Modelling Schistosomiasis in South Africa

by

Inbarani Moodley

Submitted in fulfilment of the academic requirements for the degree of Master of Science in the School of Life and Environmental Sciences, University of Natal, Durban.

December 2003

As the candidate's supervisor I have approved this dissertation for submission.

Signed: C.C. Appleton Date: 5/12/2003

Prof. C.C.Appleton

ABSTRACT

Temperature and rainfall vary spatially within South Africa and they in turn affect the parasites and intermediate host snails involved in schistosomiasis transmission. The primary goal of this study was to investigate the relationship between these two abiotic variables and schistosomiasis in South Africa using a Geographic Information System (GIS) as a spatial analytical tool. The secondary goal was to estimate the population exposure to schistosomiasis. Prevalence data for *Schistosoma haematobium* and *S. mansoni* obtained from a national hardcopy atlas and two long-term, retrospective, high resolution climate datasets were used to produce two models (temperature-suitability and regression analysis) based on different GIS methodologies.

The temperature-suitability model defined areas that are suitable and unsuitable for disease transmission by relating documented temperature regimes to the schistosomes' larval biology. The map outputs show that temperature minima corresponded better with the disease data than temperature maxima. Based on different climate and population data permutations, between approximately 3 903 734 and 4 379 079 school-aged children live in these temperature-suitable zones.

The regression model tested the hypothesis that temperatures, especially during spring and summer favoured schistosomiasis transmission more than those of autumn and winter. Positive associations were expected with the rainfall variables. A logistic equation was used to predict, as accurately as possible within the model's limitations, the probability of schistosomiasis occurring in a given area. Increasing annual rainfall, as well as spring and autumn temperature maxima and minima predicted an increase in *S. haematobium* prevalence rates. *Schistosoma haematobium* prevalence rates of 11-25% and 26-50% were predicted in the north-eastern and eastern coastal regions. A prevalence rate of 71 to 100% was predicted from Limpopo to KwaZulu-Natal. Increasing the average monthly rainfall, spring temperature maxima and autumn temperature minima, increased the likelihood of *S. mansoni* transmission. *Schistosoma mansoni* prevalence rates of 26-50% and 71 to 100% were predicted in Limpopo, Mpumalanga, KwaZulu- Natal and Eastern Cape. This is the first time GIS has been used to correlate climate variables and schistosomiasis occurrence in South Africa. The regression model requires further refinement and it is not as applicable as the temperature-suitability model for practical purposes.

PREFACE

The experimental work described in this dissertation was conducted under the Supervision of Professor Chris Appleton from the School of Life and Environmental Sciences, University of Natal, Durban. The research work was done in the Malaria Research Lead Programme, Medical Research Council, Durban.

The study represents original work by the author and has not been submitted previously, in any form to any other tertiary institution. Where use has been made of the work of others, it is acknowledged in the text.

Inbarani Moodley

December 2003

LIST OF CONTENTS

Page

ABSTRACT ... ii
PREFACE ... iii
LIST OF CONTENTS ... iv
LIST OF TABLES ... viii
LIST OF FIGURES ... ix
ACKNOWLEDGEMENTS ... xi

CHAPTER 1: Urinary and Intestinal Schistosomiasis
Burden of Disease, Life-cycles, Aetiology and Control
1.1 Introduction ... 1
1.1.1 Overview of thesis ... 2

1.2 Schistosome parasites of humans and their geographical distribution ... 3
1.2.1 Classification ... 3
1.2.2 Species affecting people worldwide ... 4
1.2.3 Species affecting people in South Africa ... 4
1.2.4 Geographic distribution of schistosomiasis in South Africa ... 5

1.3 Burden of schistososmiasis worldwide and in South Africa ... 7
1.3.1 Worldwide ... 7
1.3.2 South Africa ... 8

1.4 Life-cycle and transmission of schistosomes ... 9
1.4.1 Egg stage ... 10
1.4.2 Miracidium ... 10
1.4.3 Cercariae ... 11

1.5 Aetiology of human schistosome infections ... 11
1.5.1 Infection with *S. haematobium* ... 12
Early manifestations (Swimmer's itch and Katayama fever/syndrome) ... 12
Established *S. haematobium* infections ... 13
1.5.2 Infection with *S. mansoni* ... 13
Early manifestations of *S. mansoni* infections ... 13
Chronic *S. mansoni* infections (intestinal and hepatosplenic schistosomiasis) ... 14

1.6 Control of schistosomiasis in South Africa ... 14
1.6.1 Epidemiological considerations ... 14
1.6.2 Chemotherapy ... 15
1.6.3 Control programme efforts ... 17
1.6.4 Co-infections ... 18
1.7 Summary ... 19

CHAPTER 2: The Host Snails and Parasites in Relation to Temperature and Rainfall
2.1 Introduction ... 20
2.2 The influence of the South African climate on the host snails and parasites ... 23
2.2.1 Seasonal mean daily maximum temperature patterns ... 27
2.2.2 Seasonal mean daily minimum temperature patterns ... 30

2.2.3 Daily temperature range 31
2.2.4 Mean annual temperature 32
2.2.5 Rainfall patterns in South Africa 33
Mean annual rainfall 34
Mean monthly rainfall 34
Median rainfall 34
Rainfall patterns using median rainfall for South Africa 34
Rainfall concentration and variability 35
2.2.6 Distribution of host snails and schistosomes 36
Host snails 36
Schistosomes 37
2.2.7 Summary 38

2.3 Environmental requirements of the intermediate host snails 38
2.3.1 Temperature tolerance of the host snails 38
Optimal, high and low thermal tolerance limits 39
2.3.1.1 The *Bulinus* group: *Bulinus globosus* and *Bulinus africanus* 39
High temperature tolerance limits 39
Low temperature tolerance limits 40
Optimal temperatures for *B. globosus* and *B. africanus* 40
2.3.1.2 *Biomphalaria pfeifferi* 42
High temperature tolerance limits 42
Low temperature tolerance limits 43
Optimal temperatures for *B. pfeifferi* 43
2.3.1.3 Summary 44
2.3.1.4 Some considerations for thermal studies involving host snails and schistosomes 44
Constant and fluctuating temperatures 44
Acclimatization 45
Water temperatures versus air temperature 45
Duration of temperature 47
2.3.2 Rainfall 49
Desiccation and flooding 49
Current speed 51
2.3.3 Summary 52

2.4 Intra-molluscan development of the schistosomes 52
2.4.1 The effect of temperature on cercarial shedding from infected snails 52
2.4.1.1 *Schistosoma mansoni* 52
Seasonal transmission 53
Optimum temperatures for intra-molluscan development and cercarial shedding 54
Intra-molluscan development at high temperatures 54
Intra-molluscan development at low temperatures 55
2.4.1.2 *Schistosoma haematobium* 55
Optimum temperatures for intra-molluscan development and cercarial shedding 55
Intra-molluscan development at high temperatures 56
Intra-molluscan development at low temperatures 56
2.4.2 The role of water in parasite development and transmission 58
Cercarial shedding 58
Transmission of eggs to water 58
Intolerance to high salt content 60
2.5 Summary 61

CHAPTER 3: Building a Disease Model

3.1 Introduction 62
3.2 Constructing a disease model 63
3.2.1 Spatial analysis 64
Hypothesis generation 65
Statistics 65
Maps 66
Spatial autocorrelation 67
GIS as a health research tool 68
3.2.2 Constructing a GIS disease model 73
Data acquisition 73
Data processing and integration 74
Type of methodology 75
Vector models 75
Raster models 75
Development of map overlay 76
Raster implementation of overlay 76
Neighbourhood construction 77
3.2.3 Examples of the use of GIS in schistosomiasis modelling 78
3.3 Conclusion 81

CHAPTER 4: Methods used to Construct the Disease Models

4.1 Introduction and aim of Study 83
4.2 Study design 83
4.3 Rationale for using a GIS 83
4.4 Preliminary preparations for model building 84
4.5 Deriving the disease models 84
4.5.1 Hypothesis 84
4.5.2 Post model processing 85
4.6 Data 85
4.6.1 Disease data 85
4.6.2 Population data 88
4.6.3 Climate data 88
4.7 Generating summary statistics 89
4.8 GIS software 90
4.8.1 Putting data into GIS software 90
4.9 Deriving the disease models 90
4.9.1 Model one: Temperature-suitability model 90
Deriving the temperature-suitability model 90
4.9.2 Model two: Regression model 94
Deriving the regression model 95
Deriving the prediction equation from the regression model 96
4.10 Post model derivation processing 97
4.10.1 Population estimates 97
4.10.2 Hutchinson *et al.* (1995) versus Schulze (1997): Comparison of outputs 97
4.11 Conclusion 98

CHAPTER 5: Results

5.1 Introduction 99
5.2 Summary statistics for prevalence data 101
5.3 Results of model one: suitable temperature 104
5.3.1 *Schistosoma haematobium* temperature -suitability map 105
5.3.2 *Schistosoma mansoni* temperature -suitability map 107
5.4 Result of model two: ordered regression analysis 109
5.4.1 Ordered logistic regression analysis for *S. haematobium* 110
5.4.2 Ordered logistic regression analysis for *S. mansoni* 111
5.5 Predicting schistosomiasis occurrence using Hutchinson *et al.* (1995) climate data 112
5.5.1 Predicted prevalence categories for urinary schistosomiasis 113
5.5.2 Predicted prevalence categories for intestinal schistosomiasis 114
5.6 Comparison of outputs for *S. haematobium* using climate data from Hutchinson *et al.* (1995) and Schulze (1997) 115
5.6.1 Comparison of Hutchinson *et al.* (1995) and Schulze's data 116
5.6.2 Output from applying a predictive function to the regression analysis output using the Schulze (1997) dataset 117
5.7 Population estimates 118
5.8 Conclusion 120

CHAPTER 6: General Discussion

6.1 Introduction 121
6.2 Summary of research results 122
6.2.1 Significance of the temperature-suitability maps 122
6.2.2 Significance of the regression analysis output 124
6.3 Recommendations 127
6.4 Population estimates 129
6.5 Conclusion 131

REFERENCES 132

APPENDIX A: List of Terms and Definitions 151
References for List of Terms and Definitions 156

APPENDIX B: Procedure used to derive the temperature- suitability maps 157

APPENDIX C: Logical steps in deriving the regression model 160

APPENDIX D: Temperature-suitability Maps for Schistosomiasis in South Africa 162

LIST OF TABLES

Table 1.1 A Guide to the different South African Schistosomes and their host Snails 5

Table 3.1 Pubmed Search showing Articles on Schistosomiasis 78

Table 4.1 Prevalence categories used by Gear *et al.* (1980) 87

Table 4.2 Temperature regimes from Pitchford (1981) that are excluded in the model..... 93

Table 4.3 Temperature regimes used by Pitchford (1981) that were included in the present study..... 94

Table 5.1 Summary statistics for each of the seven prevalence categories for *S. haematobium*.. 101

Table 5.2 Summary statistics for each of the seven prevalence categories for *S. mansoni*..... 101

Table 5.3 Validation of model for *S. haematobium* based on Pitchford's (1981) data..... 106

Table 5.4 Validation of model for *S. mansoni* based on Pitchford's (1981) data 108

Table 5.5 Estimated number of school-age children living in temperature-suitable zone for *S. haematobium*..... 119

Table 5.6 Estimated number of school-age children living in areas where *S. haematobium* prevalences were predicted 119

LIST OF FIGURES

Fig 1.1 Pair of adult worms situated in their hosts's vein....3

Fig 1.2 *Bulinus africanus*....4

Fig 1.3 *Biomphalaria pfeifferi*....4

Figure 1.5a *S. mansoni* egg showing its lateral spine and the formed miracidium inside....10

Figure 1.5b *S. haematobium* egg showing its terminal spine and the fully developed miracidium inside....10

Figure 1.5c Miracidium of *S. haematobium*....10

Figure 1.5d Cercaria of *S. haematobium*....10

Figure 1.6 Child infected with *S. haematobium* holding a jar of her own urine....12

Figure 1.7 *Schistosoma haematobium* eggs in bladder wall biopsy taken at autopsy in Durban....13

Figure 2.1 Eco-regions of South Africa....24

Figure 2.2 Seasonal Means of daily maximum temperature in South Africa....28

Figure 2.3 People using infected water in the Mbogintwini River on the southern outskirts of Durban in 1985....29

Figure 2.4 Seasonal means of daily minimum temperature in South Africa....30

Figure 2.5 Mean annual temperature in the nine provinces of South Africa....32

Figure 2.6 Data adapted from Pitchford (1981) relating cercarial shedding by different proportions of snails exposed seasonally to Mdx and Mdn at Nelspruit (altitude 655m)....57

Figure 4.1: Picture of Atlas of Bilharzia....86

Figure 4.2: Map showing excluded minimum temperature regime of 5°C or less for one month or more and *S. haematobium* prevalence 51 to 70%....94

Figure 5.1 Summary Diagram showing disease model components....100

Figure 5.2 Distribution of *S. haematobium.*....102

Figure 5.3 Distribution of *S. mansoni.*....103

Figure: 5.4 Map adapted from Pitchford (1981), showing unsuitable temperature regimes for *S. haematobium* and *S. mansoni*....104

Figure 5.5 Temperature-suitability map for *S. haematobium* derived from temperatures regimes listed in Table 4.3....105

Figure 5.6 Temperature-suitability map for *S. mansoni* derived from temperatures regimes listed in Table 4.3....107

Figure 5.7 Extracted temperature variables for each *S. haematobium* point on the map..... 109

Figure 5.8 Extracted temperature variables lying under each *S. mansoni* point on the map 110

Figure 5.9 Predicted prevalence rates for *S. haematobium* 113

Figure 5.10 Predicted prevalence rates for *S. mansoni*..... 114

Figure 5.11 Output generated from running the *S. haematobium* temperature- suitability model listed in Table 4.3, with Schulze's (1997) climate dataset 116

Figure 5.12 Comparison of Schulze's (1997) and Hutchinson *et al.* (1995) output from temperature-suitability model for *S. haematobium* 117

Figure 5.13 Output from running prediction model for *S. haematobium* using Schulze (1997) dataset 118

ACKNOWLEDGEMENTS

I am thankful to the following people who assisted me with various aspects of my work:

My supervisor Professor Chris Appleton, for his valuable advice, critical comments and for access to his library of information.

