and thus reduces the transmission of malaria.

(iii) Larval control

The IRS and LLINs are very effective for indoor resting mosquitoes (WHO, 2008). However, for the most effective malaria control, it is important that outdoor resting and biting mosquitoes are also controlled. Reports indicate that the reduction in *An. funestus* and *An. gambiae* raises concerns that there might be a statistically significant increase in *An. arabiensis* (Blumberg & Frean, 2007). The larval control is more effective for exophilic and exophagic (outside resting and feeding) *An. arabiensis* (Devine & Killeen, 2010). Larval control involves applying chemicals to immature mosquito breeding habitats (Devine & Killeen, 2010). This technique assists by reducing the mosquito abundance in the environment. Reduction in these factors leads to reduction in the number of surviving mosquitoes thus reducing the entomological inoculation rates and malaria infection.

1.4.2 Case management

This arm of the intervention strategy involves accurate diagnosis of the disease and the use of effective antimalarial medicine to clinically cure and reduce malaria transmission (Blumberg & Frean, 2007). However, the selection of the chemotherapy strongly depends on disease severity, suspicion of drug resistance, parasite species and patient characteristics (Blumberg & Frean, 2007). In South Africa, for the acquired uncomplicated malaria, the artemether-lumefantrine (Coartem^{R}) or the alternative of quinine plus doxycycline or clindamycin are recommended for treatment. The quinine treatment with the addition of

doxycycline or clindamycin for severe malaria is also recommended (South African National Department of Health malaria treatment guidelines, 2007). These medicines when used at the early stage of malaria are very effective in case management (Blumberg & Frean, 2007).

1.4.3 Malaria disease surveillance in South Africa

Malaria has been a notifiable disease in South Africa since 1956 with all cases detected legally required to be reported to health authorities (Moonasar *et al*., 2012). This means that an accurate sensitive well-validated surveillance system is very important to keep track of transmission trends and predict unusual increase in malaria confirmed cases (Teklehaimanot *et al*., 2004). The notified case reports are sent to the District Health Department where analysis is performed through the District Health Information System (DHIS) (Moonasar *et al*., 2012). However, the DHIS data entry is slow so a Malaria Information System is used in South Africa in each of the malaria endemic provinces (Moonasar *et al*., 2012). In order to optimally perform key functions, the surveillance programme must possess specific attributes.

The surveillance system needs to provide active case detection and early alerts about any substantial increase in malaria cases (Teklehaimanot *et al*., 2004). Secondly, surveillance system needs to be timely (immediate reports), sensitive (reliable report of excess malaria cases) and specific (few false positive reports) (Teklehaimanot *et al*., 2004). Thirdly, the system needs to reflect continuous monitoring of malaria cases. Finally, the system needs to be involved in malaria case investigation and clear case definition, malaria surveys and

meteorological monitoring (Barclay *et al*., 2012). These attributes enable malaria control and elimination workers and public health officials to effectively control malaria through screening of cases and monitoring epidemics.

1.4.4 Epidemic preparedness and response (EPR)

This aspect of control is very important for enabling the health system to be fully prepared for malaria outbreaks and epidemics (SADOH, 2010). This will assist because prompt and fast effective interventions would be available in case of malaria epidemics (SADOH, 2010).

1.4.5 Health Promotion/Malaria Advocacy

The early presentation of malaria cases to the health facility has been reported as the best way to significantly reduce malaria morbidity and mortality in South Africa (Blumberg & Frean, 2007). The health promotion strategy supports the main malaria control interventions and involves the encouragement of health-seeking behaviour, treatment adherence and use of malaria prevention methods (Moonasar *et al*., 2012). This strategy also assists communities to recognize malaria signs and symptoms and encouraging them to seek medical attention immediately (Moonasar *et al*., 2012). The use of counselling sessions in health facilities about malaria complications, use of mass media campaigns, community outreach and education could be of assistance (Moonasar *et al*., 2012).

1.4.6 Information, education and management (IEC)

Early effective malaria case diagnosis and treatment is one of the most important cornerstones of malaria control (Blumberg & Frean, 2007), so the dissemination of information to the public is very critical to attain effective control. The IEC makes certain that the early important information reaches the public. This can be done through radio broadcasting or health workers malaria communications to the public (Hlongwana *et al*., 2011). Studies have reported that improved community knowledge regarding malaria and its mode of transmission improves malaria prevention (Hlongwana *et al*., 2011). Further studies have demonstrated that lack of community education, particularly on malaria signs, symptoms and control could threaten interventions (Hlongwana *et al*., 2011). The seeking of medical attention immediately by patients when suspecting malaria could reduce the period of infectiousness.

1.5 Historical progress on malaria elimination in Africa

The impact of malaria control since 2000 in some African countries has shown a significant reduction in malaria confirmed cases and deaths (WHO, 2011). Algeria, Botswana, Cape Verde, Namibia, Rwanda, Sao Tome and Principe, South Africa, Swaziland and United Republic of Tanzania have all shown a greater than 50% reduction in malaria confirmed cases and deaths (WHO, 2011). The above countries including South Africa, passed the stage of malaria control and have entered the stage of malaria elimination by 2020 (known as Malaria Elimination 8 (E8) (WHO, 2011)).

1.6 Imported malaria cases

Reports have shown an increase in the number of travellers between non-endemic and endemic malaria regions (Weber *et al*., 2010). In 2005, an estimated 1,256,000 nationals from mainland Africa entered South Africa (WHO, 2008). The majority were reported to come from 45 malaria endemic countries that are within the WHO-AFRO region (WHO, 2008). Labour-related opportunities and vulnerable population displacements through wars or impoverishment are major causes (Weber *et al*., 2010).

The influx of malaria-infected travellers from high transmission to low transmission areas each month or year determines the vulnerability of that place (Le Manach *et al*., 2011; WHO, 2007). It is also reported that each case imported presents a high risk of epidemics, outbreak initiation or local transmission in high receptivity areas (WHO, 2007). In South Africa, Mpumalanga Province reported that imported cases were at least double the local cases (Maharaj *et al*., 2012). The proportion of imported malaria cases in South Africa has been recorded as increasing (80% in 2011) (Maharaj *et al*., 2012).

1.7 Spatial and spatio-temporal detection of disease clusters in epidemiology

The use of spatial and spatio-temporal analysis in epidemiology has been increasingly applied in recent years (Elliot *et al*., 2000). The detection of significant clusters in space and/or time is also one of the most important exploratory methods employed in epidemiology and public health (Alexander *et al*., 1996; Hjalmars *et al*., 1996). The spatial, temporal and space-time scan statistics are nowadays mostly used tools in epidemiology to detect and evaluate statistically significant clusters of diseases (Sartorius *et al*., 2010). The space-time scan statistic software called SaTScan^{TM} can be used to analyse these methods

(Kulldorff *et al*., 1998). This software is widely used in many applications that include epidemiology and many other research disciplines (Sartorius *et al*., 2010).

1.8. Statement of the problem

The biological relationship discussed above regarding malaria transmission and environmental conditions led to numerous studies being conducted. Many of these have been done to model the spatio-temporal relationship between the environmental conditions and malaria incidence at the continental level (e.g. Mabaso *et al*., 2007). Others have been done at the country, provincial and district level (Ngomane & de Jager, 2012; Jackson *et al*., 2010; Coleman *et al*., 2009; Mabaso *et al*., 2006). In South Africa, however, there is cross-border movement of workers and tourists to and from malaria endemic countries like Mozambique that complicates the malaria picture.

The definition of malaria elimination states that the local mosquito-borne transmission has been interrupted such that the incidence of malaria infection caused by human malaria parasites in a defined geographical area as a result of deliberate efforts is reduced to zero. Nevertheless, the continued effort measures to prevent any possible re-establishment of the transmission still need to be strictly considered (WHO, 2011). While South Africa would like to become a WHO certified "malaria free" country, there is still the problem of failing to differentiate between imported and local malaria cases reported. It is fundamentally important that a clear distinction between local and imported cases is made.

1.9 Justification for the study

Studies that include mapping of malaria incidence have been conducted in malaria endemic provinces of South Africa. However, almost none investigated the correlation between environmental conditions and malaria incidence around a particular health facility. None has also investigated whether the observed malaria cases are due to environmental surroundings or are imported cases from other malaria endemic areas. This study therefore provides a relationship between malaria cases per health facility and environmental condition surrounding that facility. It also attempts to disentangle the local and likely imported cases around a particular health facility using environmental conditions as proxy measures.

This is fundamental to E8 and public health policy makers because a clear understanding of the distinction between local and likely imported cases is imperative. Sometimes the observed malaria cases might be mistakenly considered as local cases while they are imported cases. Studies indicate that local cases in South Africa could be attributed to changes in weather conditions (e.g. increased rainfall and temperature). This suggests that occurrence of cases discordant to changes in weather conditions might indicate likely imported cases. So, this will assist South African health system authorities to be able to distinguish between local and imported cases. Therefore, policy planning regarding malaria elimination could be directed either to passing strict migration laws or environmental monitoring.

1.10 Literature review

In the current literature, a lot of studies that assess the effect of climatic change or environmental conditions on the prevalence of malaria in Africa have been reported. Jackson *et al*. (2010) conducted a study to model the effect that climate change has on the prevalence of malaria in western Africa. They used rainfall, temperature and humidity as their variables for modelling and determining correlation. The correlation was obtained and the conclusion was that the climate change had an effect on malaria prevalence (Jackson *et al*., 2010). This was one of the studies that were conducted in malaria endemic areas. Nevertheless, the correlation obtained was at the country level not at the health facility level.