Dr Brian Sharp for his support, advice and for use of the Malaria Research Lead Programme's resources.

Dr Immo Kleinschmidt for his statistical input.

Mrs Marlies Craig for her expertise in GIS during the early stages of the work.

Dr Rajendra Maharaj for his critique of aspects of my work, as well as his advice and encouragement.

Mr Ishen Seocharan for his technical expertise with the images, as well as his support and assistance.

Finally, I would like to thank my fiancé as well as my family and friends for their support and encouragement during my studies.

This work is dedicated to my late parents.

CHAPTER ONE

Urinary and Intestinal Schistosomiasis
Burden of Disease, Life-cycles, Aetiology and Control

1.1 INTRODUCTION

Schistosomiasis transmission involves a parasite (bloodfluke), a vertebrate definitive host (man, Appendix A), and a molluscan intermediate host (snail) all living in an environment which supports each one's survival and growth. The Greek physician Hippocrates highlighted the importance of relating people to their environment in his book on "Airs Waters and Places" written 2400 years ago. Hippocrates stated: "Whoever wishes to investigate medicine properly should proceed thus: in the first place to consider [1] the seasons of the year, and what effects each of them produces. Then the winds the hot and cold, especially such as are common to all countries, and then such as are [2] peculiar to each locality...One should consider most attentively [3] the waters which the inhabitants use ...[4] the mode in which the inhabitants live and what are their pursuits, whether they are fond of drinking and eating to excess, and given to indolence, or are fond of exercise and labour" (McMahon and Pugh, 1970). It is now easier to heed Hippocrates' advice with the aid of better epidemiological data collection mechanisms, computer hardware and software tools all made available by modern science.

Jekel, Elmore and Katz (1996) define epidemiology as the study of (1) the distribution of disease and (2) the determinants of the disease's observed distribution in man; the goal of such studies being to limit disease spread. Alternatively, the World Health Organisation (WHO) describes the state of health as complete physical, mental and social well-being, and not merely the absence of disease (WHO, 1946). Therefore the epidemiologist should also be concerned with the pro-active approach, which is to preserve and maintain good health. However in countries like South Africa with many sick people and limited resources, this is often a luxury.

The epidemiologist describes the health status of people and seeks to understand the cause of disease and its spatial and temporal trends (Richards and Baker, 1988). Investigating the causes of disease is an intriguing process as it compels people to think beyond the presentation of the disease. Is it possible to control or even treat some diseases like schistosomiasis? Yes. But if we knew the factors that caused and exacerbated the problem in communities, then it would be

possible to mount a comprehensive attack against the disease-causing agent to control its spread within the population, and not wait until after people become infected. The parasitic and communicable infection, schistosomiasis, is affected by both biotic and abiotic factors. Therefore for this disease there is a "man-environment-disease" link.

1.1.1 OVERVIEW OF THESIS

This work brings together basic epidemiological parameters of schistosomiasis, biological observations on the intermediate host snails, the man-disease-environment-link and computer-based disease models; the aim being to use a Geographic Information System (GIS) as a research tool to study the occurrence of the disease in relation to temperature and rainfall in South Africa.

The first three Chapters review aspects of the biology of schistosomiasis, climate variables in relation to transmission and disease model building respectively. Methodology follows in Chapter 4 and includes the specific hypothesis and objectives of this work. The results, which include maps, are in Chapter 5 and finally Chapter 6 discusses the findings. Some technical terms are defined in Appendix A along with details of the methodology in Appendices B and C.

Literature on schistosomiasis is voluminous. Therefore Chapter 1 describes only six salient aspects related to the schistosomes, their host snails and transmission namely, (1) identification and classification of medically important schistosomes and host snails worldwide and in South Africa, (2) geographic distribution of schistosomiasis in South Africa, (3) the worldwide and South African burden of schistosomiasis, (4) key elements of the schistosome life-cycle, (5) how schistosomiasis manifests in people and (6) important issues related to control of the disease in South Africa.

1.2 SCHISTOSOME PARASITES OF HUMANS AND THEIR GEOGRAPHICAL DISTRIBUTION

1.2.1 Classification

Although there are other schistosome species that affect man, the two important South African human schistosomes are *Schistosoma haematobium* and *Schistosoma mansoni.* The biological classifications of these split- bodied Platyhelminthes (Fig. 1.1) are shown below (Rollinson and Southgate, 1987).

Family: Schistosomatidae	Family: Schistosomatidae
Subfamily: Schistosomatinae	Subfamily: Schistosomatinae
Genus: *Schistosoma* (Weinland, 1858)	Genus: *Schistosoma* (Weinland, 1858)
Group: *S. haematobium*	Group: *S. mansoni*
Species: *S. haematobium* (Bilharz, 1852)	Species: *S. mansoni* (Sambon, 1907)

Figure 1.1: Pair of adult worms situated in their hosts's vein

Photo: C.C. Appleton (1996)

The classification of the two main South African hosts for these blood flukes are listed below (Rollinson and Southgate, 1987).

Class: Gastropoda
Subclass: Euthyneura (includes the Pulmonata, Müller, 1781)
Family: Planorbidae
Subfamily: Bulininae
Group: *Bulinus africanus*
Genus: *Bulinus* (Müller, 1781)
Species: *B. africanus* (Krauss, 1848)
B. globosus (Morelet, 1866)

Figure 1.2: *Bulinus africanus*
Photo: D. Herbert, Natal Museum in Appleton (1996)

Class: Gastropoda
Subclass: Euthyneura (includes the Pulmonata, Müller, 1781)
Family: Planorbidae
Subfamily: Planorbinae
Genus: *Biomphalaria* (Preston,1910)
Species: *B. pfeiferri* (Krauss, 1848)

Figure 1.3: *Biomphalaria pfeifferi*
Photo: D. Herbert, Natal Museum in Appleton (1996)

1.2.2 Species affecting people worldwide

Species of digenetic flatworms or blood flukes known as schistosomes are disease causing agents in humans. There are two forms of the disease which are diagnosed based on where the parasite lives in the body. Urinary schistosomiasis, caused by *S. haematobium*, occurs in 53 countries in Africa and the Eastern Mediterranean. Intestinal schistosomiasis caused by *S. mansoni* is prevalent in 54 African countries, the Caribbean, the Eastern Mediterranean and South America (WHO, 1996). Two Asian forms of intestinal schistosomiasis exist and are caused by *Schistosoma japonicum* and *Schistosoma mekongi*. The presence of one form of the disease does not necessarily imply the presence of the other.

1.2.3 Species affecting people in South Africa

Some of the differences between *S. haematobium* and *S. mansoni* include their different egg shapes, their reliance on different host snails and the mode of transmission out of the body i.e urine or faeces (Table 1.1).

Table 1.1: A Guide to the different South African Schistosomes and their host Snails

(Rollinson and Southgate (1987); Sturrock (1993); Brown (1994))

Schistosome	Mature egg	Snail Host	Incubation period in definitive host (days)
S. haematobium	Ovoid Size = 144 X 58 µm Terminal spined Normally passed in urine	*B. africanus* group viz., *B. africanus* *B. globosus*	56
S. mansoni	Ovoid Size = 142 X 60 µm Lateral spined Normally passed in faeces	*B. pfeifferi*	34

Schistosoma haematobium parasitises certain snails of the *B. africanus* group (namely *B. africanus* and *B. pfeifferi*). The larval stages of *S. mansoni* develop in *B. pfeifferi* snails. The form of intestinal schistosomiasis found mainly in animals is caused by *Schistosoma mattheei,* but Pitchford (1966) also found evidence of these parasites in people in South Africa. However, human infection rates are not as high as that of *S. haematobium* and *S. mansoni* (Pitchford, 1986). The *B. africanus* group snails also serve as the intermediate host for *S. mattheei.* Appleton, Sharp and Le Sueur (1995) added that *S. mattheei* infection in people is probably self-limiting but their interaction is beyond the scope of this work as *S. haematobium* and *S. mansoni* are more common. Both species of host snails are freshwater hermaphrodites that become susceptible to schistosome parasites from the time they are a day old (Gear and Pitchford, 1979).

1.2.4 Geographic distribution of schistosomiasis in South Africa

Appleton *et al.* (1995) maintain that schistosomiasis could have probably been carried to the country by the Iron Age people as they migrated southwards at about 600 AD. Hence it has been in South Africa for centuries. However of significance is the fact that both the parasite and the snail hosts originate from the tropics and South Africa represents their southerly limits. More information on this and their different geographic locations follow in Chapter 2 but the occurrence of each disease is briefly given here to describe its geographic extent.

The geographical locations of South Africa's nine provinces are shown in Fig. 1.4. *Schistosoma haematobium* has been reported in areas extending from Uitenhage in the Eastern Cape, northwards through the eastern coastal belt and into the coastal and midland parts of KwaZulu-Natal (Pitchford, 1986). However, this parasite does not appear in the mountainous regions of

the Drakensberg nor is it found south of the Magaliesberg (in what is now Gauteng), Lesotho, Free State or the Western Cape (Pitchford, 1986). The numbers in Fig. 1.4 relate to Chapter 2, Section 2.2.1.

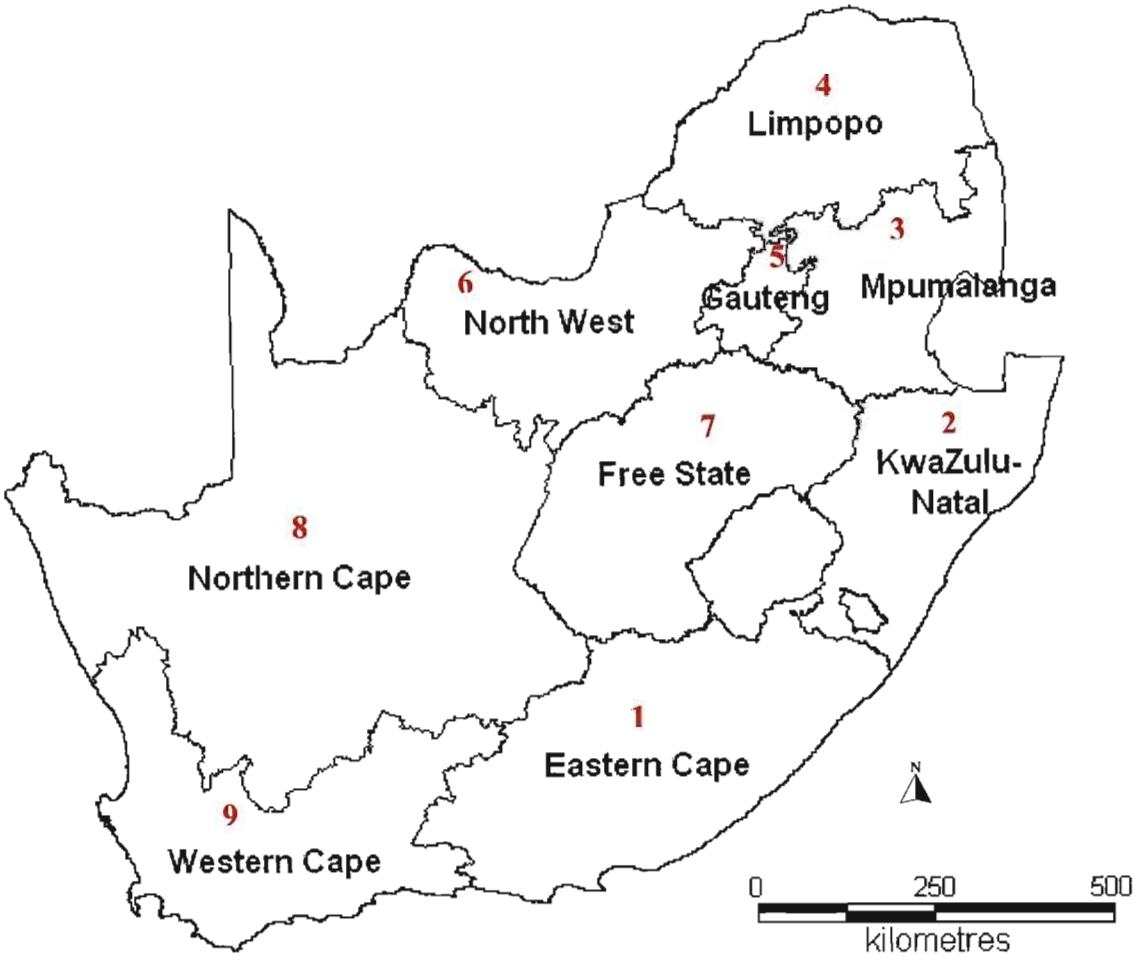

Figure 1.4: South Africa's nine provinces

Schistosoma haematobium may also be found in the low- and middle- lying areas of neighbouring Swaziland as well as the lowveld of Mpumalanga and the Limpopo province in the north (Pitchford, 1986). Interestingly, the distribution of *S. mattheei* follows that of *S. haematobium,* except for extending further to some other areas in the Eastern Cape (Pitchford, 1986). *Schistosoma mansoni* is found mainly in Mpumalanga and the Limpopo Province. There are a few additional sites in central Gauteng, the low-lying parts of Swaziland and coastal regions of KwaZulu-Natal where *S. mansoni* has been reported (Pitchford, 1986). This parasite is also absent from the Western Cape Province and the central highland plateau (Fripp, 1979). From this description it is apparent that *S. mansoni* is confined to a smaller area compared to *S. haematobium*.

1.3 BURDEN OF SCHISTOSOMIASIS WORLDWIDE AND IN SOUTH AFRICA

Schistosomiasis has been known since the ancient times of the pharaohs of Egypt (Sturrock, 1993; Fripp, 1979). This section discusses the worldwide and South African burden of schistosomiasis.

1.3.1 Worldwide

The disease currently ranks as the second most important human parasitic disease in both tropical and subtropical areas (WHO, 1996). Both urinary and intestinal diseases are widespread in these areas although different distributions are reported as is the case in South Africa. It is commonly quoted that over 200 million people are infected and approximately 500 to 600 million people are at risk of being infected. Of the infected people, 20 million suffer from severe disease sequelae and 120 million people are asymptomatic (WHO, 1996). An estimated 80% of all cases present in Africa, where the burden of the disease is felt the worst.

Updated morbidity and mortality estimates are restricted by data deficits due to limited survey data especially in some African countries. Utroska *et al.* (1989) maintain that prevalence data on schistosmiasis are limited, which is certainly the case in South Africa. Therefore researchers rely on extrapolations from existing prevalence data. For instance van der Werf and de Vlas (2001) calculated the total number of people at risk of infection with S. *haematobium* to be 452 million, while 111 million people are infected in Africa. In describing disease due to *S. mansoni*, van der Werf and de Vlas (2001) estimate that 409 million people are at risk of infection while 54 million people are infected. Furthermore these authors estimated that about 200 000 people die of schistosomiasis each year in sub-saharan Africa.

WHO (2002) estimated that 1 389 000 disability life adjusted years (DALYs, Appendix A) were lost among 602 million people in endemic African countries in 1998. Each DALY represents the loss of one year of healthy life due to premature death and disability (World Health Report, 2002) and is a useful tool for estimating disease burdens quantitatively and for comparison purposes. Updated information suggests a bleaker picture. The more recent World Health Report (2002) considered the African burden of disease for schistosomiasis to be 1 760 000 DALYs with 15 000 deaths. These DALYs have increased by 21% since 1998, in other words more years are being lost due to the burden of schistosomiasis. The mortality estimates also differ greatly. Despite these estimates being available, the Expert Committees on the Prevention and Control of Schistosomiais and Soil-Transmitted Helminths expressed concern that the

disability adjusted life years lost due to schistosomiasis had been underestimated (WHO, 2002). The important point from these statistics is that many people are still affected by schistosomiasis but Africa still carries the worst burden.

1.3.2 South Africa

Schistosomiasis is not a notifiable disease in South Africa. Therefore reliable estimates of people at risk or infected in the country are currently unknown. The lack of systematic or periodic large scale screening programmes and the current living conditions of many people make the actual burden difficult to quantify. This difficulty is evident in the studies mentioned below.

Given the lack of appropriate case data, one has to rely on the available literature and anecdotal evidence to estimate the number of infected people. As expected the figure has changed over the years, with earlier estimations being that 3 million people were infected (Gear and Pitchford, 1979). Waner (1999) reported that the schistosomiasis situation may have improved in certain parts of the country due to better living conditions, but at the same time the prevalence, especially in rural areas may have increased due to population growth.

This estimate is now considered conservative. For instance, Schutte, Fripp and Evans (1995) believed that the prevalence of schistosomiasis in South Africa had not decreased, but rather may have increased. Although the percentage of heavily infected people in an endemic area may vary considerably, Schutte *et al.* (1995) estimated that between 10 and 15% of people will present with clinical signs and symptoms of schistosome infection. Schutte *et al.* (1995) indicated a prevalence of four million but they also highlighted the lack of survey results and consequently their inability to assess whether the figure is a true reflection of reality or not. The authors used these estimates to conclude that between 400 000 and 600 000 people will have pathology related to schistosomiasis in such an endemic area. Wolmarans and de Kock (2000) do not discount the earlier estimate of Gear and Pitchford (1979) when they state that between three and four million people are infected in the country. Their projections were based on incidence data among school children in the schistosomiasis endemic areas of the country.

The results from another school-based survey in Ingwavuma district depict the prevalence at a smaller geographical scale, i.e Ingwavuma district in KwaZulu-Natal (Fig. 1.4). An overall prevalence of 68.3% (n = 1109) urinary schistosomiasis among children was found (Saathof *et al.*, 2002). In terms of specific estimates of infections, Utroska *et al.* (1989) calculated the

average prevalence in the country to be 17.50% with 1 575 000 infected children under 15 years. These and the work mentioned above highlight the difficulty in reaching consensus on the burden of schistosomiasis in South Africa without proper case data. Furthermore in South Africa a new focal point for the disease has arisen. School nurses in Humansdorp district (24.35°, -33.98°) in the Eastern Cape (Fig. 1.4) observed urinary schistosomiasis in school children in October 2002. This surprised health authorities as small numbers of *B. africanus* do occur there but no disease was reported until now (Appleton, 2002). Therefore, it seems that conditions in this marginal area of disease are now conducive for the parasite to complete its life-cycle.

1.4 LIFE-CYCLE AND TRANSMISSION OF SCHISTOSOMES

The schistosome life-cycle is indirect as it uses a snail host as an intermediary for certain growth stages and a definitive host (man) for its final growth stages. Although this itself makes the schistosome life-cycle complex, the schistosomes' free-living stages are further subjected to the environment that their snail hosts live in - water. The discipline of disease ecology considers the schistosomes' growth and reproduction in relation to the changing environments in which they live (Jones and Moon, 1987, Appendix A). The two major factors involved in successful disease transmission are the life-cycle of the parasites and the influence of geogens (geographical factors) forming a complex relationship in time and space (Jones and Moon, 1987). The disease cycle consists of the following four components:

1. the host who gets the disease,
2. the "disease agents" which cause the disease directly, eg. the schistosome parasite- either *S. haematobium* or *S. mansoni,*
3. vehicles such as water which assist transmission, and
4. the host (whether intermediate or definitive) in which the disease agent develops.

The life-cycles of both diseases are well documented in other work. Only the free- living stages are discussed here because these stages are exposed to the environment. The species of schistosomes affecting people and their respective complex life-cycles display some similarities in the chain of infection. All three species mentioned in Section 1.1 develop over the following seven stages: egg, free swimming miracidium, first stage (mother) sporocyst, second stage (daughter) sporocyst, cercaria, schistosomulum and adult. Aspects of three of these stages (egg, miracidium and cercaria) are discussed in the following section because these are the stages which are exposed to the environment.

1.4.1 Egg stage

The eggs of the different species have characteristic shapes as is evident in the pictures below (Table 1.1; Figs. 1.5a and 1.5b).

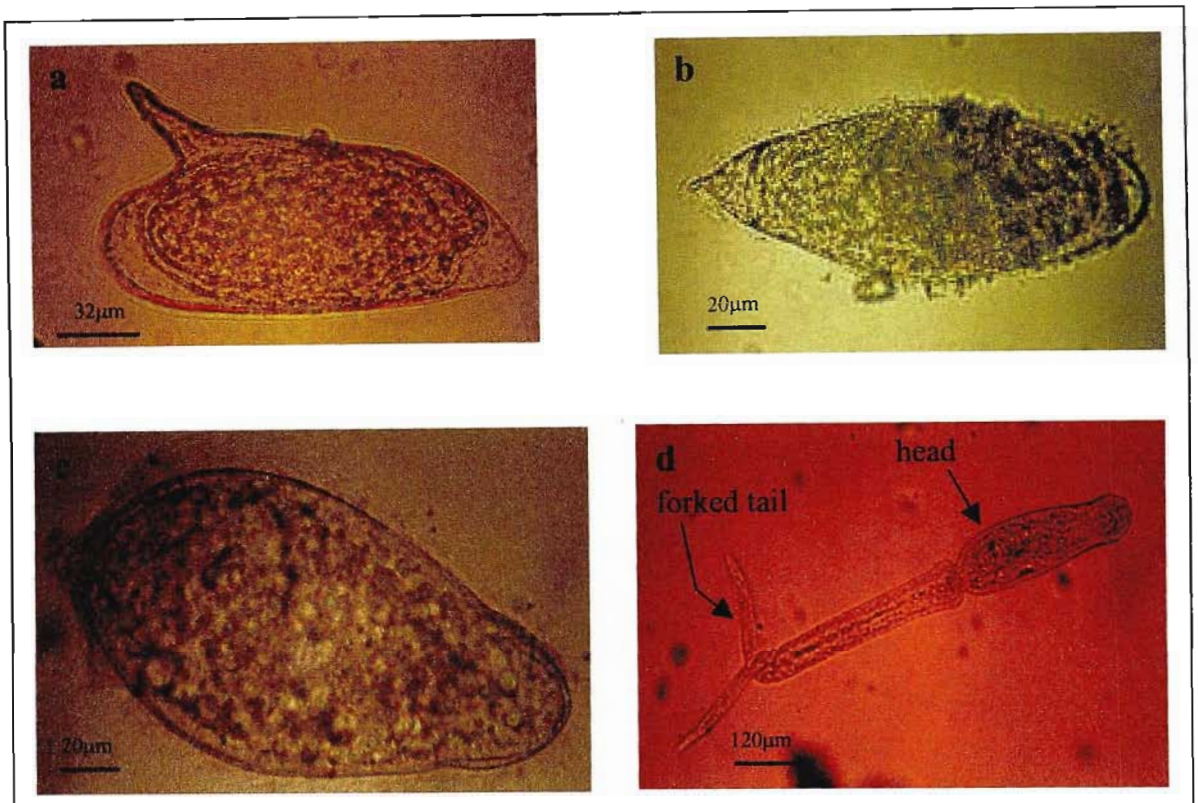

Figure 1.5: (a) *S. mansoni* egg showing its lateral spine and the formed miracidium inside, (b) *S. haematobium* egg showing its terminal spine and the fully developed miracidium inside, (c) miracidium of *S. haematobium* and (d) cercaria of *S. haematobium* Photos: C.C.Appleton, University of Natal

The eggs of both species are relatively large oval, yellowish, non-operculate and have a spine (Sturrock, 1993). These characteristics are used for diagnoses.

1.4.2 Miracidium

The miracidium (Fig. 1.5c) develops inside the egg over about six days. The eggs of the schistosomes in the excreta of an infected person hatch in water and release miracidia, which are non-feeding organisms. Hatching occurs when the osmotic pressure of the environment falls and when certain environmental conditions are met, viz., temperature (between 25°C and 30°C), light and an osmotic pressure close to that of natural water (Southgate and Rollinson, 1987). These tiny larvae must find a suitable snail which themselves have a discontinuous distribution. Porter (1938) found they could live for up to three days before penetrating a snail host via its foot. Southgate and Rollinson (1987) commented on the sometimes contradictory reasons for

miracidial location of their snail host but suggested that two kinds of responses are at play, one of which is a temperature cue.

After penetration the miracidia reproduce asexually to produce thousands of new parasites (cercariae) over the course of four to six weeks, depending on temperature. While the schistosomes are in their snail hosts they constitute what is commonly called the "intramolluscan stage" during which time they undergo different developmental transformations. These stages include mother sporocyst, asexual differentiation of daughter sporocysts, sporocystogenesis and cercariagenesis (Southgate and Rollinson, 1987). These developmental stages are vulnerable to the external environment within their snail hosts and they are only able to grow to mature cercariae if the conditions are tolerable. Snails can remain infected for many months. Chapter 2 includes a discussion on the effects of temperature on infected snails.

1.4.3 Cercaria

The non-feeding cercariae (Fig. 1.5d) leave the snail following a daily photoperiodic and thermoperiodic-related rhythm (Southgate and Rollinson, 1987). They then swim into the surrounding water in search of a human host as they can only survive optimally for about two days at most, especially in the warm tropics. They can penetrate an individual's skin within a few minutes and continue their biological cycle once they have made their way to the victim's blood stream (Sturrock, 1993).

In order for the complex schistosome life-cycle to become established, the definitive host must come into contact with fresh water. People are infected during contact with infested water in the course of their normal daily activities for personal or domestic purposes, such as hygiene and recreation (swimming), or in professional activities such as fishing, rice cultivation and irrigation.

1.5 THE AETIOLOGY OF HUMAN SCHISTOSOME INFECTIONS

Only about half of the eggs laid by the female worms are excreted in the faeces (intestinal schistosomiasis), or in the urine (urinary schistosomiasis). The rest become trapped in the body tissues of the host, damaging other vital organs instead of being excreted. It is these eggs - and not the worm - which cause damage to the liver, bladder and other organs. Disease due to

schistosomiasis is indicated either by the presence of blood in the urine possibly leading to bladder cancer or kidney problems (urinary form) or, in the case of the intestinal form, by initial atypical symptoms such as intermittent (bloody) diarrhoea, which can lead to serious complications of the liver and spleen.

Figure 1.6 shows a child holding a jar containing red urine. Studies have shown the presence of blood in the urine can be used as an indirect method to estimate the prevalence of *S. haematobium* infection (Red Urine Study Group, 1995). There is a range of disease manifestations in schistosome-infected people but only some of the more salient signs of early manifestations and established infections are described here because their details are outside the scope of this work.

Figure 1.6: Child infected with *S. haematobium* holding a jar of her own urine

Source: C.C. Appleton, University of Natal

1.5.1 Infection with *S. haematobium*

Early manifestations (Swimmer's itch and Katayama fever/syndrome)

The first sign of infection is severe itching which appears within 12 hours of cercarial penetration and can last up to two or three days before disappearing (Appleton, 1984; Doherty, Moody and Wright, 1996). This immediate manifestation is commonly found with migrants or tourists who have not developed any immunity to infection (Ross *et al.*, 2001). Hence it is not commonly seen in endemic areas where people have acquired immunity (Appendix A). It is also characteristic of invasion by cercariae of non-human schistosomes. Swimmer's itch generally occurs during summer months throughout the world, but its risk is underestimated in South Africa (Appleton, 1984). The other early manifestation, Katayama fever or toxemic schistosomiasis is a form of acute schistosomiasis diagnosed in patients who present with symptoms such as fever in the evenings, headache, malaise, cough, enlarged liver and spleen

and abdominal pains about four to six weeks after severe initial exposure (von Lichtenberg, 1987; Farid, 1993; Doherty *et al.*, 1996; Ross *et al.* 2001).

Established *S. haematobium* infections

Schistosoma haematobium targets three urinary tract organs, namely (1) the bladder which is the most frequently affected organ, (2) the ureters and (3) kidneys. In the bladder, the disease presents in the form of sandy patches and polypoid or nodular lesions (Fig. 1.7) (Farid, 1993). Sandy patches are the most common lesions and are irregular, yellowish-grey, variable sized rough mucousal patches surrounding heavily calcified egg deposits (Farid, 1993; Ross *et al.*, 2001).