It has also been indicated that climatic changes are positively associated with increased risk of vector-borne diseases that includes malaria (Kearney *et al*., 2009). Other studies associated increase mosquitoes with malaria rates (CDC, 2004). Rogers & Randolph (2000) conducted a study that modelled the distribution of *P. falciparum* and climate change. Their model was highly sensitive to detecting the relationship between climate variables and their impact on malaria transmission. Their findings indicated remarkably few changes and strong relationship between these two variables. This study only focused on the transmission of the parasite in new places at the global level and again not at health facility level.

Mabaso *et al*. (2006) conducted a study of the spatio-temporal analysis and the role climate played in inter-annual variation in malaria incidence in Zimbabwe. The mean average temperature, rainfall and vapour pressure were strong positive predictors of increased annual malaria incidence (Mabaso *et al*., 2006). In other words, these environmental

variables increased the incidence of malaria. This study was conducted among children under the age of five years positive for malaria disease in 58 districts in Zimbabwe. This study demonstrated a very good relationship between malaria occurrence and climatic conditions. However, the authors did not demonstrate this relationship at the level of the health facility. According to Mabaso *et al*. (2006), in southern Africa very few studies that assess the relationship between malaria and climatic factors have been published.

Zacarias & Andersson (2010) conducted a study to investigate an association between malaria incidence and weather parameters in tropical Maputo province, Mozambique. This study was conducted to compare malaria incidence in dry and wet seasons. In wet seasons, malaria transmission was shown to be high and in winter seasons no association was observed. Nevertheless, these scholars did not attempt to take into consideration health facilities as well.

Coleman *et al*. (2009) conducted a study using the SaTScan method to detect local malaria clusters to guide malaria control programmes in Mpumalanga Province, South Africa. This was a very good malaria case cluster study at the level of the district and using cases collected from local health facilities. However, Coleman and colleagues did not consider the issue of imported cases due to immigration from neighbouring malaria endemic countries.

All these studies demonstrated a positive relationship between malaria incidence/occurrence and climatic/environmental conditions and that is not surprising. Authors in these studies looked at this relationship at the country, province, districts and some health facility level. However, none of the authors attempted to disentangle imported

malaria cases from endemic ones using environmental conditions as proxy measures. This study is not only particularly important to South Africa but also for many other southern African countries that are considering malaria elimination.

1.11 Research question, objectives and hypothesis

1.11.1 Research question

There was a noticeable gap that included the lack of studies addressing malaria occurrence and climatic conditions at health facility level to disentangle imported cases from endemic cases. This gap led to the development of the research question to be answered by this study. This study assessed the correlation between environmental conditions and malaria incidence in a given health facility from each of the selected sub-districts of Mpumalanga Province. It also determined whether the reported malaria cases were attributed to migrants from other malaria endemic areas or not, using environmental factors as a proxy measures. Therefore, the research question was that is there a correlation between malaria incidence and environmental conditions around particular health facilities from each sub-district in this province.

1.11.2 Overall objective

The overall objective was to determine whether malaria incidence at given health facilities could be ascribed to local transmission (using rainfall and other environmental factors as proxy measures) or was likely to be imported.

Specific objectives:

- To describe the socio-demographic characteristics of the underlying population at risk by sub-district of Mpumalanga Province, South Africa, between 2001 and 2010
- To assess malaria annual incidence and trends at selected sub-districts in Mpumalanga Province between 2001 and 2010
- To summarize and construct maps of selected environmental conditions in the affected selected sub-district by month and year between 2001 and 2010
- To assess correlation between malaria incidence due to endemic cases and surrounding selected environmental conditions at selected sub-districts between 2001 and 2010
- To identify and quantify the relationship between malaria cases and environmental or climatic conditions between 2001 and 2010 to disentangle imported from local cases
- To identify any spatial and space-time clustering of malaria cases at the sub-district level between 2001 and 2010

1.11.3 Research hypothesis

It was hypothesized that there is a correlation between malaria incidence and environmental conditions around particular health facilities from each sub-district in Mpumalanga Province. Thus, any excess of malaria cases without an increase on temperature, rainfall and humidity would be considered as imported cases.

CHAPTER TWO

METHODOLOGY

Overview of the Chapter

In this Chapter, the description of Mpumalanga Province is provided. The type of the study design that was employed to answer the research question is presented. The study population of Mpumalanga Province where malaria data were obtained and study outcomes is discussed. Study procedures which included data collection, measurements of variables and data sources together with study limitations are reviewed. Data management, processing and statistical analysis techniques employed to answer the research question are presented. The Chapter ends by giving ethical considerations involved in the project.

2.1 Study setting

Mpumalanga Province is one of nine South African provinces. It lies in the eastern part of the country with an area of 76,495 km^2 (Figure 2.1). The population of Mpumalanga as reported by Stats SA census 2011 was at 4,039,939. The most spoken language is IsiSwati (27.7% of the population) followed by IsiZulu with 24.1% and 10.1% IsiNdebele (StatsSA, 2011). The black population forms the majority in the population of Mpumalanga. This province borders Mozambique in the east and Swaziland in the south. Mpumalanga Province is divided into high-lying grassland Highveld and subtropical Lowveld regions (http://www.sa-venues.com/weather/mpumalanga.htm, accessed 31 October 2012). The

Highveld experiences rains during the summer period (October to February/March) and winter from May to August. The temperatures average around 26°C in summer and 8°C in winter. The Lowveld subtropical regions have a rainy summer season from September to March (http://www.sa-venues.com/weather/mpumalanga.htm, accessed 31 October 2012). The rainfall averages at 620 mm between September and March and temperatures range from 17 – 30°C in summer and 8 – 17°C in winter (http://www.sa-venues.com/weather/mpumalanga.htm, accessed 31 October 2012). The relative humidity of the Lowveld region is about 80% in summer. The two regions of Mpumalanga Province are divided into three districts known as Ehlanzeni, Nkangala and Gert Sibande. These districts are also divided into eighteen local municipalities (sub-districts). The estimated number of health facilities from which malaria cases data were used in this study was ten per region.

Figure 2.1. Map of South Africa with Mpumalanga Province (shaded in grey) (source: http://www.info.gov.za/aboutsa/provinces.htm accessed 8 July 2013).

2.2 Study design

The study is a retrospective ecological correlation study design. This study assessed the correlation between environmental exposures and health facility based malaria incidence at the sub-district level. The study utilized secondary data for South African health facility based sub-district population estimates from Stats SA, Mpumalanga Provincial Department of Health (SADOH) (malaria cases), nearest weather stations and remote sense (satellite) data for Mpumalanga Province. The population risk estimates were calculated using malaria cases as a numerator and Statistics SA data or year census total population data for each sub-district as a denominator over ten years (2001 - 2010). The daily records of rainfall and temperature from nearest weather stations were added to calculate monthly records. The monthly records were aggregated according to specific months making the season. For example, from mid-October to mid-February was considered a summer season. The rainfall, temperature and relative humidity data obtained were collected from Nelspruit, Lydenburg, Witbank and Ermelo weather stations. The time at which these data were measured was from 8:00 am till late in the afternoon daily. Remotely sensed data were extracted from CRU - TS 3.0 for nearest satellites information to health facilities. The remotely sensed satellite data were based on satellite information and not on physical measurements. These data were extracted for regions of Mpumalanga Province of South Africa.

2.3 Study population

The study populations comprised residents of Ehlanzeni, Gert Sibande and Nkangala Districts staying in the vicinity of selected health facilities. The Sekhukhune District was put under Limpopo Province in 2004 and moved from Mpumalanga Province. It is

therefore not included in all the analysis and it only appear on descriptive summary of demographics. The total population of Ehlanzeni, Gert Sibande and Nkangala Districts in 2001 according to 2007 community survey census data was estimated to be 1,447,053; 900,007 and 1,018,826, respectively (StatsSA, 2007). At Ehlanzeni and Nkangala, it was reported to have increased to ±1,526,200 and 1,226,500 respectively in 2007 (StatsSA, 2007). The population of Gert Sibande was shown to have decreased to 890,700 in 2007. These data were obtained from Stats SA Community Surveys data for the period between 2001 and 2007. However, the population data used in this study was linearly adjusted to account for demographic changes in the province.

2.4 Study outcomes

The primary outcomes of this study were malaria incidence/intensity in the selected sub-districts around a particular health facility. The potential explanatory climatic variables that were used to answer the objectives were the rainfall, temperature and relative humidity over a ten year period of 2001 to 2010.

<u>Explanatory variables and data sources</u>

- Health facility – Mpumalanga Provincial DOH
- Month and year when cases were diagnosed – Mpumalanga Provincial DOH
- Monthly rainfall – South African Weather Services
- Monthly temperature – South African Weather Services
- Monthly relative humidity – South African Weather Services
- Mpumalanga District Population data as a denominator – Statistics South Africa

Outcome variable

- Malaria cases – Mpumalanga Provincial DOH

2.5 Study procedures

2.5.1 Data collection

The study utilized secondary data obtained from Mpumalanga Provincial Health Department, Stats SA, Nelspruit weather stations and remotely sensed satellite data. No primary data collection was done by the investigator in this study since this is a secondary data analysis study.

(i) Malaria data

Malaria data were received and contained case numbers, age, diagnosis date, death status, place of residents, gender, country, district, health facility name and date of diagnosis grouped by month and year. These data were then process, cleaned and merged using STATA IC 12.0.

(ii) Climatic data

The climatic records data for the period 2001 to 2010 were obtained from the South African Weather Service. The records consisted of individual monthly rainfall (mm), individual monthly temperature (^{o}C) (both minimum and maximum) and individual monthly relative humidity (%) in months and grouped by year. The monthly rainfall must be bigger than 80 mm to be suitable for malaria transmission. The mean temperature must

range between 18 and 32^{o}C and monthly relative humidity greater than 60% (Bruce-Chwatt 1988).