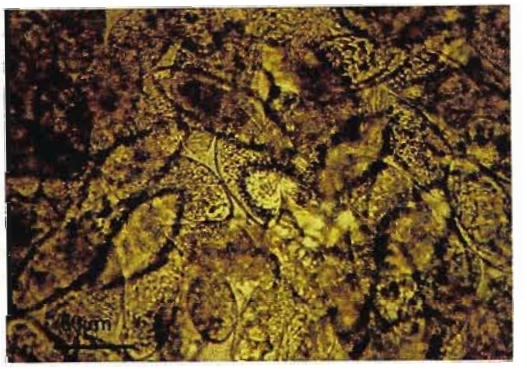

Figure 1.7: *Schistosoma haematobium* eggs in bladder wall biopsy taken at autopsy in Durban

Photo: C.C.Appleton, University of Natal

Two active and inactive stages are characterised. Active stages are observed mainly in young patients who present with dysuria and haematuria (Farid, 1993). Haematuria was accepted as "normal" in the lives of school children in endemic Ingwavuma and Ubombo districts in KwaZulu-Natal (Cooppan, Bhoola & Mayet, 1984). After studying urinary schistosomiasis in school children in Durban, Cooppan *et al.* (1984) showed that clinical morbidity correlated well with the intensity of infection. Furthermore, although the relationship between colo-rectal cancer and schistosomiasis has been debated for decades, Ross *et al.* (2001) maintain that there is an association between *S. haematobium* infections and bladder squamous cell carcinoma.

1.5.2 Infection with *S. mansoni*

Early manifestations of *S. mansoni* infections

The symptoms described above also occur after *S. mansoni* infection.

Chronic *S. mansoni* infections (intestinal and hepatosplenic schistosomiasis)

In the case of intestinal schistosomiasis, the worms reside in the blood vessels draining the lower intestine and rectum and they produce eggs which induce inflammatory and fibrotic lesions in the body (Lambertucci, 1993; Ross *et al.*, 2001). Chronic schistosomiasis is divided into two syndromes, namely intestinal and hepatosplenic forms (Lambertucci, 1993).

For intestinal schistosomiasis the main lesions are inflammation, fibrosis and colonic polyposis. Hepatosplenic schistosomiasis is characterised by liver fibrosis and enlarged spleen and is the best known form of chronic heavy *S. mansoni* infection (Lambertucci, 1993). Referred to as clay-pipe-stem fibrosis, it is the only human liver disease directly caused by schistosome infection (von Lichtenberg, 1987). Ross *et al.* (2001) state that clay-pipe-stem fibrosis is associated with heavy infections and can take years to develop.

Most people who suffer from these often severe and complex manifestations of schistosome infections rely on health ministries to control and cure the disease. There are many studies showing how effective treatment can be. In some people these manifestations can be reversed thereby alleviating the burden of disease and improving their quality of life. The following section discusses some measures to control schistosomiasis in South Africa.

1.6 CONTROL OF SCHISTOSOMIASIS IN SOUTH AFRICA

1.6.1 Epidemiological considerations

Schistosomiasis control is dynamic and requires multiple inputs (Mott, 1987). The various forms of control of the disease are well documented by other authors. Therefore a brief discussion is included here with reference to the current status of control in South Africa. WHO (1996) reports the eradication of the disease in Japan, Lebanon, Montserrat and Tunisia. Puerto Rico, Venezuela, Saudi Arabia and Morocco are having success in their control efforts and are nearing the eradication phase. Endemic countries such as Brazil, China, Egypt and the Philippines are maintaining national control programmes which have helped to maintain morbidity at low levels. In 1996, WHO aimed to revive interest in schistosomiasis in sub-Saharan Africa where, following Engels *et al.* (2002) control is almost non-existent. The specific and non-specific control measures that exist are discussed adequately in the literature, but a few points of note are included below.

Specific measures of control include chemotherapy (to reduce or eliminate schistosome eggs in people) and snail control but the WHO (1996) adds that control strategies must be adapted according to the epidemiology, resources and culture of each country. Non-specific measures are associated with health education and improved sanitation. Control of the molluscan snail hosts needs to occur at a particular time of year and for a certain period of time not only to be effective against the parasite but also to be environmentally friendly. The following characteristics of schistosomiasis epidemiology are important in terms of control:

1. number of snails that survive in the cold winter months;
2. number of snails that survive winter or carry infections from one wet season to another after aestivation;
3. rate of infection of a new snail generation;
4. cercarial development time.

The importance of these characteristics as they relate to disease modelling, are expanded further in Chapter 2.

There may be some areas where the hydrology and temperature remain the same over long time periods, in these places the snail populations and cercarial output may remain at a steady rate. In such cases, chemical means such as molluscicides, may be needed for snail control. These chemicals are used to render the snails' habitat unsuitable and have a long history of use as a control measure. Appleton (1985) described the South African situation with respect to molluscicides and maintained that this method of control should be incorporated with chemotherapy and provision of safe water to be effective. Currently in the South African situation there are three topics deserving discussion, i.e. (1) chemotherapy, (2) the absence of a control programme and (3) the implication of co-infection with other diseases.

1.6.2 Chemotherapy

Whereas previously host snail elimination was the first choice of control (Anon, 2002a) chemotherapy is now playing the most important role (WHO, 1996). Despite considerable effort there is no vaccine to target the schistosomula as yet. The current drug of choice for treatment is praziquantel, a pyrazinoisoquinoline derivative for which many generics are available. Praziquantel is active against all schistosome eggs and worms but not the schistosomulae. Murray *et al.* (2000) reported that praziquantel reduced egg counts by 95% with a high (85%) parasitological cure rate. However, it does not prevent re-infections. Therefore the drug is useful against reducing morbidity but not as effective for chemoprophylaxis (Appendix A). Shuhua,

Booth and Tanner (2000a) stated that praziquantel's non-prophylactic effect against *S. japonicum* reduced its efficacy in high transmission areas.

Nevertheless, praziquantel has become cheaper over the past decade making it more accessible to poor countries. Therefore presumptive treatment may be provided in endemic areas or according to other epidemiological criteria and still be cost-effective and safe. In countries such as Brazil mass treatment was given to the whole population where prevalence was >20% among 7-14 year old children under the "Special Schistosomiasis Control Programme." If there was prevalence of 4-20%, people between 5 years and 25 years were treated (Jordan and Webbe, 1982). WHO (2002) stated that the earlier treatment occurs, the greater the chances of reversal of the disease manifestations mentioned in the previous Sections 1.5.1 and 1.5.2.

The use of one antischistosomal drug may lead to resistance and is already a cause for concern from the scientific community (Utzinger *et al.*, 2001) as it has been in the market for more than 20 years (Ross *et al.*, 2001). Further disadvantages of the singular use of praziquantel include its short half -life and the fact that it does not target the juvenile schistosomula. Hence, alternative curative and preventative drugs need to be sought and careful monitoring for early detection of resistance is necessary in schistosomiasis endemic countries.

There is evidence to suggest *S. mansoni* tolerance of praziquantel in Egypt (Utzinger *et al.*, 2000). Although Gryseels *et al.* (2001) did not find convincing evidence to suggest praziquantel-resistant *S. mansoni* in Senegal, Doenhoff (2002) suggests that there are low levels of resistance in this country. Gryseels *et al.* (2001) attributed low *S. mansoni* cure rates not to praziquantel resistance in Senegal, but rather to high initial worms loads and heavy transmission. Such vigilance is needed to ensure that praziquantel continues to be useful as a drug for treatment of schistosomiasis.

Studies have shown that artemether has a good safety profile for malaria and is effective against the juvenile stages of the schistosome life-cycle (Utzinger *et al.*, 2001). Higher drug doses are required for malaria treatment than that required for the schistosomes. Theoretically combination therapy with praziquantel and artemeter will be most effective in high transmission areas as Shuhua *et al.* (2000b) found in laboratory experiments with *S. japonicum* infected rabbits. However, use of artemether for schistosomiasis and malaria requires careful monitoring to prevent selection of the malaria parasites.

Artemether is being used in South Africa for malaria. It is also being used in China (Shuhua *et al.*, 2000a) for schistosomiasis but its use here in South Africa has not been investigated as praziquantel is still effective. Hence praziquantel is likely to remain the drug of choice in South Africa until resistance appears.

1.6.3 Control programme efforts

The success of any schistosomiasis control programme depends on long- term commitment (WHO, 1996) as well as available human and financial resources. The Department of Health in KwaZulu-Natal implemented a pilot helminth control programme in endemic areas of the province in 1998, which was the first of its kind in the country. The main aim of the programme was to treat about 1.5 million primary school children with praziquantel on a regular basis to maintain low infection intensities in the high intensity areas. Kvalsvig *et al.* (2001) found a decline in infection during this intervention. Unfortunately, this programme did not gain the necessary momentum and there is currently no treatment strategy of any kind in any area of the country (Kvalsvig *et al.*, 2001).

Engels *et al.* (2002) state that adequate clinical care is an important first step of control. In addition the WHO (1996) states that optimal schistosomiasis control is achieved when it involves the general health care system and when the primary health care system performs specific control tasks. A document called The "Primary Health Care National Norms and Standards in South Africa" includes the management of communicable diseases such as schistosomiasis and emphasises prevention, early diagnosis and initiation of measures to prevent transmission and serious morbidity, disability and death (Anon, 2002b).

The following excerpt from the abovementioned document is significant as it includes important treatment and control strategies in relation to the disease's complex epidemiology:

(1) Clinic staff should know whether the clinic is in an endemic area for schistosomiasis.

(2) The clinics in these endemic areas for schistosomiasis should have a copy of "Schistosomiasis in South Africa" (Gear and Pitchford, 1979).

(3) Schistosomiasis endemic clinics receive extra protocols on management from the District Health Offices, and an environmental health officer should visit them at least every month between December and March (presumably as this is the high transmission season).

(4) Clinic personnel should take more complete patient and family histories and should visit the home and environment to identify other cases and causes which can be prevented.

(5) Staff should give the correct information to patients on the life-cycle of worms and how to prevent future infections.

This strategy includes an integrated approach involving treatment, prevention and active surveillance. Unfortunately, there is no such system in the country. In order for South Africa to show that schistosomiasis has been eradicated or effectively controlled, no new infections should be observed over a certain time period (Engels *et al.*, 2002) or the prevalence should be reduced. This information relies on a surveillance system similar to that described above and the WHO (1996) recommends that surveillance and maintenance must continue for 10-20 years. Another report by WHO (2002) states that repeated treatment is effective even in such areas where control has been interrupted for a long time which is promising for the South African control effort should it be re-instated.

1.6.4 Co-infections

Co-infections with the Hepatitis Viruses B (HBV) or C (HCV) and *S. mansoni* are associated with deteriorating hepatic function (Ross *et al.*, 2001). Studies also suggest that helminth infections could have a negative impact on the immune systems of people also infected with the HIV/AIDS. The efficacy of praziquantel treatment depends on the immune system's response (Gundel and Hermann, 2002). Hence the treatment may not be as effective as it could be if the person is immuno-compromised. Lambertucci (1993) stated that failure to respond to praziquantel in the usual doses is expected in *S. mansoni*-infected people. He also stated that there have been changes in the clinical presentation, pathological aspects and therapeutic approach to most infectious diseases in an immuno-compromised host.

Furthermore Grant and de Cock (2001) put forward the theory that HIV infection could increase the incidence of tropical diseases. That relationship is complex and has important implications for disease control. Although Gundel and Hermann (2002) state that genital schistosomiasis is a risk factor in HIV transmission, other evidence showed that HIV positive people with *S. mansoni* excreted fewer eggs than HIV negative people (Grant and de Cock, 2001) and treatment of *S. mansoni* did not influence the load of HIV type 1 (Ross *et al.*, 2001). Interestingly, the common symptoms of early manifestations of HIV are weight loss, night sweats and diarrhoea which are common schistosomiasis manifestations as well.

The association and effectiveness of treatment for schistosomiasis in people co-infected with HIV are only now being in studied in South Africa. Fincham (2001) reported that there is

accumulating evidence showing helminthiasis treatment could help to alleviate some associated symptoms of HIV and Tuberculosis. Clearly, this is a complex relationship but mass de-worming of school children does contribute to their overall health and well-being. Schistosomiasis is endemic in parts of KwaZulu-Natal which also has one of the highest HIV prevalence rates in the country (Statistics SA, 2001) but as mentioned earlier there is no schistosomiasis control programme in that or any province in the country.

1.7 SUMMARY

As mentioned in the beginning of this Chapter, Hippocrates highlighted the need to consider the seasons of the year and the water that people use when studying the man-environment link with respect to disease. Temperature is an indicator of seasonal change and rainfall is an indicator of water availability. Following the reviews of Appleton (1976a, 1978) and the experimental work of Pflüger (1980, 1981), Pitchford, (1981) and O' Keeffe (1985a, 1985b), this study will use temperature and rainfall to build disease models for schistosomiasis in South Africa. These authors identify temperature and rainfall as being most important to schistosomiasis transmission and are discussed further in Chapter 2, Sections 2.1 and 2.3.

Comparable studies which use GIS to model schistosomiasis have also largely confined themselves to various temperature permutations, as well as rainfall. These studies are outlined in Chapter 3, Section 3.2.3. Therefore the goal of this study was to assess the relationship between rainfall, temperature and schistosomiasis in South Africa, by using available knowledge about the disease and its snail hosts.

CHAPTER TWO

The Host Snails and Parasites in Relation to Temperature and Rainfall

2.1 INTRODUCTION

This chapter is divided into the following three sections:

(1) the influence of the South African climate on host snails and schistosomes,
(2) the host snails' response to changing temperature and rainfall conditions, and
(3) the schistosomes' intra-molluscan development under varying temperature and moisture conditions.

The purpose of these three sections is to review the tolerance of schistosomes and their host snails to the changing temperature and moisture conditions that preside in their habitats.

For a person to become infected with schistosomiasis, the parasite must grow and reproduce from the time the miracidium hatches from the egg to the adult worm stage. When the life-cycle was discussed in Chapter 1, it was noted that *S. haematobium* and *S. mansoni* exhibit biologically complex life-cycles and in addition the various phases of their life-cycles were vulnerable to different environments, namely that within their host snails (mother and daughter sporocysts) and that outside their hosts, i.e. in water (miracidia and cercariae). The hosts in turn have to respond to the changing environments in which they find themselves. Being poikilotherms, the host snail's body temperature follows that of its environment. This has implications for both the snail's survival in a habitat and for the schistosomes during intra-molluscan development. Therefore, for successful transmission, suitable climatic conditions (especially temperature and rainfall) and biological events must coincide.

A habitat's suitability or unsuitability for schistosomiasis transmission depends on how well the snails and parasites respond to changes in their environment. For example some snails enter into a period of inactivity (aestivation or anhydrobiosis) which allows them to survive in small nutrient-rich waters that temporarily dry out (Brown, 1994). If aestivation is prolonged due to the water not being replenished in these small water bodies, many individual snails die.

In addition, evolutionary biology describes some of the mechanisms that parasites have evolved to survive in their environments. For instance (1) prolific egg production is possibly a r-selected strategy to improve the chances that at least some eggs will hatch and survive to the adult stage (2) the response of ciliated miracidia to certain cues given off by the host snails which facilitate their location and penetration of the host snails in water. These are examples of strategies that have evolved in response to selection pressures. The latter are imposed by evolutionary mechanisms mediated by environmental change.

In turn, environmental changes are caused both by climatic events like floods and droughts and human activities like the construction of dams. The schistosomes and host snails tolerate such environmental changes differently due to their individual sets of requirements for survival. Ecological theory states that the presence and success of an organism or group of organisms in a niche depend on a complex of abiotic conditions and biotic factors (Appendix A; Odum, 1983). These dynamic and frequently interactive biotic factors and abiotic conditions constitute the external environment that organisms must adapt to and tolerate.

There is a range of tolerances for every abiotic condition including an optimum range at which the organisms are most abundant (Odum, 1983). According to Shelford's Law of Tolerance (1913) for any organism to survive and succeed in an environment each of a complex set of conditions must occur within the organism's tolerance range and if any factor exceeds the minimum or maximum tolerance level, it will not thrive (Odum, 1983). Each species' optima and tolerance ranges differ according to its adaptation to its environment. Once a condition reaches or exceeds these limits of tolerance it becomes a "limiting factor" (Odum, 1983).

Furthermore the compound effect of too many limiting factors in a habitat may render it unsuitable for the host snail to live. Both host snails and parasites experience stress once a tolerance limit is reached in their respective microhabitats. The host snails may have a wide range of tolerance for one factor, but a narrow range for another which may explain their flexibility and wide yet patchy distribution in some areas of South Africa. An organisms' survival in a niche is particularly constrained by its limited ability to tolerate extreme changes in specific parameters, especially those which affect their survival most. From an ecological perspective, Shiff (1964a) stated that temperature is one of the most important physical influences of any biotope. The availability of water is the second most important factor.

Evidence as to how temperature affects snail and parasite survival is discussed in the following sections but some important conclusions from other researchers' work are mentioned briefly here by way of introduction to Section 2.3 in this chapter.

Brown (1994) comprehensively evaluated the chemical and physical factors affecting snail distribution and highlighted the importance of temperature on the distribution of host snails in the tropical and temperate regions of southern Africa. He also considered the influence of temperature on the schistosomes' intra-molluscan stages as a determinant of the parasites' spatial distribution. Appleton's (1976a; 1978) reviews on the South African situation highlighted the strong influence of temperature and current velocity on host snails. In another study, Pflüger, Roushdy and El-Emam (1984) emphasised that it is important to consider the effects of seasonal temperature variations in a subtropical schistosomiasis-endemic area, like that found in South Africa. An important conclusion arising from these studies was that thermal variation influences both parasite biology and the intrinsic rate of natural increase (designated *r*) of snail species (Appleton, 1976a).

Shiff (1964a) described *r* as the rate of increase of an unrestricted snail population of stable age distribution in a specified environment. Under natural field conditions, populations of organisms live according to a general life pattern and their numbers will naturally become restricted due to biotic potential and environmental resistance (Shiff, 1964a). He also maintained that the snails probably have longer life-spans and reproduce better under favourable environmental conditions than unsuitable environmental conditions. This parameter *r* offers an objective measure of a population's growth rate under specific conditions. Hence *r* is important for applied ecological research involving biotic tolerance.

Much work has been done on establishing the temperature tolerance ranges of the host snails and parasites. Michelson (1961) identified four stages in the transmission cycle that are susceptible to thermal variation:

(1) egg hatching success, the rate of miracidial development, miracidial locomotion and penetration,
(2) intra-molluscan larval development,
(3) length of the prepatent period in snails (to cercarial emergence), and
(4) cercarial infectivity of the final (definitive) host.

Aside from temperature, rainfall also affects seasonal patterns of cercarial production and plays a role in changing schistosomiasis transmission foci. Evidence of the importance of both temperature and rainfall was provided by O' Keeffe's (1985a) study on Kenyan *B. globosus*. He concluded that these two variables were the most significant factors affecting snail population fluctuations in tropical areas.

Once these important environmental factors are identified, distinct ecological zones may be geographically delineated (Appendix A). These zones can be designed to reflect the specific abiotic conditions known to be suitable or unsuitable to the organisms being studied. Hence, they can form the basis for disease models, which are discussed further in chapter 3. Appleton and Kvalsvig (1994) were the first to present the idea of spatially illustrating ecological zones for human intestinal parasites in South Africa. They used transect lines across the study area, (KwaZulu-Natal, Fig. 1.4) to represent areas expected to differ in transmission potential. Therefore, these ecological zones or eco-regions (Appendix A) reflect the suitability of the regional pattern of climate for intestinal parasite transmission. The value of ecological zones in disease modelling and the planning of control programmes were recently recognized by WHO (2002). An ecological zone map can be used to define the spatial scope of disease models as well as to identify gaps where survey data and new models are required (Brooker, Hay and Bundy, 2002a).

In light of the studies mentioned above, this chapter considers the effects of temperature and rainfall on the development of host snails and schistosomes. Firstly, a description of the South African climate is provided because it represents the environment to which these organisms are exposed.

2.2.1 THE INFLUENCE OF THE SOUTH AFRICAN CLIMATE ON THE HOST SNAILS AND PARASITES

The importance of climate to schistosomiasis epidemiology is well known (Pflüger, 1980). This section describes the prevailing South African climate, notably the patterns of temperature and rainfall where host snails and schistosomes are found.

South Africa, located at the southern tip of Africa, is characterised mainly by its complex temperate and subtropical climates. The main eco-regions (Fig. 2.1) of the country include:

1. the so-called great escarpment which is a continuous series of mountain ranges that ring the interior plateau and stretches from about 20°E to 31°E at about 200 to 300 km

inland from the south and east coasts (Schulze, 1997). It is also the major watershed of South Africa running along the east, south and west of the highveld (see 2 below). It separates the two largest river systems, the Gariep (Orange) and the Limpopo. The Gariep River system includes the main Gariep River itself and the Vaal and Caledon tributaries which flow in a westerly direction. The Luvuvhu, Letaba and Olifants are the major rivers of the Limpopo river system.

2. the vast interior plateau covering about two-thirds of the country and consisting of the highveld, lowveld and middleveld which describe its varying elevations. The highveld covers most of the plateau where mainly high altitude areas occur.
3. a generally narrow coastal strip of low altitudes

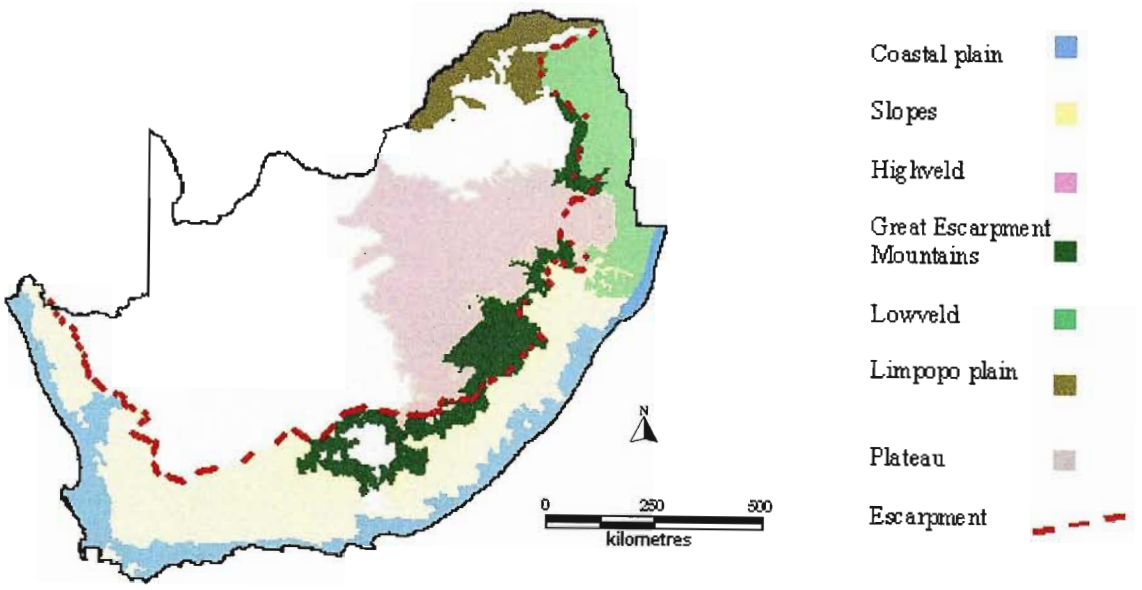

Figure 2.1: Eco-regions of South Africa (after Kleynhans and Hill, 1999)

The Western Cape (Fig. 1.4 in Chapter 1 shows the province's location) has a temperate climate, and experiences winter rainfall and dry summers. The east coast is characterised by its subtropical climate that becomes increasingly warm and humid northwards. The South African host snails and schistosomes are mainly tropical animals (Brown, 1994) displaying patchy distributions within the zones illustrated in Fig. 2.1.

Snails in their natural environment are subjected to the day-to-day weather of South Africa which is in turn influenced by subtropical, tropical and temperate features of the atmospheric circulation over the sub-continent (Preston-Whyte and Tyson, 2000). Spatial and temporal variation of the southern African climate occurred during the 20th century, which has possibly

impacted on many organisms' microhabitats (Preston-Whyte and Tyson, 2000). Biological processes therefore have to function within changing climate systems.

Climate describes the cumulative effect of weather conditions observed at places over a long time period. Weather information is an important consideration when conducting fieldwork on biological organisms. For instance air temperature recordings on a particular day are the most basic of information needed to calculate the degree-day index or `heat unit' for an organism. This index describes the accumulation of mean temperatures above or below a particular lower threshold over a time period (usually days or weeks) (Higley, Pedigo and Ostlie, 1986). The degree-day or degree-hours per week indices describe the total heat to which an organism is exposed to during part or all of its life-time. This index is also applied to vegetation such as maize. Degree-day indices for the host snails are described in Section 2.3.1.1.

Generally, prolonged low temperatures reduce the growth rate of plants and animals. The development of miracidia to cercariae in the schistosome life-cycle slows down during cool weather. This is discussed further in Section 2.4.1. Some organisms depend on their habitat's accumulated mean temperatures exceeding a particular threshold to initiate or complete particular developmental phases in their life-cycle (Schulze, 1997). Such development will continue provided the temperature remains within the organism's tolerance range.

Climate data spanning many years are useful for looking at trends and for describing both typical and atypical conditions or climate events in relation to epidemiology. Over 1.2 million km^2 of South Africa comprises a plateau (Fig. 2.1) lying between 1000m and 2500m (Doumenge *et al.*, 1987). The Western and Eastern Cape provinces together with KwaZulu-Natal, have even more variable altitudes. KwaZulu-Natal (Fig. 1.1 in Chapter 1), situated on the east coast and influenced by the Indian Ocean, has a humid climate. The coastal plain of northeastern KwaZulu-Natal is an area where the host snails *B. pfeifferi* occur but there is no intestinal schistosomiasis (Pitchford, 1976). *Biomphalaria pfeifferi* has a discontinuous distribution in this area and is found mostly in cooler and deeper waters compared to the waters *B. globosus* are found in. However, even if *B. pfeifferi* does occur in shallow waters as on the Pongolo floodplain, its density is low (Appleton *et al.*, 1995).

Below are descriptions of the temperature and rainfall patterns observed in the country. This detailed information was obtained from the South African Atlas of Agrohydrology and -

Climatology (Schulze, 1997), which contains maps of these climate parameters and therefore will not be presented here.

The descriptions are based on mean maximum and minimum temperatures respectively and grouped to reflect the seasons as follows:

(1) Spring - September to November, a period of rapidly increasing temperatures. In spring, cool wet weather is experienced in most parts of the country.

(2) Summer - December to February, a period of relatively stable, high temperatures. Generally South African summers are hot with thunderstorms in the afternoons.

(3) Autumn - March to May, a period of rapidly falling temperatures. In autumn there is low rainfall and it is warm during the days but cooler in the evenings.

(5) Winter -June to August, a period of relatively stable, low temperatures. During winter the higher-lying areas are cold and dry although sunny. Low rainfall is experienced in the lowveld (Fig. 2.1), and snowfalls can occur in the mountains.

South Africa is located between -22° and -35° latitude and it is influenced by the subtropical anticyclones that dominate air movements over the country. Varying rainfall and temperatures are experienced in South Africa depending on the altitude, exposure to prevailing winds and geographic location (latitude and longitude), (Schulze, 1997). Air temperature decreases as both altitude and latitude increases in South Africa.

Lower temperatures are observed at high altitudes hence much of the highveld has a cooling influence on temperatures. For instance, Johannesburg (situated at approximately 28° longitude - 26.2° latitude) should have predominantly warm temperatures but because of its high altitude, relatively low temperatures prevail. It then follows that flora and fauna are affected by these high altitudes and low temperatures. Since high altitudes imply cool temperatures that are possibly too cold for the snail or parasite to survive, one would expect these areas to be disease free. Prevalence studies done in high- and low-lying parts of the coastal KwaZulu-Natal confirm this. Kvalsvig *et al.* (2001) noted that urinary schistosomiasis was prevalent and showed high intensities in primary schools in KwaZulu-Natal. In their study, the prevalence and intensity of urinary schistosomiasis decreased as altitude increased (> 800m) probably due to the adverse effect of the low temperatures experienced at these high altitudes.

The low temperatures limit the geographical range of both the host snails and schistosomes because they are adapted to warm tropical conditions. Latitude in turn, influences seasonal

temperature variation. Seasonality reflects the way the weather changes over time during the year. Schulze (1997) described the relationship between latitude and seasonality by stating that high latitudes are associated with cool winters and not with cool summers.

Since the average daily temperature may fluctuate by several degrees, it is difficult to it use for comparative purposes. It is more useful to aggregate daily temperature recordings when studying temperature patterns. In this work, four temperature variables are used to describe the temperature regimes within the country. These are:

(1) seasonal mean daily maximum temperature patterns,
(2) seasonal mean daily minimum temperature patterns,
(3) daily temperature range and
(4) mean annual temperature.