(iii) Remotely sensed satellite data

The remotely sensed data were extracted from the global Climatic Research Unit (CRU) - TS 3.0 time series data (http://www.cgiar-csi.org/data/uea-cru-ts-v3-10-01-historic-climate-database) using R 2.15.3 software. The extracted data were mean monthly minimum and maximum temperature (^{o}C), precipitation/rainfall (mm) and vapour pressure (hecta-Pascals). These are gridded data set that has been collected and available by month of each year since 1901 to 2009. The spatial resolution that was used for the data set extracted for this project was estimated to be approximately 30 km.

2.5.2 Measurements and data sources

Data that were utilized were health facility based malaria case data for the past 10 years (2001 - 2010). Explanatory variables of interest that were used were average monthly rainfall, temperature and humidity. All these variables were numerical. The denominator used was the total population of each district of Mpumalanga Province. These data were obtained from the Statistics South Africa Community surveys of 2001 and 2007. The monthly average rainfall measurements, maximum and minimum temperatures and humidity were used to estimate seasonal time measurements. Seasonality was addressed by creating one dummy variable for a year and one for a month over a ten year period.

Malaria symptoms in adult patients included cases that presented with fever, headache, rigors, myalgia, dizziness and weakness, loss of appetite, diarrhoea sore throat and

vomiting. Among children, fever, vomiting, weakness, lethargy, diarrhoea, cough and poor feeding were symptoms of malaria. The clinical signs in adults and young patients were fever, splenomegaly and/or hepatomegaly for uncomplicated malaria. Fever, severe prostration, splenomegaly and/or hepatomegaly, pallor, jaundice, increased respiratory rate, change in the level of consciousness, reduced urine output, bleeding and shock were symptoms for severe malaria (South African National Department of Health malaria treatment guidelines, 2007). Malaria could not be diagnosed solely on the basis of clinical findings so laboratory diagnosis was performed to confirm cases. Malaria confirmed cases included cases that were positive for RDTs and/or laboratory confirmed microscopic examination.

2.6 Data processing methods and analysis plans

2.6.1 Data management and processing

The statistical software STATA IC version 12.0 was used for all data management, processing and analysis. Data from primary sources were converted to STATA IC 12.0 format for processing and analysis. The remotely sensed data were extracted using R 2.15.3 computer software. The extracted data were then written or exported to excel from R format. The malaria cases, rainfall and temperature data were expressed as monthly unit of time to capture annual unit. The merging of malaria cases data with weather data was done using the district, year and month variables as unique identifiers. The management and processing of data included cleaning and generation of variables. The cleaning of data was done by combining data sets that were separated. The data sets were separated by year and month and were all combined into one dataset.

2.6.2. Data analysis

The analysis comprised descriptive summary statistics for socio-demographic details (means or medians, standard deviations or inter-quartile ranges for numerical data and proportions and percentages for categorical data). Analysis of variance for continuous/numerical variables was used to determine the differences in mean rainfall, temperature and humidity across all the months. The Kruskal Wallis non-parametric test was used in case ANOVA was not suitable for the analysis. The Chi-square test of associations was used to determine associations among categorical variables. The Fisher's exact test was used in cases where the Chi-squared was not suitable for the analysis. The cumulative malaria incidence was computed by dividing the number of health facility-based malaria cases per year by total population at risk around the health facility. The 95% confidence interval was computed using exact Poisson limits to estimate the baseline incidence of malaria in the selected sub-districts. The Chi-square test of trends of cumulative incidence over time was performed to assess linear temporal trends by year.

MapInfo Professional 9.5 software was used to develop maps of malaria incidence over time by sub-district selected and health facility. The Pearson correlation co-efficient was used to assess for significant correlations between malaria cases and environmental conditions at the district and monthly level.

A negative binomial was used for all risk factor analysis and re-run for the year dummy model. The significance level was assessed at the 5% level (where alpha is equal to 0.05). The univariate and multivariate Poisson regression model was used to identify and quantify factors significantly associated with malaria risk. The model assumptions were assessed and if there was evidence of over dispersion (variance bigger than the mean), thus the

negative binomial approach was used. In case where the variables were collinear (r bigger that 0.60), they were removed from the model. A univariate and multivariable modelling approach was used. This was performed to assess the relationship between malaria incidence and climatic conditions when other potential confounders are controlled for. Those factors that were significant at a 0.15 level in the univariate analysis were included in the multivariable model. The general of form of the Negative Binomial regression takes the formula: $Log_eY = \beta_0 + X_1\beta_1 + X_2\beta_2 \ldots X_p\beta_p$. This then translate to $Y = (e^{\beta 0})\ (e^{X1\beta 1})\ (e^{X2\beta 2}) \ldots (e^{Xp\beta p})$. The incidence risk in the exposed divided by the incidence risk in the non-exposed defined the estimated incidence risk ratio (IRR). It is calculated using the formula: IRR = Incidence Risk in the exposed (R_1)/Incidence Risk in the unexposed (R_o). The model goodness-of-fit was checked using suitable diagnostic methods (i.e. fitstat). Local and imported malaria cases were disentangled by assessing malaria distribution by season and related climatic data. The increase in the number of cases for a particular season unrelated to climatic conditions surroundings meant that the increase was more likely to be imported.

The Kulldorff spatial and space-time scan statistic was used to identify significant clusters of malaria overall and by year (month) (Kulldorff, 1997). This statistical technique places circular windows on the map which their centres move across the study districts. These circles could contain different sets and number of sub-districts. Each of these circles represents a potential cluster of overall malaria by year around a particular health facility. This spatial scan statistics calculates the probability/likelihood of observing the number of malaria cases inside and outside each circle. The circle with the maximum likelihood represents most likely cluster that did not occur by chance (Kulldorff, 1997). The Poisson based model was used in this analysis. The SaTScan provides the most likely cluster

together with its p-value and the significant level was set at 5%. The other clusters (i.e. secondary, tertiary etc.) that did not overlap with the most likely cluster were also indicated if obtained. The software SaTScan was used to perform the spatial clustering analysis (http://www.satscan.org). The computer software ArcMap 10 (ArcGIS 10) was used to draw maps of significant clusters identified by SaTScan software.

2.7 Ethical considerations

The study was reviewed and approved by the School of Public Health assessor groups and the Faculty of Health Sciences of University of the Witwatersrand (approved on: 21/08/12).The ethical clearance was sought from and granted by Human Research Ethics Committee of the University of the Witwatersrand. The ethical clearance was granted on 31/08/12, the reference number was R14/49 and clearance certificate was M120853. The project protocol and ethical clearance certificate were sent to Mpumalanga Provincial Department of Health to apply for ethical clearance to use malaria data. Access to the DoH malaria case data was authorized by the Malaria Programme Managers for each sub-district and the ethical approval was sought from the HREC of the University of the Witwatersrand, South Africa. The DoH malaria case data did not have any patients' names therefore it was anonymous and confidentiality was maintained as confirmed by Malaria Programme Managers. The data security was ensured by the use of access password.

CHAPTER THREE

RESULTS

Overview of the Chapter

This chapter will present the findings obtained from the analysis performed with the data used. This section will be separated into two parts, the first part demonstrating findings of the relationship between malaria incidence and climatic conditions utilizing weather stations data and the second part showing the findings of the relationship between malaria incidence and climatic conditions utilizing remotely sensed data. The description of the study population, trends in annual incidences and spatial analysis in the form of a map will be presented. The correlation between incidences and environmental or climatic conditions will also be shown. Disentangling of imported and local cases and the inferential statistical analysis (univariate and multivariate approach) will be presented. At the end of the chapter, the space and space-time analysis of data will be illustrated.

3.1 Part 1: Analysis using weather stations climatic data

3.1.1 Description of socio-demographic characteristics of the study population

The socio-demographic characteristics of the study population by district are presented in Table 3.1. The mean (standard deviation) age was 25.63 (15.67), 30.15 (14.03), 29.06 (17.06) and 29.06 (16.17) years for Ehlanzeni, Gert Sibande, Nkangala and Sekhukhune Cross Boundary Districts, respectively. In a total of 21,586 males, 98.47% were from Ehlanzeni, 0.75% from Gert Sibande, 0.38% from Nkangala and 0.40% from Sekhukhune

Cross Boundary. The total number of females was 15,651 and 99.07%, 0.48%, 0.21% and 0.24% were from Ehlanzeni, Gert Sibande, Nkangala and Sekhukhune Cross Boundary, respectively. The number of reported malaria cases for 2001 to 2010 was 37,237 and about 99% comes from Ehlanzeni District. There were 245 health facilities that were involved in reporting malaria cases during the period 2001 to 2010. Approximately 88.57% were from Ehlanzeni, 6.12% from Gert Sibande, and 5.31% from Nkangala Districts. The Ehlanzeni District reported a high number of malaria deaths (about 96%) as compared to other two districts (Table 3.1).

Table 3.1. Description of socio-demographic characteristics of malaria reported cases by district in Mpumalanga Province, South Africa between 2001 and 2010

Variable	Districts				P-value
	Ehlanzeni	Gert Sibande	Nkangala	Sekhukhune Cross Boundary	
Population size					
2001	944700	900014	1020590	221710	
2007	1526236	890699	1226500	221710	
Age					
N (%)	36761 (98.84%)	237 (0.64%)	107 (0.29%)	89 (0.24%)	
Mean (SD)	25.63 (15.67)	30.15 (14.03)	29.06 (17.06)	29.06 (16.17)	0.001[i]
Gender					
Males (%)	21256 (98.47%)	162 (0.75%)	82 (0.38%)	86 (0.40%)	0.001[j]
Females (%)	15505 (99.07%)	75 (0.48%)	34 (0.22%)	37 (0.24%)	0.001[j]
Number of health facilities					
N (%)	205 (83.67%)	15 (6.12%)	13 (5.31%)	12 (4.90%)	
Reported malaria cases					
N (%)	36761 (98.72%)	237 (0.64%)	116 (0.31%)	123 (0.33%)	
Reported malaria deaths					
Yes	184 (96.34%)	1 (0.52%)	3 (1.57%)	3 (1.57%)	0.003[h]
No	36577 (98.73%)	236 (0.64%)	113 (0.31%)	120 (0.32%)	0.003[j]

Statistical test used: i – ANOVA, j – Chi-squared test, h – Fisher Exact chi-squared test.