Figures 2.2 and 2.4 in Sections 2.2.1 and 2.2.2 respectively show the seasonal mean daily temperature variations in each of the nine South African provinces. Since Schulze (1997) cautioned against using the data to obtain exact locational parameters (discussed in Chapter 4, Section 4.6.3), this seasonal grouping is a useful way to broadly describe the climatic similarities and differences among the nine provinces as illustrated in his Atlas. Hence, the information presented here do not account for small-scale variation in temperature and rainfall within each province.

Some descriptions of daily mean minimum and maximum temperatures are also provided in Sections 2.2.1 and 2.2.2 below. The provinces are numbered from 1 to 9 in a counterclockwise direction on the South African map as illustrated in Fig. 1.4. Rainfall patterns are discussed in relation to medians, concentrations and variability of precipitation in Section 2.2.5.

2.2.1 Seasonal mean daily maximum temperature patterns

The daily maximum seasonal temperature patterns of the nine provinces (Fig. 2.2) are arranged from the eastern coastal provinces, then inland and to the west. In spring, mean daily maximum temperatures rise to over 20°C throughout the country. Compared with the other provinces, relatively low spring temperatures are evident in northern KwaZulu-Natal, Eastern Cape and Western Cape, which lie along the coastal belt.

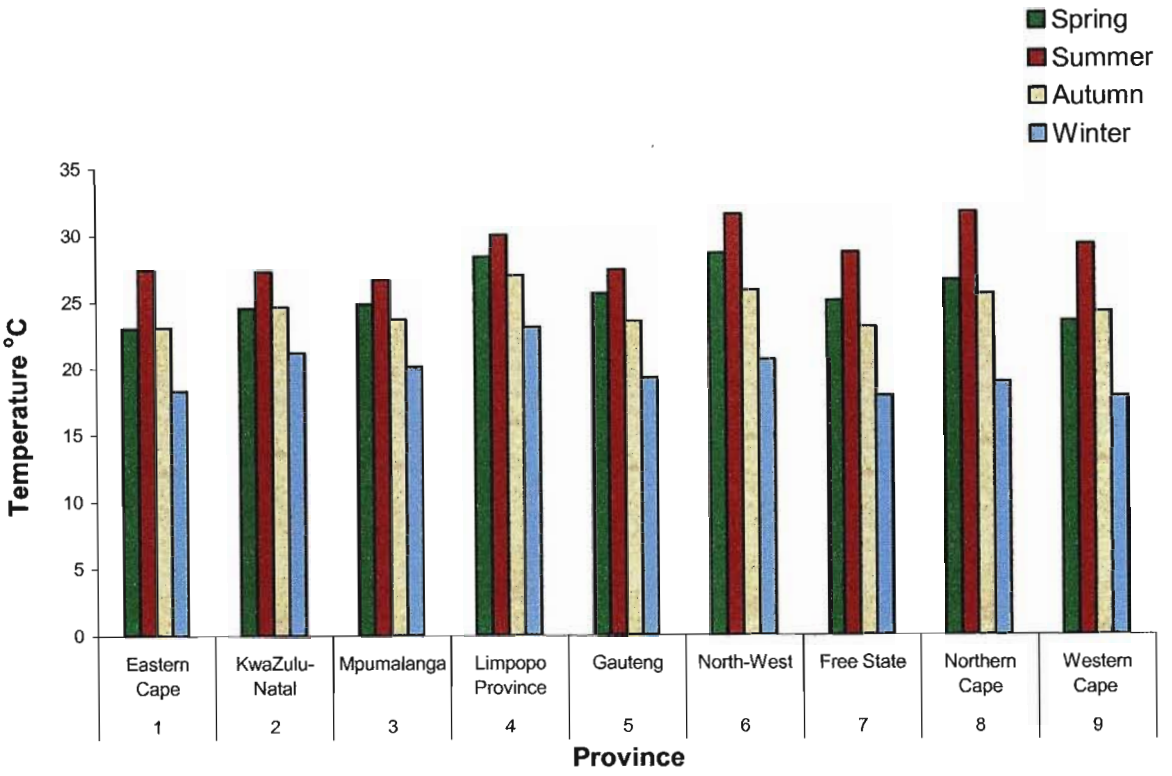

Figure 2.2: Seasonal means of daily maximum temperature in South Africa (after Schulze, 1997)

Stuckenberg (1969) observed that most organisms breed, feed and move about more when warmer temperatures occur. The Drakensberg mountain range and escarpment (Fig. 2.1) presents a natural zoogeographical barrier that affects the distribution patterns of many organisms including the tropical host snails (Appleton, 1976a). During the summer months mean maximum temperatures along the Drakensberg mountains in KwaZulu-Natal range between 22°C and 26°C (Schulze, 1997). Such high summer temperatures are moderated by the influence of altitude and the cloud cover along the east coast. No schistosomiasis has been reported along these mountains (Gear, Pitchford and van Eeden, 1980).

Mean temperatures over 34°C are evident in some parts of the North West province (34.9°C) and Limpopo Province (35.3°C) where the hottest mean daily maximum and minimum temperatures occur (Schulze, 1997). High maxima in the lowveld and Limpopo plain (Fig. 2.1) can be critical for snail hosts and schistosomes as will be evident later in Section 2.3. In mid summer, about 45% of the Northern Cape province experiences mean daily maximum temperatures over 32°C. The western and eastern regions of the North West province exhibit similarly high mean daily maximum values. Towards the latter part of summer the eastern parts of the country exhibit temperatures ranging between 18°C and 30°C (Fig. 2.2).

During the warm spring and hot summer months, children are on school holidays and they spend much more time swimming and engaging in other water sports than they do during the cooler seasons in South Africa. However, this does not preclude them from becoming infected during the cooler months. They may also swim in these waters whilst on their way home from school or they collect water for their daily use. The risk of infection increases if they contact contaminated water during the high transmission season. According to the national census of 1996, only 56% of people in the country have piped water, while even less (45%) have a flush or chemical toilet (Census, 1998). Therefore, in some areas where the lack of reticulated water is a problem, both girls and boys are potentially exposed to contaminated water whenever they play, bath, or wash clothes (Fig. 2.3), irrespective of the season. Appleton (1996) stated that about 80% of school children in the Mbogintwini River illustrated in Fig. 2.3 suffered from intestinal schistosomiasis in 1985. Another national census was done in 2001 but the results were only released in June 2003 and were thus not available for this study.

Figure 2.3: People using infected water in the Mbogintwini River on the southern outskirts of Durban in 1985 (Photo: C.C Appleton, 1996)

In autumn, mean daily maximum temperatures of 26°C to 28°C occur along the east coast while areas along the Eastern Cape coastal belt experience temperatures between 24°C to 26°C (Schulze, 1997). Towards mid- and late autumn, the temperatures drop by a further 5°C or 6°C along the eastern coast belt (Schulze, 1997) so that KwaZulu-Natal and Eastern Cape provinces

experience mean temperatures between 22°C and 25°C during this time (Fig. 2.2). The mean daily maximum temperature pattern for autumn approximates that for spring in the Eastern Cape, KwaZulu-Natal and Western Cape provinces.

During early winter the Limpopo Province, Mpumalanga, and KwaZulu-Natal have comparatively high (>18°C) mean daily maximum temperatures. Hot 'berg' winds produce the anomaly of the highest maximum temperatures recorded in winter along parts of the east coast and are features of coastal climates. They are most common during early spring and late winter (Preston-Whyte and Tyson, 1988). 'Berg' wind warming along the coastal areas gives rise to rapid increases in daily temperature. Inland regions exhibit cooler temperatures ranging between 10°C and 18°C during winter. Hence, inland areas experience relatively low daily maximum temperatures compared to the rest of the country during this time.

2.2.2 Seasonal mean daily minimum temperature patterns

The seasonal mean daily minimum temperatures (Fig. 2.4) have a broader range than the seasonal mean daily maxima (Fig. 2.2) and range between 1°C and 18°C while the daily maxima range between 18°C and 32°C. During summer, minima over 16°C occur in the Limpopo Province and the KwaZulu-Natal. Limpopo Province experiences the hottest daily minimum temperatures during summer.

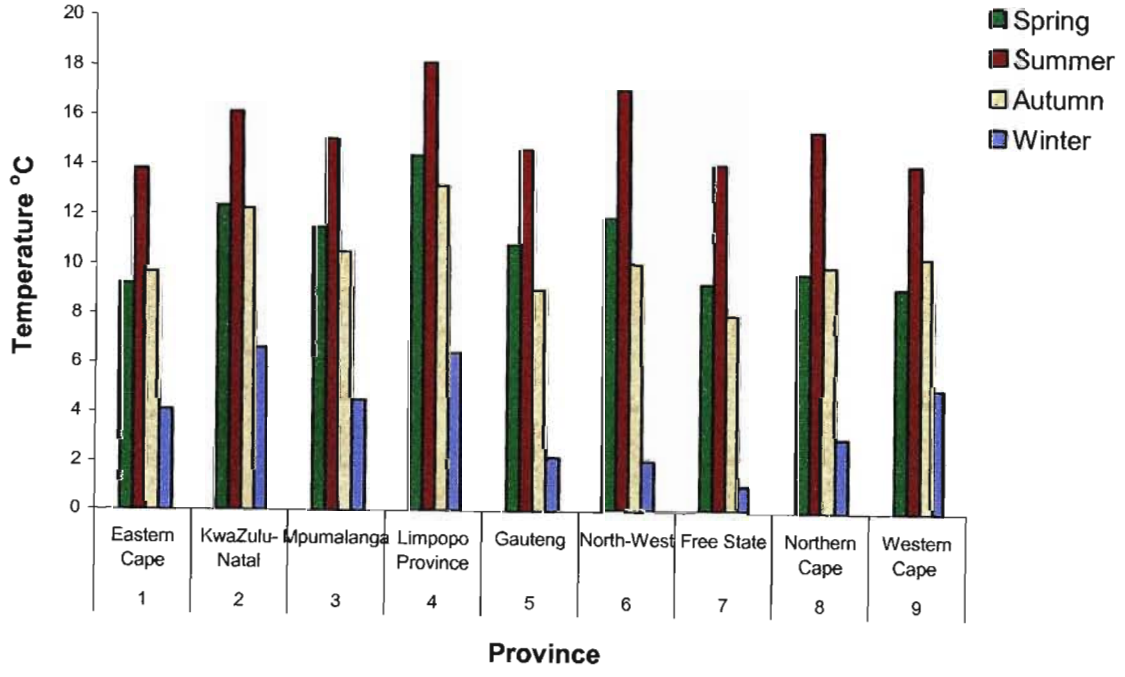

Figure 2.4: Seasonal means of daily minimum temperature in South Africa (after Schulze, 1997)

As autumn approaches cool mean minimum temperatures (below 20°C) are evident as one progresses further inland, with only parts of Lesotho (Mt. Aux Sources region) having very low daily minimum temperatures (Schulze, 1997). However even in mid-autumn, high minimum temperatures are seen further down the east coast of KwaZulu-Natal and into the Eastern Cape (Fig. 2.4). By May, a marked decrease in the overall mean daily minimum temperature for the country is observed.

During winter, the daily minimum temperatures range from 1°C (Free State) to 6.5°C (KwaZulu-Natal). Hence the Free State is the coldest province and KwaZulu-Natal the warmest province during winter. The interior regions of the country are colder than the coastal areas. Overall mean minimum daily temperatures range between -6.4°C and 3.3°C during winter (Schulze, 1997). Most organisms found there have special strategies and adaptations to survive these cold winter periods.

During early spring, the mean daily minimum temperatures range from -3.2°C in KwaZulu-Natal to 7.0°C in the Northern Province (Schulze, 1997). By mid-spring there is a general increase in temperature throughout the country, with the range of daily minimum temperatures being as cold as -1.8°C to 10.4°C (Schulze, 1997). By late spring, relatively high temperatures are evident in the Northern Province, Mpumalanga and KwaZulu-Natal, while the Free State and Western Cape continue to experience cool temperatures.

In this discussion on mean daily maximum and minimum temperature patterns, winter minima (< 7°C) represent the lowest of the low temperatures and summer maxima (> 25°C) represent the warmest of the high temperatures. It is also useful to consider the magnitude of the temperature change between these highs and lows. Interestingly, the coldest mean daily maximum temperature (about 16°C) experienced in winter is only a few degrees colder than the hottest mean daily minimum temperature in summer (about 18°C).

2.2.3 Daily temperature range

Daily temperature range is the difference between the mean daily maximum and minimum temperatures. Hence, it reflects the change in observed temperature during the course of a twenty-four hour period. Coastal areas do not have the large daily temperature ranges that the inland areas do because the sea has a moderating effect on daily and seasonal temperature ranges. The largest temperature ranges are observed in a north-south trend in November (spring), but this shifts to a north-west/south east alignment from December to February

(summer) and then back to a north-south trend in March (autumn). In winter months (June to August) higher ranges are observed in an east-west alignment. In nature temperatures do not remain constant throughout the day but vary over a range which itself changes from day to day and also seasonally. Temperature range is a good variable to replicate studies of snail and parasite tolerance limits because it represents the magnitude of the temperature fluctuation to which the organisms are exposed and introduces a time component.

2.2.4 Mean annual temperature (MAT)

The MAT is a broad index because it smoothes out the diurnal, monthly and seasonal patterns of maximum and minimum temperatures shown previously in Figures 2.2 and 2.4. In Fig. 2.5 it can be seen that KwaZulu-Natal has the third highest maximum MAT (MAT > 21°C) and lowest minimum MAT (3°C) in the country. As stated earlier both snails and schistosomes are seen to occur along this northeast coastal belt and along the eastern border and from this it can be inferred that they tolerate the province's broad MAT temperature range. However, low minimum MATs are observed along the Drakensberg escarpment and over Lesotho where the snails do not occur. Such variations may be attributed to topographic variation. The interior has high minimum and maximum MATs.

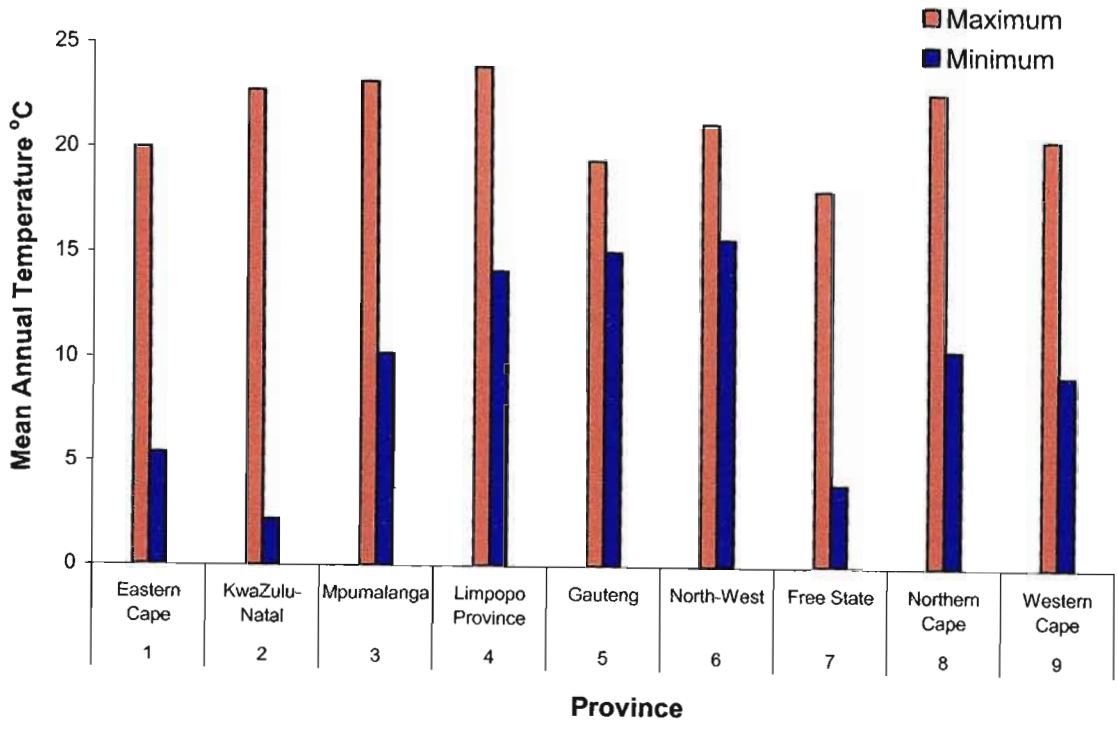

Figure 2.5: Mean annual temperature in the nine provinces of South Africa (after Schulze, 1997)

Global circulation models predict that the greenhouse effect could cause an increase of 1.02°C to 3.5°C in the global mean temperature by 2100 (Haines, McMichael and Epstein, 2000). From these calculations, mean annual temperatures over South Africa are predicted to increase by 2°C (Hulme, 1996). Haines *et al.* (2000) state that global warming will cause increases in ambient temperatures and rainfall at high elevations. Consequently, host snails and their parasites will be subjected to higher temperatures than they are currently acclimated to and their survival will depend on their adaptation to and tolerance of the thermal change. Martens (1995) modelled the effect of global warming on schistosomiasis worldwide using different climate change scenarios. He predicted a spatial expansion of the areas currently supporting schistosomiasis. Martens (1995) concluded that transmission would increase at the edges of current high altitude endemic areas, but would decrease in other endemic areas. The predicted temperature increases in parts of currently endemic areas would decrease the transmission potential because these temperatures would rise above the parasites' and snails' upper thermal tolerance ranges (see Section 2.3). Consequently, in such areas perennial transmission may become seasonal and seasonal transmission in the fringe areas may become perennial.

2.2.5 Rainfall patterns in South Africa

This section addresses the following three aspects of rainfall that are relevant to schistosomiasis transmission in the country:

(1) the duration and amount of rainfall,

(2) the spatial distribution of rainfall and

(3) the seasonal distribution of rainfall.

Rainfall is important to this study because it is a surrogate indicator of the availability of water for disease transmission, especially in rain-fed habitats.

Rainfall also exerts a strong influence on vegetation cover. Freshwater snails are usually associated with macrophytes. These leafy aquatic plants provide the host snails with egg-laying sites and also shelter them from solar radiation and current velocities (Brown, 1994). The snails also feed on decaying plants. Maps of rainfall can be correlated with vegetation indices such as the Normalized Differentiation Vegetation Index (NDVI) (Appendix A) which represents the amount of chlorophyll in an area. Little or no rain implies dry conditions during which time snails may be able to aestivate. Some of the commonly used rainfall indices are mean annual rainfall, mean monthly rainfall and median rainfall and these will be discussed in the sections that follow.

2.2.5.1 Mean annual rainfall

Mean annual rainfall decreases westwards across South Africa, where schistosomiasis becomes increasingly less common. This rainfall contrast from east to west has profound effects on the growth of many types of flora and fauna.

2.2.5.2 Mean monthly rainfall

The mean rainfall for any given month is the average of the daily rainfall for that month. Consideration of cumulative rainfall indices is sometimes more useful than using short rainfall indices like daily rainfall. The reason is that the rainfall over a period of one month can have more of an effect on habitat stability or permanence than steady rainfall over a shorter time span of a few days. Monthly data also allow comparisons of intra-year rainfall distribution. If these data are then grouped into seasons, it offers a useful time- step to describe temporal rainfall patterns, based upon often irregular, daily rainfall patterns. Monthly rainfall patterns can indicate the start and end of the rainy season. In addition, analyses of the rainfall coverage over one month for each province allow the wet and dry parts of the country to be identified and comparisons to be made.

One disadvantage of using monthly rainfall data is that large differences can exist between one month and the next, which may be lost in analyses if too general figures are calculated. Mean values are also influenced by any extreme climate event. Thus, the mean may not be a true reflection of the general rainfall pattern over the whole month.

2.2.5.3 Median rainfall

Instead of monthly rainfall, Schulze, (1997) describes rainfall in the country using the median i.e. the midpoint of a series of data ranked from highest rainfall to lowest rainfall. Schulze (1997) considers the median to be the statistically expected value, which is the reason it is discussed further here. However, when using rainfall for model building it is worthwhile to consider what type of measurement will add the greater value to the model. This also depends on the relevant data being available and affordable.

Rainfall patterns using median rainfall for South Africa

In January, there is a distinct east-west gradation of rainfall from higher to lower respectively, correlating with both schistosomiasis distribution and the peak transmission period. The high rainfall areas extend from the north-east part of the Eastern Cape, northwards through KwaZulu-Natal, Mpumalanga and Limpopo provinces. This follows the distribution of *B. pfeifferi* and *S.*

mansoni (Gear *et al.*, 1980). A similar pattern exists for *B. africanus* and *S. haematobium* but in this case both the snail and the disease are distributed further westward along the coast of the southern part of the Eastern Cape.

Generally, there is a shift from a summer rainfall pattern to one of winter rainfall, i.e. parts of the country receive more rain from February to May, while others receive most rain in winter. The following description of seasonal rainfall patterns illustrates this shift: during summer, KwaZulu-Natal in the east coast (Fig. 1.4) experiences the most rainfall during summer while the Western Cape experiences the least rainfall at this time. The situation is reversed as the seasons change. The Western Cape experiences the most rain in autumn when the province is significantly wetter than the other provinces. During late spring and summer there are general increases in rainfall in all provinces, with the exception of the Western Cape, which becomes dry again.

2.2.5.4 Rainfall concentration and variability

The rainfall concentration index as defined by Schulze (1997) refers to the duration of the rainy season and describes whether rainfall is concentrated over a long period or short period of the year. An index of 100% implies that all of a region's rain falls predominantly in one month. Alternatively, an index of 0% implies that the rainfall in an area is spread over time and that the rainfall for each month of the year may be similar. The northern regions of Limpopo Province (a high rainfall area) and Northern Cape (a low rainfall area) have the highest rainfall concentrations implying that these provinces receive intensive rainfall over only a few months. The southern parts of Western Cape and Eastern Cape have the lowest rainfall concentrations, less than 10 %, since their rainfall is evenly spread through the year.

Rainfall variability describes how much variation or deviation occurs in the average amount of rainfall. The greater the variability is, the more unreliable the rainfall. The areas where schistosomiasis occurs display reliable rainfall concentrations compared to areas where no schistosomiasis occurs (the western parts of the country) (Gear *et al.*, 1980). As one moves from east to west in South Africa, the rainfall becomes less reliable. This together with the variable temperatures experienced in these parts of the country, and discussed in this section, impose restrictions on snail survival in the types of habitats that occur there.

2.2.6 Distribution of host snails and schistosomes

Maps of the distribution of South African *B. pfeifferi* and *B. africanus* group snails occur in the Atlas of Bilharzia (Gear *et al.*, 1980) but are the intellectual property of the former Snail Research Unit at Potchefstroom University (C.C. Appleton, University of Natal, pers comm[1]). Therefore, they are not repeated here.

Host snails

Brown (1994) studied the distribution of the freshwater host snails in Africa and divided them into two groups, namely tropical species and temperate species based on the climate where they occur. As mentioned in Section 2.2.1, both temperate and tropical climates occur in South Africa. However, both *B. pfeifferi* and the *B. africanus* group snails occur mainly in the subtropical eastern coastal parts of South Africa where the climate is generally more suitable for snail survival than the western regions which has a temperate climate. Tropical areas are warmer than the temperate areas therefore snails living in tropical areas are able to tolerate the higher temperatures found there. Both organisms reach the southern limits of their distribution in South Africa.

The suitable east coast areas form a "tropical corridor" up to 100km wide (Brown, 1994). For example, *B. pfeifferi* is found across south-central Africa from the Okavango River System to Mozambique and southwards down the narrow eastern parts of South Africa, to the Mngazi River (31° 29`S) in Eastern Cape (Appleton, 1996). As was shown in Section 2.2.5, the inland parts of the country are generally drier than the east coast and *B. pfeifferi* may also be found in some isolated habitats.

Bulinus africanus is found over both the highveld and the lowveld extending south to KwaZulu-Natal and Eastern Cape. It is however, absent from the narrow coastal plain between Lake St. Lucia and the Mozambique border. The species occurs, apparently sporadically in the Eastern Cape where it extends to the Kromme River (Gear *et al.*, 1980; Appleton, 2002). Brown (1994) attributed the limited occurrence of host snails in the central and western parts of South Africa to the "drought" corridor.

[1] Prof. C.C. Appleton, School of Life and Environmental Sciences
University of Natal, Durban, 4041, South Africa

A second species belonging to the *B. africanus* group occurs in South Africa, i.e. *B. globosus*. This species is found in the Mpumalanga lowveld (where it is sympatric with *B. africanus*) and extends down the lowlands to Lake St. Lucia on the east coast of KwaZulu-Natal (Brown, 1966).

Host snail species have a discontinuous distribution and they occur in some areas where no schistosomiasis occurs (Pitchford, 1976), probably due to intrinsic environmental factors that do not support parasite fitness. As long ago as 1938 Porter recognised that the snail hosts were more widely distributed than the schistosomes, possibly due to the different tolerance limits each organism had for their abiotic environment.

Schistosomes

The distribution pattern of *S. haematobium* covers much of eastern South Africa and resembles that of their snail hosts of the *Bulinus africanus* group. The occurrence of *S. haematobium* was described in chapter 1, from which it can be concluded that the parasite occurs mainly in the following five eastern provinces, namely; Limpopo, North-west, Mpumalanga, KwaZulu-Natal and Eastern Cape. Previously the southerly limit was thought to be the Kei River (32° 40`S) but recently Appleton (2002) reported urinary schistosomiasis in children living along the Kabeljous River in the Humansdorp district of Eastern Cape (Fig. 1.5) which now also represents the new southern limit for the disease.

Morgan *et al.* (2001) stated that *S. mansoni* is the most widely distributed of all the human schistosomes and is particularly abundant in sub-Saharan Africa. This relates to the fact that only *S. mansoni* and not *S. haematobium* was translocated to South America (Rollinson and Southgate, 1987). However, a comparison of the spatial distribution of *S. mansoni* and *S. haematobium* in South Africa (Gear *et al.*, 1980) reveals a different picture. The distribution of *S. mansoni* here is not as wide as that of *S. haematobium*, commonly occurring in only two provinces namely, Limpopo and Mpumalanga, but also sporadically KwaZulu-Natal as mentioned in chapter 1. Furthermore, the occurrence of neither parasite approximates the distribution pattern of their snail hosts, which have a wider distribution (Gear *et al.*, 1980). Brown (1994) suggested that this was due to the climate transition from tropical to temperate; the schistosomes being more sensitive to this climatic transition than the planorbid intermediate hosts.

2.2.7 Summary

The temperature parameters discussed above, namely mean daily maxima and minima temperature, temperature range and mean annual temperature help to define the seasonal thermal variations within each province. Some rainfall parameters were also discussed to describe the generally wet and dry provinces. Although both these parameters are discussed separately here for the purposes of the next section, an important consideration is the combined effects of temperature and rainfall together on organisms. Odum (1983) noted that temperature has a more severe limiting effect on organisms when there is either too much or too little moisture compared to moderate amounts of moisture. Likewise rainfall has more of a limiting effect under temperature extremes. This could account for some anomalies in areas where there is no disease despite suitable host snails being present and for the patchy distributions of *S. haematobium* and *S. mansoni*.

Temperature and rainfall act directly but also indirectly on the snails through changes in the surrounding habitat's flora and fauna (O'Keeffe, 1985b). For instance, snails feed on the associated periphyton growing on the associated vegetation (as well as decaying vegetation) and this in turn is affected by rain and temperature. Furthermore, the vegetation in the water can also moderate the water temperature if these plants produce shade (Appleton, 1997). The effect of shaded water on snail distribution is discussed in greater detail later. The important point to highlight here is that the varying temperature and rainfall patterns observed in different parts of the country impact on the growth of juvenile snails and the reproductive potential and survival of adults. The following section discusses how temperature and rainfall affect the snail hosts and schistosomes.

2. 3. ENVIRONMENTAL REQUIREMENTS OF THE INTERMEDIATE HOST SNAILS

A review of the available literature was conducted to determine the temperature conditions that are suitable for the South African host snails to function optimally whether they are either infected or uninfected with schistosomes. Snails will die if temperatures go above or below critical limits. Hence, there is an optimal temperature range for their survival. This section discusses the host snails' tolerance limits under different temperature conditions.