3.1.2 Assessing annual incidence and trends due to endemic cases in Mpumalanga over ten years

The annual incidence and trends of malaria cases reported in Mpumalanga Province over 10 years is shown in Table 3.2 and Figure 3.1. There is a reduction in the incidence of malaria from 2001 to 2010. The incidence of malaria decreased from 1,304 per 100,000 population at risk in 2001 to 136 per 100,000 population at risk in 2009 (Table 3.2). However, there was a small rise in incidence from 136 per 100,000 population at risk in 2009 to 201 per 100,000 population at risk in 2010. The trend of malaria incidence by month is also shown in Figure 3.2 below. In every month of each year, the incidence of malaria was always up at around 800 per 100,000 population at risk in January and decreased to 400 per 100,000 population at risk in February. The incidence levelled off between February and May. From May to September, the malaria incidence decreased noticeably from 500 per 100,000 population at risk to less than 100 per 100,000 population at risk. It started increasing again at the beginning of September and was around 250 per 100,000 population at risk in October.

Table 3.2. The annual cumulative incidence in Mpumalanga Province over time between 2001 and 2010.

Year	Incidence per 100, 000 population at risk	95% CI
2001	1304	1278 – 1330
2002	886	865 – 908
2003	483	467 – 498
2004	477	462 – 493
2005	227	216 – 238
2006	499	484 – 515
2007	212	203 – 221
2008	174	166 – 182
2009	136	130 – 143
2010	201	192 – 210

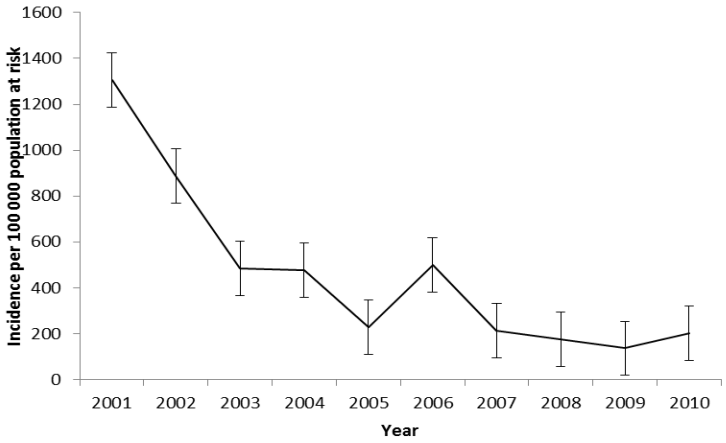

Figure 3.1. Cummulative incidence of malaria by year between 2001 and 2010, Mpumalanga Province.

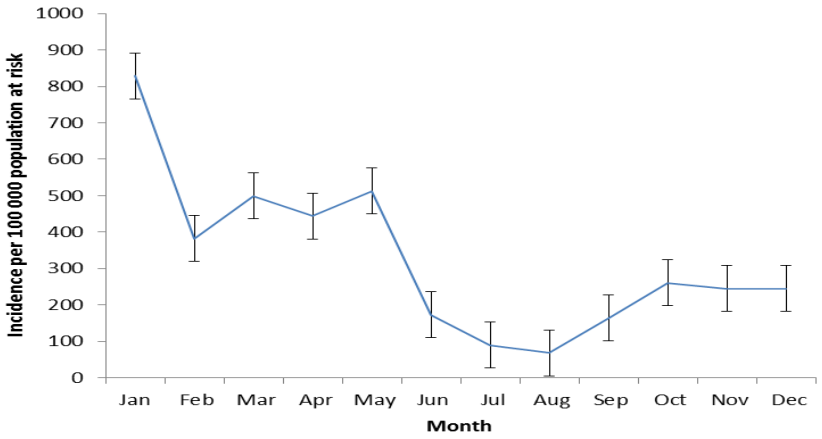

Figure 3.2. Cummulative incidence of malaria by month between 2001 and 2010, Mpumalanga Province.

3.1.3 The summary of selected environmental/climatic conditions

The summary of environmental conditions by month between 2001 and 2010 from Mpumalanga Province is shown in Table 3.3. The median maximum and minimum monthly temperature decrease from 26.2^{o}C and 15.5^{o}C in January to 18.8^{o}C and 5.1^{o}C in July, respectively. The median rainfall decreased from 4.2 mm in January to 1 mm in

September in all study years. The rainfall started increasing in October from 2.3 mm to 4.4 mm in December for all study years. The median monthly humidity exhibited a different trend. It started low at 82% in January, increased in March and April to 84%. The month of September had the lowest humidity of 64% as compared to other months in all study years. The minimum and maximum temperature, rainfall and humidity were significantly different in all months of the study period of Mpumalanga ($p<0.005$).

Table 3.3. The summary of selected environmental/climatic conditions in the affected selected sub-districts of Mpumalanga Province by month between 2001 and 2010.

Month	Maximum Temperature (°C) N Median (IQR)$^{\psi,k}$	Minimum Temperature (°C) N Median (IQR)$^{\psi,k}$	Daily rainfall (mm) N Median (IQR)$^{\psi,k}$	Daily Humidity (%) N Median (IQR)$^{\psi,k}$
January	1138	1138	471	1048
	26.2 (23.9 - 27.9)	15.5 (14.2 - 16.9)	4.2 (1.2 - 11.8)	82 (73 - 90)
February	1077	1079	371	961
	26.1 (24 - 27.9)	15.1 (13.6 - 16.6)	3.6 (0.8 - 10.8)	81 (73 - 89)
March	1176	1174	353	1058
	25.2 (22.9 - 27.2)	13.6 (11.9 - 15.3)	3.2 (0.6 - 8.4)	84 (75 - 91)
April	1186	1186	275	1065
	23.5 (21.3 - 25.4)	11.2 (9.5 - 13.2)	2 (0.4 - 4.8)	84 (75 - 92)
May	1229	1230	114	1104
	21.5 (19.4 - 23.3)	7.7 (5.7 - 9.8)	1.5 (0.4 - 6)	76 (61 - 88)
June	1177	1177	84	1059
	18.8 (16.7 - 21.1)	5.1 (3.2 - 5.1)	1.4 (0.25 - 5.4)	76 (61 - 87)
July	1185	1187	47	1064
	19 (16.6 - 21.3)	4.6 (2.2 - 6.4)	1.4 (0.2 - 5.8)	71 (55 - 83)
August	1178	1178	61	1048
	21.7 (19.1 - 24.4)	7 (4.8 - 9.3)	1.4 (0.6 - 6)	71 (49 - 84)
September	1183	1183	90	1061
	25 (21.6 - 27.7)	9.6 (7.6 - 11.7)	1 (0.2 - 2.8)	64 (44 - 78)
October	1232	1232	380	1098
	25.7 (22.3 - 28.4)	12.3 (10.7 - 14.1)	2.3 (0.4 - 9.3)	72 (59 - 83)
November	1120	1122	445	988
	25.4 (22.5 - 27.6)	13.7 (12.1 - 15.2)	3.7 (1 - 11.4)	77 (67 - 86)
December	1184	1185	489	1111
	26.1 (23.8 - 27.9)	14.8 (13.3 - 16.4)	4.4 (1 - 11)	77 (68 - 85)

ψ, k – Statistically significant at $p<0.05$ with Kruskal-Wallis test

3.1.4 Spatial analysis of the distribution of malaria cases

The spatial analysis for the distribution of malaria cases by sub-district of Mpumalanga is shown in Figure 3.3. The sub-district of high malaria risk was Nkomazi sub-district municipality. It was followed by Mbombela, Bushbuckridge and Umjindi sub-district municipalities. These are sub-districts located in the Lowveld regions bordering Mozambique and Swaziland and Mozambique is a known malaria endemic country.

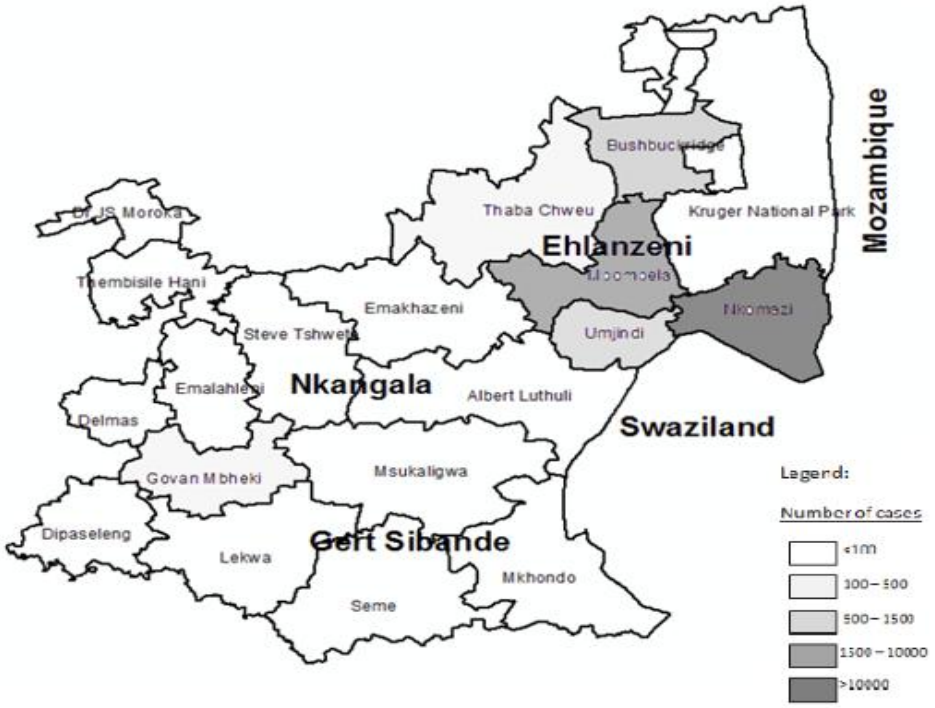

Figure 3.3. Spatial distribution of malaria cases by sub-district of Mpumalanga Province between 2001 and 2010.

3.1.5 Correlation analysis

The assessment of correlation analysis between malaria cumulative incidence and climatic/environmental conditions, district, month, year and seasonality is depicted in Table 3.4. All factors were statistically significant at 0.05 except for seasonality ($p>0.05$).

The minimum and maximum temperature, rainfall and humidity showed a positive correlation with malaria cases. Therefore, the increase in each factor led to an increase in the number of malaria cases. The variables district, month, year and season showed a negative correlation so the change in each factor led to a decrease in the number of malaria cases.

Table 3.4. Pearson correlation co-efficients for the correlation between monthly malaria cases and monthly climatic/environmental conditions for Mpumalanga Province between 2001 and 2010.

Variable	Cases	
	Correlation co-efficient (r)	P-value
Minimum temperature	0.2630	0.001
Maximum temperature	0.1916	0.003
Rainfall	0.1426	0.028
Humidity	0.4288	0.001

3.1.6 Disentangling imported cases from local cases

3.1.6.1 Disentangling imported cases from local malaria cases using the curves

The incidence risk ratio (IRR) for malaria in Mpumalanga Province between 2001 and 2010 is shown in Figure 3.4. The IRR fluctuated markedly between seasons from 0.89 in May to 0.38, 0.22 and 0.19 in June, July and August, respectively. The IRR started to increase from 0.29 to 0.45 between September and November during the study period.

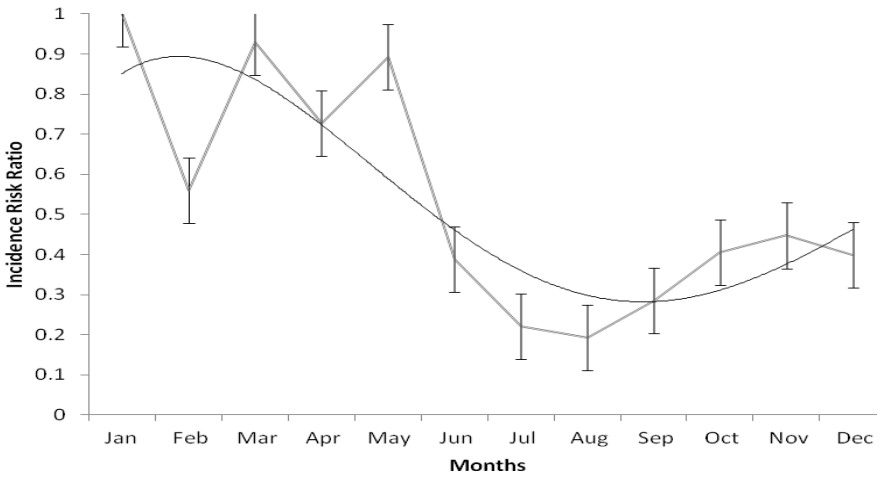

Figure 3.4. The Incidence Risk Ratio (IRR) of malaria by month in Mpumalanga Province between 2001 and 2010.

When disentangling local from imported malaria cases, the actual number of cases of malaria were also plotted by months over time in Figure 3.5. It was observed that from March to the end of June, the number of malaria cases exceeded the expected number (fitted line). The number of cases started to increase in August and exceeded the expected around September and October over time.

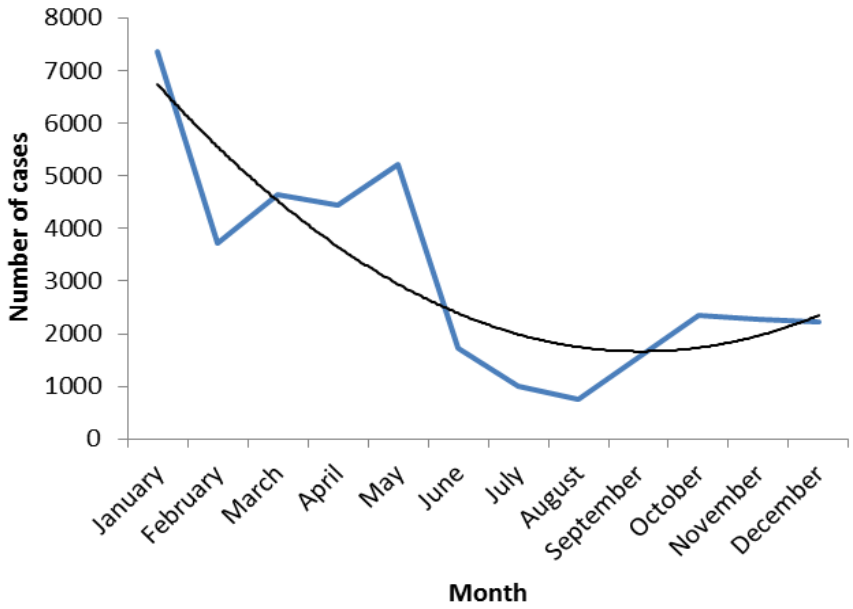

Figure 3.5. The number of malaria cases by month in Mpumalanga Province between 2001 and 2010

3.1.6.2 Disentangling local cases from imported malaria cases using the model prediction.

Given temperature, rainfall and humidity, the model computed the expected numbers of cases. In other words, these are theoretical cases that would have been seen under the conditions of the above mentioned variables over time. The positive numbers in the last column of Table 3.5 suggest excess from expected and the negative suggests less from expected. The Ehlanzeni District demonstrated an excess number of cases in three months. In January, May and June, 194, 1,752 and 104 cases were in excess of case expected, respectively.

Table 3.5. The observed and modelled expected number of malaria cases by District and month of Mpumalanga Province over time between 2001 and 2010.

District	Month	Actual observed malaria cases	Modelled expected number of malaria cases	Difference between observed and expected O – E*
EHLANZENI	**January**	**7218**	**7024**	**194**
EHLANZENI	February	3661	3998	-337
EHLANZENI	March	4612	8150	-3538
EHLANZENI	April	4382	6438	-2056
EHLANZENI	**May**	**5166**	**3414**	**1752**
EHLANZENI	**June**	**1718**	**1614**	**104**
EHLANZENI	July	981	1112	-131
EHLANZENI	August	749	2039	-1290
EHLANZENI	September	1542	1861	-319
EHLANZENI	October	2283	3543	-1260
EHLANZENI	November	2251	2962	-711
EHLANZENI	December	2198	5943	-3745
GERT SIBANDE	January	75	333	-258
GERT SIBANDE	February	34	269	-235
GERT SIBANDE	March	16	80	-64
GERT SIBANDE	April	30	214	-184
GERT SIBANDE	May	20	62	-42
GERT SIBANDE	June	16	37	-21
GERT SIBANDE	July	7	10	-3
GERT SIBANDE	August	3	7	-4
GERT SIBANDE	September	5	28	-23
GERT SIBANDE	October	14	86	-72
GERT SIBANDE	November	8	35	-27
GERT SIBANDE	December	9	41	-32
NKANGALA	January	32	92	-60
NKANGALA	February	11	90	-79
NKANGALA	March	4	25	-21
NKANGALA	April	15	33	-18
NKANGALA	May	10	24	14
NKANGALA	June	2	6	-4
NKANGALA	July	4	4	0
NKANGALA	August	1	5	-4
NKANGALA	September	11	24	-13
NKANGALA	October	10	50	-40
NKANGALA	November	11	40	-29
NKANGALA	December	5	64	-59

*The positive numbers indicate excess and negative numbers indicate less from expected

3.1.7 Regression or modeling analysis

3.1.7.1 Univariate negative binomial regression analysis

The unadjusted univariate Incidence Risk Ratios are shown in Table 3.6. When the effect of other factors was ignored, the minimum and maximum daily temperatures were significantly associated with malaria cases. For every $1^{o}C$ increase in minimum monthly temperature, there was a 14% increase in the risk of malaria infection and when maximum monthly temperature increase by $1^{o}C$, there was a 20% increase in malaria risk. As the difference between maximum and minimum temperature widen, there was a 0.79 times less likely risk of malaria.

The monthly rainfall and monthly humidity were both marginally significantly associated with malaria cases when the effect of other variables was ignored. These factors demonstrated that for every 1 mm and 1% increase in each one factor respectively, the risk of malaria increase by 1% for rainfall and 2% for the humidity, respectively (IRR = 1.01, 95%CI = 0.99 – 1.02; IRR = 1.02, 95%CI = 1.01 – 1.03). There was a 99% reduction in malaria risk at both Gert Sibande and Nkangala Districts as compared to Ehlanzeni District. Finally, when the time of the year was winter season, there was a 31% reduction in the risk of malaria as compared to summer season (Table 3.6). The risk of malaria was observed decreasing as the month and year variables changed (Table 3.6).

3.1.7.2 Multivariate Negative Binomial regression analysis

The variables minimum temperature, district, season and month were removed from the model due to multicollinearity. This means that these explanatory variables in the model are linearly related to each other, in other words, the combination of two or more

explanatory variables put together in a model have a strong positive or negative relationship or same effect. This is a phenomenon that is not required in all statistical regression analysis. The minimum temperature collinear with maximum temperature (r = 0.89), rainfall (r=0.66) and season (r= -0.81). The variable humidity collinear with the variable district (r= -0.83). The variable season collinear with the variable maximum temperature (r= -0.74). The adjusted IRR for factors associated with malaria cases in Mpumalanga are shown in Table 3.6. When the effect of other factors was adjusted for, the maximum temperature, temperature range and rainfall were associated with malaria cases. Therefore, for every 1^{o}C increase in maximum temperature, there was a 21% increase in the risk of malaria (IRR = 1.21, 95% CI=1.13 - 1.29). As the range between maximum and minimum temperature was increasing, there was a 0.86 less likely risk of malaria when adjusting for other factors.

For the rainfall variable, for every 1 mm increase, there was a 5% increase in the risk of malaria when other factors are controlled for (IRR = 1.05, 95%CI = 0.99 – 1.08). This variable was marginally significantly associated with malaria risk. For every 1% increase in humidity, there was a 1% increase in the risk of malaria (IRR = 1.01, 95%CI = 1.00 – 1.02). This variable did not reach any statistical significance when adjusting for other factors. The risk of getting malaria decreased from 2001 to 2010 when adjusting for other factors.

Table 3.6. The univariate and multivariate negative binomial regression analysis model for the relationship between malaria incidence and climatic/environmental conditions in Mpumalanga Province between 2001 and 2010

Variable	IRR	95% CI	P-value	IRR	95% CI	P-value
Minimum temperature (°C)	1.14	1.08 - 1.20	<0.001	-	-	-
Maximum temperature (°C)	1.20	1.10 - 1.31	<0.001	1.21	1.13 - 1.29	0.001
Temperature range (°C)	0.79	0.71 - 0.88	<0.001	0.86	0.78 – 0.94	0.003
Rainfall (mm)	1.01	0.99 - 1.02	0.072	1.05	0.99 - 1.08	0.081
Humidity (%)	1.02	1.01 - 1.03	<0.090	1.01	1.00 – 1.02	0.102
District						
Ehlanzeni	1 (Ref)			-	-	-
Gert Sibande	0.01	0.01 - 0.02	<0.001	-	-	-
Nkangala	0.01	0.004 - 0.009	<0.001	-	-	-
Sikhukhune Cross Boundary	0.03	0.003 - 0.27	0.002	-	-	-
Season						
Summer	1 (Ref)			-	-	-
Winter	0.79	0.48 - 1.29	0.347	-	-	-
Month						
January	1 (Ref)					
February	0.54	0.22 - 1.35	0.185	-	-	-
March	0.98	0.36 - 2.71	0.968	-	-	-
April	0.73	0.28 - 1.88	0.517	-	-	-
May	0.96	0.36 - 2.52	0.928	-	-	-
June	0.41	0.14 - 1.17	0.097	-	-	-
July	0.22	0.08 - 0.63	0.005	-	-	-
August	0.19	0.06 - 0.56	0.003	-	-	-
September	0.30	0.11 - 0.82	0.018	-	-	-
October	0.41	0.15 - 1.11	0.079	-	-	-
November	0.47	0.17 - 1.30	0.147	-	-	-
December	0.41	0.15 - 1.09	0.073	-	-	-
Year						
1	1 (Ref)			1 (Ref)		
2	0.78	0.30 - 1.98	0.599	0.81	0.59 - 1.10	0.181
3	0.49	0.19 - 1.31	0.157	0.56	0.40 - 0.78	<0.001
4	0.55	0.19 - 1.51	0.243	0.55	0.39 - 0.76	<0.001
5	0.13	0.05 - 0.30	<0.001	0.43	0.31 - 0.59	<0.001
6	0.31	0.13 - 0.73	0.007	0.58	0.43 - 0.79	<0.001
7	0.10	0.04 - 0.22	<0.001	0.32	0.23 - 0.45	<0.001
8	0.11	0.04 - 0.28	<0.001	0.21	0.15 - 0.29	<0.001
9	0.11	0.04 - 0.28	<0.001	0.18	0.13 - 0.25	<0.001
10	0.14	0.06 - 0.37	<0.001	0.21	0.15 - 0.29	<0.001

3.1.8. Spatial and spatio-temporal scan statistics analysis

3.1.8.1 Spatial only analysis

The most likely and secondary clusters observed for the purely spatial analysis are shown in Table 3.7. A statistically significant (at 5% level) most likely cluster of high malaria risk comprised two sub-districts for the period 2001 – 2010 (observed cases = 28,193, expected cases = 4,194.10, RR = 24.57, $p<0.001$). The secondary cluster, statistically significant, comprised two sub-districts for the period 2001 – 2010 (observed cases = 7,006, expected cases = 6352.14, RR = 1.12, $p<0.001$). All these sub-districts were located in the Lowveld region of Mpumalanga adjacent to borders of Mozambique and Swaziland (see also Figure 3.3).

3.1.8.2 Space-time analysis

The most likely and secondary clusters of high malaria risk obtained from space-time scan analysis are shown in Table 3.7. The statistically significant most likely cluster comprised of only one sub-district for the period 2001 – 2004 (observed cases = 19,139, expected cases = 2,094.22, RR = 17.77, $p<0.001$). The secondary cluster comprised two sub-districts for the period 2001 – 2002 (observed cases = 3,098, expected cases = 1,671.63, RR = 1.93, $p<0.001$). These clusters were also located in the Lowveld region of Mpumalanga bordering Mozambique.

Table 3.7. Clusters of malaria cases using purely spatial and space-time scan analysis for high rates over ten years for Mpumalanga Province between 2001 and 2010

Analysis type	Years	Type of cluster	Number of sub-districts	Observed cases	Expected cases	Relative risk (RR)	P-values
Purely spatial	2001 - 2010	Most likely	2	28193	4194.10	24.57	<0.001
	2001 - 2010	Secondary	2	7006	6362.14	1.12	<0.001
Space-Time	2001 - 2004	Most likely	1	19139	2094.22	17.77	<0.001
	2001 - 2002	Secondary	2	3098	1671.63	1.93	<0.001

3.1.9 Significant clusters of high malaria risk in Mpumalanga Province

Significant clusters of malaria by sub-district were pictorially shown in Figure 3.6. The lowveld region sub-districts of Mpumalanga bordering Mozambique were found to be significant using SaTScan statistical analysis. The appropriate significant p-values by sub-district in the map were shown for each malaria high risk cluster detected. The Nkomazi, Bushbuckridge, Mbombela, Govan Mbheki and Umjindi sub-districts had significant p-values at $p=0.05$ ($p<0.001$).

Figure 3.6. Significant clusters of malaria by sub-district detected in Mpumalanga Province between 2001 and 2010 (significant p-values of significant clusters indicated in the sub-district).

3.2 Part 2: Analysis using remote sensed data

3.2.1 The summary of selected environmental/climatic conditions for remote sensed data

The summary of environmental or climatic conditions by month between 2001 and 2009 from Mpumalanga Province using remote sensed data is shown in Table 3.8. The median maximum and minimum monthly temperature decrease from 30.3^{o}C and 19.2^{o}C in January to 24.2^{o}C and 6.6^{o}C in July, respectively. The median precipitation (related to rainfall in weather stations data) decreased from 102 mm in February to 2.8 mm in August in all study years. The monthly precipitation starts increasing in October from 44.3 mm to 117.6

mm in December for all study years. The median monthly vapour pressure (related to humidity in weather stations data) decreased from 225hPa in January to 107hPa in July. It started increasing in August to December. The minimum and maximum temperature, rainfall and humidity were significantly different in all months of the study period of Mpumalanga ($p<0.05$).

Table 3.8. The summary of selected environmental/climatic conditions in the affected selected sub-districts of Mpumalanga Province by month between 2001 and 2009 for the remote sensed data

Month	Maximum Temperature (°C) N Median (IQR)[ψ,k]	Minimum Temperature (°C) N Median (IQR)[ψ,k]	Monthly rainfall (mm) N Median (IQR)[ψ,k]	Monthly Vapour Pressure (hPa) N Median (IQR)[ψ,k]
January	1548	1548	1548	1548
	30.3 (27.7 - 31.8)	19.2 (16.4 - 20.4)	87.2 (60.6 - 121.8)	218 (186 - 234)
February	1548	1548	1548	1548
	30.3 (27.7 - 31.8)	19.5 (16.4 - 20.8)	102.5 (66.9 - 160)	225 (191 - 235)
March	1548	1548	1548	1548
	29.0 (26.9 – 30.2)	18.1 (14.45 - 18.9)	71.4 (45.6 – 101.9)	216 (177 - 227)
April	1548	1548	1548	1548
	27.8 (25.2 - 29.2)	15.0 (12.1 - 16.2)	28.8 (18.3 - 42.7)	177 (152 - 195)
May	1548	1548	1548	1548
	26.4 (23.2 - 27.9)	10.4 (7.5 - 11.5)	7.3 (4.1 – 18.1)	136 (110.5 - 154)
June	1548	1548	1548	1548
	24.3 (20.8 – 25.3)	7.2 (4.8 - 8.6)	12.2 (4.3 - 18)	114 (89 - 127)
July	1548	1548	1548	1548
	24.2 (20.9 - 25.2)	6.6 (3.8 - 8.0)	3.7 (1.9 – 10.2)	107 (82 - 116)
August	1548	1548	1548	1548
	26.1 (23.6 – 27.4)	9.5 (7.0 - 10.8)	2.8 (1.6 – 9.3)	125 (99 - 133)
September	1548	1548	1548	1548
	27.5 (25.4 - 28.8)	12.1 (9.7 - 13.5)	12.2 (4.7 – 19.8)	142 (113.5 - 154)
October	1548	1548	1548	1548
	28.4 (26.4 - 29.5)	15.2 (12.2 - 16.2)	44.3 (30.6 – 75.6)	175 (144 - 183)
November	1548	1548	1548	1548
	28.7 (26.6 - 29.9)	17.2 (14.45 - 18.45)	104 (77.2 – 144.5)	197 (167 - 207)
December	1548	1548	1548	1548
	29.7 (27.5 – 31.4)	18.9 (15.9 - 20.1)	117.6 (82.3 –169.4)	220 (187 - 232)

ψ, k – Statistically significant at $p<0.05$ with Kruskal-Wallis test

3.2.2 Correlation analysis using remote sensed data

The Pearson correlation co-efficients for the assessment of correlation between malaria cumulative incidence and climatic conditions from extracted satellite data was shown in Table 3.9. All factors were statistically significant at 0.05 except for seasonality ($p>0.05$). The minimum and maximum temperature, precipitation (rainfall) and vapour pressure (humidity) showed a positive correlation with malaria cases. Therefore, the increase in each factor led to an increase in the number of malaria cases.

Table 3.9. Pearson correlation co-efficients for the correlation between malaria cases and climatic/environmental conditions using remote sensed data for Mpumalanga Province, 2001 – 2009.

Variable	Cases	
	Correlation co-efficient (r)	P-value
Minimum temperature	0.3207	<0.001
Maximum temperature	0.3232	<0.001
Precipitation	0.4070	<0.001
Vapour pressure	0.5772	<0.001

3.2.3 Disentangling imported from local cases

3.2.3.1 Disentangling imported cases from local cases using remote sensed data from the fitted curve analysis

The IRR for malaria in Mpumalanga Province between 2001 and 2009 using remote sense data is shown in Figure 3.7. Between January and May, the IRR was fluctuating (i.e. decreasing and increasing) and a sharp decrease from 1.12, 0.45, 0.27, and 0.22 is observed in May, June, July and August, respectively. The IRR started to increase from 0.31 to 0.50 between September and November during the study period.

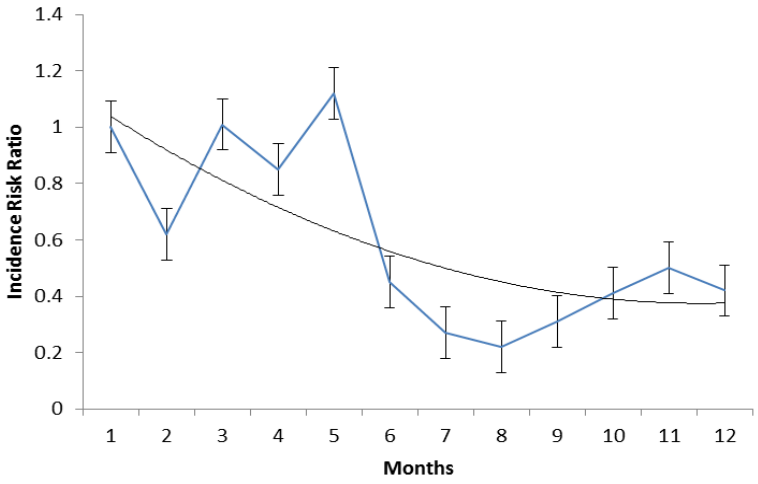

Figure 3.7. The Incidence Risk Ratio (IRR) of malaria by month in Mpumalanga Province between 2001 and 2009 using remote sense data.

3.2.3.2 Disentangling imported malaria cases from local cases using remote sensed data from the modelled data analysis

The results to disentangle imported malaria cases from local cases were shown in Table 3.10. When using remote sensed data, Ehlanzeni District is still the district that is experiencing a lot of excess cases from observed. Starting from March to the end of July, excess cases were observed. From March, April, May, June and July, about 1,131; 3,036; 4,009; 994 and 235 excess cases were observed, respectively. These are winter months and an excess during this period is more likely to indicate imported cases.

Table 3.10. The observed and modelled expected number of malaria cases by District and month of Mpumalanga Province over time between 2001 and 2009 using remote sensed data

District	Month	Number of observed cases	Number of modelled expected cases	Difference between observed and expected cases*
EHLANZENI	January	7218	84820	-77602
EHLANZENI	February	3661	10619	-6958
EHLANZENI	**March**	**4612**	**3481**	**1131**
EHLANZENI	**April**	**4382**	**1346**	**3036**
EHLANZENI	**May**	**5166**	**1157**	**4009**
EHLANZENI	**June**	**1718**	**724**	**994**
EHLANZENI	**July**	**981**	**746**	**235**
EHLANZENI	August	749	1189	- 440
EHLANZENI	September	1542	1567	-25
EHLANZENI	October	2283	2657	-374
EHLANZENI	November	2251	5032	-2781
EHLANZENI	December	2198	11436	-9238
GERT SIBANDE	January	75	344	-269
GERT SIBANDE	February	34	252	-218
GERT SIBANDE	March	16	78	-62
GERT SIBANDE	April	30	165	-135
GERT SIBANDE	May	20	73	-53
GERT SIBANDE	June	16	43	-27
GERT SIBANDE	July	7	15	-8
GERT SIBANDE	August	3	45	-42
GERT SIBANDE	September	5	148	-143
GERT SIBANDE	October	14	136	-122
GERT SIBANDE	November	8	108	-100
GERT SIBANDE	December	9	75	-66
NKANGALA	January	32	707	-675
NKANGALA	February	11	587	-576
NKANGALA	March	4	403	-399
NKANGALA	April	15	329	-314
NKANGALA	May	10	87	-77
NKANGALA	June	2	32	-30
NKANGALA	July	4	60	-56
NKANGALA	August	1	11	-10
NKANGALA	September	11	490	-479
NKANGALA	October	10	239	-229
NKANGALA	November	11	274	-263
NKANGALA	December	5	394	-389

*The positive numbers indicate excess and negative numbers indicate less from expected

3.2.4 Univariate negative binomial regression model

The univariate negative binomial regression model to assess the relationship between malaria cases and climatic conditions around health facilities reporting malaria using remote sensed data was shown in Table 3.11. When the effect of other climatic factors is ignored, most variables were significantly associated with malaria incidence. The risk of malaria increased with increasing temperature, precipitation and vapour pressure. It was decreasing with district changing and season changing from summer to winter. The minimum temperature variable showed that for every 1^{o}C increase, the risk of malaria increase by 16% (IRR = 1.16, 95%CI= 1.10 – 1.22). The maximum Temperature demonstrated a 37% increase in the risk of malaria for every 1^{o}C increase (IRR = 1.37, 95%CI = 1.24 – 1.50). The precipitation variable also showed that for every 1 mm increase, an 8% increase in the risk of malaria was observed (IRR = 1.08, 95%CI = 1.02 – 1.12) (Table 3.10). Those patients who were staying at Gert Sibande and Nkangala Districts were at 0.02 and 0.007 respectively less likely to be at risk of malaria infection compared to those who were staying at Ehlanzeni District (Table 3.11). Finally, for the change in a season from summer to winter, the risk of malaria decreased by 11% (IRR = 0.89, 95%CI = 0.56 – 1.42). The risk of malaria was observed decreasing across all months except March and May.

3.2.5 Negative Binomial multivariate regression model using remote sense data

The negative binomial multivariate regression model to assess the relationship between malaria cases and climatic conditions around health facilities reporting malaria using remote sensed data is shown in Table 3.11. The variables maximum and minimum temperature, vapour pressure, district and season were removed due to collinearity. The

minimum temperature collinears with maximum temperature (r=0.92) and temperature range (r=-0.84). The vapour pressure collinears with rainfall (r=0.75). The variable district collinears with rainfall (r=-0.59) and vapour pressure (r=0.82). The variable season collinears with the variable maximum temperature (r=0.62).

When the effect of other climatic factors was taken into account, maximum temperature, precipitation and year were significantly associated with malaria incidence. The maximum temperature indicated that for every 1^{o}C increase, there is a 35% increase in the risk of malaria infection (IRR = 1.35, 95%CI = 1.22 –1.50). Similarly, monthly precipitation (rainfall) demonstrated that for every 1 mm increase, the risk of malaria increased by 3% (IRR = 1.03, 95%CI = 1.01–1.06).

Table 3.11. The univariate and multivariate negative binomial regression model for the association between malaria incidence and climatic/environmental conditions using remote sensed data in Mpumalanga Province, 2001 – 2009.

Variable	IRR	95% CI	P-value	IRR	95% CI	P-value
Minimum temperature (°C)	1.16	1.10 - 1.22	<0.001	-	-	-
Maximum temperature (°C)	1.37	1.24 - 1.50	<0.001	1.35	1.22 - 1.50	<0.001
Temperature range (°C)	0.84	0.76 - 0.92	<0.001	1.28	1.15 – 1.43	<0.001
Precipitation (mm)	1.08	1.02 – 1.12	<0.001	1.03	1.01 - 1.06	<0.001
Vapour pressure (hPa)	1.02	1.01 – 1.04	<0.001	-	-	-
District						
Ehlanzeni	1 (Ref)					
Gert Sibande	0.02	0.01 - 0.03	<0.001	-	-	-
Nkangala	0.007	0.005 - 0.009	<0.001	-	-	-
Sikhukhune Cross Boundary	-	-		-	-	-
Season						
Summer	1 (Ref)			-	-	-
Winter	0.89	0.56 - 1.42	0.626	-	-	-
Month						
January	1 (Ref)			-	-	-
February	0.62	0.27 - 1.44	0.266	-	-	-
March	1.01	0.41 - 2.48	0.987	-	-	-
April	0.85	0.35 – 2.03	0.719	-	-	-
May	1.12	0.45 - 2.72	0.805	-	-	-
June	0.45	0.17 - 1.18	0.104	-	-	-
July	0.27	0.10 - 0.74	0.011	-	-	-
August	0.22	0.08 - 0.64	0.005	-	-	-
September	0.31	0.13 - 0.74	0.009	-	-	-
October	0.41	0.18 - 0.98	0.044	-	-	-
November	0.50	0.20 - 1.23	0.132	-	-	-
December	0.42	0.17 - 0.99	0.049	-	-	-
Year						
2001	1 (Ref)			1 (Ref)		
2002	0.66	0.29 - 1.47	0.308	0.81	0.59 - 1.11	0.192
2003	0.44	0.18 - 1.04	0.061	0.52	0.40 - 0.78	<0.001
2004	0.40	0.17 - 0.96	0.040	0.42	0.39 - 0.76	<0.001
2005	0.11	0.05 - 0.24	<0.001	0.33	0.31 - 0.59	<0.001
2006	0.25	0.11 - 0.56	<0.001	0.42	0.43 - 0.79	<0.001
2007	0.11	0.05 - 0.24	<0.001	0.32	0.23 - 0.45	<0.001
2008	0.12	0.05 - 0.28	<0.001	0.21	0.15 - 0.29	<0.001
2009	0.13	0.05 - 0.30	<0.001	0.18	0.13 - 0.25	<0.001

CHAPTER FOUR

DISCUSSION AND CONCLUSSIONS

The findings in this study indicated the significance of disentangling imported cases from local cases. The results in this study were consistent with the findings of other studies in Mpumalanga Province (Ngomane, 2012). In both studies, the highest number of malaria cases was reported from Ehlanzeni District as were the number of deaths reported. These high numbers could be attributed to the close proximity of the district to the Kruger National Park and Mozambique and to the fact that it is a low-altitude area (Blumberg & Frean, 2007).

There was a significant reduction in malaria prevalence later in year 2000 following a major malaria epidemic in 1999/2000. During the epidemic, more than 60,000 malaria cases were reported (Coetzee, 2005) and between 11% and 50% of resistance to pyrethroid in *An. funestus* were reported (Hargreaves *et al*., 2000). The reduction could be attributed to re-introduction of DDT replacing pyrethroid later in year 2000. The successful programmes on vector control, drug policy change to fight drug resistance and cross-border malaria control initiatives also contributed to the malaria reduction. These sustainable well-structured and effective control strategies resulted in malaria reductions seen even today.

A positive correlation obtained between malaria cases and temperature, rainfall and humidity is consistent with previous studies. The study done by Taylor & Mutambu (1986) in Zimbabwe; Craig *et al*. (2004) in KwaZulu-Natal, South Africa; and Kearney *et al*. (2009) depicted the positive correlation between malaria incidence and climatic factors. Mabaso *et al*. (2006) in Zimbabwe conducted a study exploring and studying malaria incidence and relationship with climatic factors in the past 30 years. This author's findings showed that annual mean temperature, rainfall and vapour pressure were strong positive predictors of increased malaria incidence. This positive correlation suggested that as the increase in these factors occurs, the number of malaria cases also increase. This is what would be expected in every study involved on studying malaria and climatic conditions.

The observed malaria cases exceeded the expected number of malaria cases from March to June in the period of ten years. This suggests an increase in the number of malaria cases inconsistent with the given climatic conditions around health facilities. During the beginning of May to June, the climatic conditions (i.e. temperature, rainfall and humidity) are normally low. In other words, this is the time of the year when the temperature and humidity are starting to drop drastically and cold conditions are experienced in the country. The rainfall also is drastically reduced during these times of the year. Therefore, the excess malaria cases reported are most likely imported cases from areas north of South Africa. This supports the recent study by Maharaj *et al*. (2012) where it was revealed that up to 80% of the cases reported from 2005 – 2011 are imported. Most importantly, the local cases reported from 2005 – 2011 has decreased from 31% – 20%.

The previous studies by Zhou *et al*. (2004) in the East African highlands further emphasized the known epidemiological understanding of the relationship between climate

and malaria. They clearly determined that every one unit increase in minimum or maximum temperature, rainfall or humidity led to an increase in the risk of malaria. These findings were in accordance with the findings from the present study. The synergistic effects of a combination of temperature and rainfall to increase malaria incidence was also observed in this study.

The high malaria risk areas identified in space and space-time were the areas already mentioned by Maharaj *et al*. (2012) as areas that require urgent intervention. These are the areas that were also detected when doing malaria spatial analysis. Therefore, a close monitoring and evaluation of the malaria control programmes in these areas to achieve elimination is strongly recommended.

Limitations of the data involved health facility-based case data that did not distinguish the imported and local cases. It only assumes that people did not cross borders and go to use other health facilities from other district. The Stats SA population data did not separate between the migrating and non-migrating nationals as it sample everybody in the district. The issue of population undercount as not everyone get counted during census also identified. The weather stations data had a lot of missing values. It was not a best representation of the climatic conditions surrounding health facilities. For example, some of the facilities are many kilometres away from the weather station recording data. The unit of analysis was health facility and the conclusions were based at the individual case thus creating ecological bias.

From the findings in the present study it was clear that the occurrence of malaria cases around a particular health facility were not particularly due to the surrounding climatic

conditions. These were most likely imported cases from malaria endemic countries. So, it is strongly recommended that sensitive surveillance systems applicable to the elimination phase are instituted.

Secondly, it is absolutely imperative that cross-border movement with neighbouring countries needs urgent attention and that cross-border malaria control programmes initiatives need to be strongly supported to minimize case importation. Thirdly, research studies that focus on mosquito vectors and insecticide resistance distribution are encouraged. Finally, strategic elimination planning that quantifies population movement patterns to and from our country needs to be established.

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http://www.info.gov.za/aboutsa/provinces.htm

http://www.sa-venues.com/weather/mpumalanga.htm

Appendix 1

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

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Mr Khumalo Mbhekiseni

CLEARANCE CERTIFICATE	**M120853**
PROJECT	Correlations between Surrounding Environmental Conditions and Malaria Incidence in Selected Sub-Districts of Mpumalanga and Limpopo Provinces, South Africa (2000-2010)
INVESTIGATORS	Mr Khumalo Mbhekiseni.
DEPARTMENT	School of Public Health
DATE CONSIDERED	31/08/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

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

DATE 31/08/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr B Sartorius

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

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix 2

MPUMALANGA PROVINCIAL GOVERNMENT

Building No.3
No. 7 Government Boulevard
Riverside Park Extension 2
Nelspruit
1200
Republic of South Africa

Private Bag X 11285
Nelspruit, 1200
Tel: 013 766 3429
int: +27 13 766 3429
Fax: 013 766 3458
int: +27 13 766 3458

Department of Health

Litiko Letemphilo | Umnyango WezaMaphilo | Departement van Gesondheid

Enquiries: Molefe Machaba (013) 766 3009/3511

12 November 2012

Mr. Mbhekiseni Khumalo
P O Box 1813
NQUTU
3135

Dear Mr. Mbhekiseni Khumalo

APPLICATION FOR RESEARCH & ETHICS APPROVAL: CORRELATION BETWEEN SURROUNDING ENVIRONMENTAL CONDITIONS AND MALARIA INCIDENCE IN SELECTED SUB-DISTRICTS OF MPUMALANGA AND LIMPOPO PROVINCES, SOUTH AFRICA (2000 – 2010).

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

Kindly ensure that you provide us with the report once your research has been completed.

Kind regards

Molefe Machaba
Research and Epidemiology

12/11/2012
Date

We care Do you? Siyanakekela

MPUMALANGA
A Pioneering Spirit

Appendix 3

South African Weather Service

Disclosure Statement

SCHEDULE 1

Please note: The South African Weather Service will only act upon customer requirements noted on this disclosure statement and not from any other correspondence.

FULL PERSONAL DETAILS OF USER

Full Names: **Khumalo Mbhekiseni Phikelamangwe**

University/school/organization: **University of the Witwatersrand, School of Public Health**

Student Number: (where applicable) **472973**

Email address: **Mbhekiseni.Khumalo@students.wits.ac.za**

Postal Address: **P O BOX 1813, NQUTU, 3135**

Supervisor: **Professor Maureen Coetzee and Doctor Benn Sartorius**

Project/Thesis Title: **Correlation between surrounding environmental conditions and malaria incidence in selected sub-districts of Mpumalanga province, South Africa (2000 – 2010).**

Registered Course: (where applicable) **Master of Science in Epidemiology and Biostatistics**

THE PURPOSE

(Please indicate a detailed description of the purpose for which the data will be used).

The data will be used for a Masters Research project contributing to malaria epidemiology in South Africa. The overall objective is to determine whether malaria incidence at given health facilities can be ascribed to local transmission or is likely to be imported. Rainfall and temperature will be used to support and prove this objective therefore they are important and central variables to this Project.

DATA REQUIRED

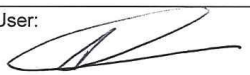
(Please include the weather elements (e.g. rain, temperature), place/s and period)

1. **Rainfall (mm) daily data from January 2000 – December 2010**
2. **Temperature (°C) daily data from January 2000 – December 2010 – Maximum and minimum temperature daily data**
3. **Daily records of relative humidity (%) data**

Data that are required are for the Mpumalanga Province particularly from Ehlanzeni, Gert Sibande, Sekhukhune Cross Boundary and Nkangala districts for the period January 2000 to December 2010.

I hereby accept that:

- SAWS will be acknowledged in the resulting thesis/project or when published, for the data it provided.
- SAWS will be provided with a copy of the final results in printed or electronic format.
- The data received shall not be provided to any third party.

Signature of the User:  Date: 10/12/12

(Please sign the document and do not type your name in as this is a legal document and requires a signature.)