2.3.1 Temperature tolerances of the host snails

Generally, temperature affects the size of a snail population and the fecundity of adult snails. There is a series of optimal temperature tolerance ranges known to support the survival and

reproduction of different snail species. Aquatic organisms tend to have narrower temperature tolerance ranges than their terrestrial counterparts (Odum, 1983). This is shown by the experimental work done on South African snail species dating back several decades (e.g. Porter, 1938). The results of relevant studies on temperature and rainfall are discussed below.

Optimal, high and low thermal tolerance limits

The effects of moderately high or low temperatures are of more interest for water- related diseases than short-lived extreme temperatures. Generally, extreme temperatures are rare in aquatic environments due to their heat capacity and evaporative properties (Appleton, 1976a). The tolerance ranges for each host snail species are described in terms of three categories in the following sections namely; high temperatures, low temperatures and optimal temperatures. As mentioned earlier the host snails are poikilothermic and their body temperature fluctuates as the environmental temperature changes.

2.3.1.1 The *Bulinus africanus* group: *Bulinus africanus* and *Bulinus globosus*

High temperature tolerance limits

High temperatures are however more detrimental to snail survival than to parasite survival, so while the parasites can thrive at 26°C and 28°C their snail hosts do not. These species of snails generally do not colonise habitats with very high temperatures. It was found that temperature has the most marked influence on snail growth during the first month of a snail's life (Brown, 1994). Therefore, snail's thermal adaptation to stress at a young age will determine whether it reaches maturity and reproduces or not.

Joubert *et al.* (1986) maintained that daily water temperatures in excess of 30°C are not unusual in areas that are endemic for *B. globosus* and *B. pfeifferi*. Joubert *et al.* (1986) found that *B. globosus* is more tolerant of such high temperatures than both *B. pfeifferi* and *B. africanus*. Laboratory studies by these authors showed that *B. globosus* could tolerate constant high temperatures of 34°C to 40°C better than *B. pfeifferi* or *B. africanus,* living for 40 days at 34°C but no snails survived at 40°C beyond 6 to 8 hours. Shiff and Husting (1966) concluded that *B. globosus,* although being stenothermal, could colonise thermally harsh environments because they have a relatively high *r* at high temperatures. Due to their differing high heat tolerances, one would expect the *Bulinus africanus* group snails and *B. pfeifferi* to be distributed differently throughout the country, but this is not the case as *B. pfeifferi* is found in the hot parts of South Africa albeit patchily distributed. However, there is evidence that in these situations, *B. pfeifferi*

survives in habitats that experience relatively cooler temperature regimes such as deeper pools and lakes (Appleton, 1977b).

Low temperature tolerance limits

Bulinus africanus tolerates constant very cold temperatures (0°C to 8°C) better than *B. globosus*. According to the findings of Joubert *et al.* (1984) the ranking of the three South African host snails in terms of cold tolerance is as follows: *B. africanus* > *B. globosus* > *B. pfeifferi*. These authors conclude that theoretically, *B. africanus* and *B. globosus* could survive at temperatures between 0°C and 8°C in the laboratory but this is unlikely to be the case in the field where they prefer warmer temperatures (see following section on optimal temperatures).

In Shiff's (1964b) field study in Zimbabwe *B. globosus* survival improved as autumn (a season of rapidly falling temperatures) approached. During March and May, the snail survival rates were high compared with December (mid-summer) when fewer snails survived. Thus as the temperature decreased, survival of this species was favoured. The egg-laying season is between November to May, which corresponds to spring, summer and autumn (Shiff 1964b). However, as it gets cooler from March to August, there is a decline in egg production possibly due to little or no breeding during the subtropical winters. Furthermore, Joubert *et al.* (1984) attributed the absence of host snails in otherwise suitable habitats in certain parts of the South African highveld, to the low winter temperatures prevailing there. During winter the highveld is also dry and the pools of water harbouring these host snails are too shallow to offer them the protection they would normally get at greater (and possibly warmer) depths. None of the cohorts in their study survived for more than 8 days at 8°C.

Optimal temperatures for *B. globosus* and *B. africanus*

Generally *B. globosus and B. africanus* have a narrow range of optimal temperatures (i.e. they are stenothermal) and are able to maintain population peaks at 25°C (Brown, 1994)

As mentioned earlier the *r* value of particular snail cohorts provides an indication of the direct influence of temperature on the organism's biology within a niche. In general, *r* for the *B. africanus* group snails approaches zero at low temperatures (17 - 18°C) and peaks at approximately 25°C (Shiff, 1964a; Sturrock, 1966a; Sturrock & Sturrock, 1972). De Kock (1973) found the lower limit for the growth and survival of South African *B. africanus* to lie between 17°C and 20°C and for *B. globosus* it is approximately 20°C. However, within this range Shiff (1964a) had found the intrinsic rate of natural increase to be comparatively higher

for Zimbabwean *B. globosus* in the laboratory (Shiff 1964a) compared to that observed for the South African snails pertinent to this work.

Shiff (1964a) showed that survival of B. *globosus* was better at a constant temperature of 22.5°C compared to 25°C or 27°C. However, the optimum temperature *r* for this species was 25°C, with maturation occurring earlier as the temperature rose. In the field, Shiff (1964b) found rapid increases in egg production as the temperature increased up to the 25°C threshold. Similarly in South Africa, Prinsloo and van Eeden (1969) observed good survival of uninfected *B. tropicus* at 25°C but these snails began to die at warmer temperatures around 27°C. On the coast of Kenya, O'Keeffe (1985a) studied the environmental factors affecting *r* of *B. globosus* in two reservoirs in Nguni and Benes. He found an inverse relationship between water temperature and *r*, which implied that long-term warm temperatures during the year inhibited snail population growth. When the mean water temperature increased to over 28.5°C during the cohort's early reproductive phase, their *r* was negative.

In addition Shiff (1966) found that laboratory-bred *B. globosus* could detect temperature differences as small as 4°C in a habitat, and will tend to remain in warmer water (near the surface). In summer, these snails are randomly distributed in the water body, while in winter they cluster near the surface, possibly because the temperature is higher there than at lower depths.

These studies suggest that the temperature range at which high *r* is maintained varies amongst the different snail species. Nevertheless high *r* may be considered to be a selective advantage to these poikilothermic animals enabling them to live in the harsh environments found in temporary water bodies on the highveld (Appleton, 1978). In summary, the optimal temperature for the *B. africanus* groups snails is 25°C. Low temperatures (< 8°C) up to 17°C and high temperatures (>34°C) are detrimental to these snail populations. This correlates with the known distribution of the snail species in South Africa (Gear *et al.*, 1980). The Western Cape province has a mean daily maximum temperature of 34°C and no *B. africanus* group snails are found there. However, the eastern parts of the country experience temperatures that are more suitable to these snails (18°C to 30°C) and are endemic for schistosomiasis (Fig. 2.2).

2.3.1.2 *Biomphalaria pfeifferi*

High temperature tolerance limits

Even though *B. pfeifferi* snails are widely distributed in the country they do not fare well in areas where too high temperatures occur (Brown, 1994). Once the temperature rises too high, *B. pfeifferi* is vulnerable and areas where such temperatures occur represent unsuitable snail habitats. Some studies that show this are described below.

Sturrock's (1966b) work on the effect of constant temperatures (19°C to 35°C) on Tanzanian *B. pfeifferi* demonstrated the snails' vulnerability to high temperatures. Snail mortality was highest at 30°C. The conclusion was drawn that at lower temperatures (e.g. 19°C), the snails could maintain their numbers but could not expand them rapidly. Although that study showed that *B. pfeifferi* could tolerate maximum temperatures in the range 30°C to 35°C in the laboratory, the threshold in the field is more likely to be lower (approximately 28°C). Moderate temperatures (20.5 - 25.5°C with a 5°C/ day fluctuation) favoured the growth rate and fecundity in de Kock and van Eeden's (1986) study. At temperatures rising to 25°C, there was a rapid increase in egg production, and egg maturation occurred earlier as the temperature increased.

Appleton's (1977a) work in the coastal plain of north-eastern KwaZulu-Natal showed that the high temperatures found there to be too high for *B. pfeifferi* to survive. He found that the high temperatures of natural shallow water bodies were negatively correlated with the fecundity of *B. pfeifferi*. Appleton (1977a) found that snail went into hypothermia at constant 29°C while fecundity and survival were reduced even at 27°C. The temperature regimes in natural shallow waters like ponds, pans (less than 2m deep) and streams rose to such high levels in summer that *B. pfeifferi* gametogenesis was retarded and survival was compromised (Appleton and Eriksson, 1984).

Observations on the situation in north-eastern KwaZulu-Natal led Appleton (1977a; 1977b) to conclude that *B. pfeifferi* preferred cooler, deeper waterbodies which accounts for their discontinuous distribution on the coastal plain there. However smaller populations are sometimes found in shallow habitats like those on the Pongolo floodplains where high spring and summer temperatures occur (Appleton, 1997a). Earlier work (Appleton, 1977a) showed that under such conditions both fecundity and survival were reduced at 27°C and at 29°C there was severe stunting of growth with few or no eggs being laid. The amount of above-optimal heat (fluctuating between 45 to 50 degree hours above 27°C per week) that occurred during the spring breeding period in this region impaired development of the ovotestis and consequently,

egg production as well. *Biomphalaria pfeifferi* cannot survive temperatures of 40°C for more than 6 to 8 hours (Joubert *et al.*, 1984).

Low temperature tolerance limits

De Kock and van Eeden (1986) studied the effect of programmed circadian temperature fluctuations on *B. pfeifferi* and concluded that these snails could actually benefit from a daily temperature fluctuation of more than 10°C. The lower temperature regimes (18-28°C, i.e. a 10°C/day fluctuation) favoured longevity. At the temperature regime that is optimal for egg production, the snails died more quickly i. e longevity is low but *r* was at a peak under these conditions. Early work by de Kock (1973) suggested that the lower temperature limit for growth and survival of South African *B. pfeifferi* lies between 15 °C and 17°C.

The work of Joubert *et al.* (1984) using constant low temperatures (ranging from 0°C to 8°C) on *B. pfeifferi*, showed that snails died as the temperature decreased. These experimental temperatures were less favourable for *B. pfeifferi* than for the *B. africanus* group snails. None of the three planorbid species tested could survive in nature at these temperatures. Nevertheless, the authors concluded that theoretically *B. pfeifferi* could survive for 96 hours at 6°C in contrast to *B. africanus* which survived for longer (144 hours at 6°C). Furthermore, *B. africanus* survived for 102 hours at 8°C without any mortality.

Optimal temperatures for *B. pfeifferi*

Biomphalaria pfeifferi, being a eurytherm, can tolerate wider temperature fluctuations than the South African *B. africanus* group snails. Temperature tolerance for *B. pfeifferi* is generally expressed in the literature as an optimality "range" and not as a specific temperature as was the case for the *B. africanus* group snails described above. The reason is that *r* for *B. pfeifferi* has a plateau of near- optimal *r* values (Appleton, 1978).

Appleton (1977a) suggested that *B. pfeifferi* may perform optimally, or near-optimally at a range of temperatures from 22.8°C to 27°C. Later the work of de Kock and van Eeden (1986) showed the best results for the population parameters for *B. pfeifferi* were obtained under a fluctuating regime of 18°C - 28°C. These authors also stated that 27°C is considered near optimal for this species. However, evidence reviewed by Brown (1994) endorsed the existence of a plateau of optimality but with an even broader range of 20°C to 29°C. The higher temperature of 29°C was contributed by Appleton and Eriksson (1984) who found that the end-point of the plateau of near optimal *r* values for *B. pfeifferi* lay around 29°C (corresponding to

45-50 degree hours above 27°C per day). Sturrock's (1966b) work on Tanzanian *B. pfeifferi* showed that its life table values were higher and the mean generation time shorter at 25°C compared with lower temperatures. Thus the optimum temperature for Tanzanian *B. pfeifferi* was 25°C, perhaps an adaptation to life in more tropical conditions than Zimbabwe or South Africa.

De Kock and van Eeden (1986) maintained that *B. pfeifferi* are adapted to colonize warm, relatively stable habitats as they exhibited a relatively low *r* and a long generation time (Tc), even at optimal temperatures. These snails exhibit a discontinuous distribution in the country, which could reflect their need for the stable thermal conditions often found in permanent habitats. The results of the studies mentioned in this section suggest that temperatures over 28°C are too high and temperatures cooler than 6°C are too low for this species. Temperature has been shown to be an important limiting factor in the distribution of *B. pfeifferi* in south-eastern Africa (Appleton, 1977a; 1977b).

2.3.1.3 Summary

To summarise, these studies show that reproduction and growth of *B. globosus* peaked at 25 °C, whereas for *B. pfeifferi* they remained optimal over the range 20°C to 27 °C (Shiff, 1964a; Shiff and Garnett, 1967). Also *B. pfeifferi* has a broader tolerance of fluctuating temperatures than the *B. africanus* group snails. It seems too that *B. globosus* is more tolerant of high temperatures than *B. africanus*. The review of these studies raised four important points that need to be considered in relation to biological studies of these organisms' tolerance of their environment, namely:

(1) constant versus fluctuating temperatures,
(2) acclimatization,
(3) studies done using air temperature measurements rather than water temperature and
(4) the duration of measured temperatures in the field.

2.3.1.4 Some considerations for thermal studies involving host snails and schistosomes

Constant and fluctuating temperatures

Many laboratory studies involving both snails and schistosomes make use of constant temperatures rather than fluctuating temperatures. However, long periods of constant temperatures do not normally occur in field conditions. Brown (1994) cautioned against extrapolating experimental results on the effects of constant temperatures on snail hosts (and

their schistosome parasites) to explain their natural distribution. In the field, organisms are subjected to variable temperatures so they respond differently to them than they do to constant temperatures. Hence, experiments using fluctuating temperatures are useful as they reveal how the host snails respond to the changes in their environment.

Appleton (1978) suggested that a combination of both fluctuating temperatures in the laboratory and longitudinal field studies could provide the best reflection of reality. Frank (1966) found that the intra-molluscan development stages of *S. haematobium* and *S. mansoni* depended on diurnal temperature fluctuations for optimum cercarial output. A fluctuating temperature regime (for example 10 to 20°C, average 15°C) does not have the same effect on an organism as a constant temperature of 15°C.

Acclimatization

Conclusions from such studies depend on where the snails originate from, for instance if *B. pfeifferi* originates from an area representing the colder part of its temperature tolerance range, it could be better acclimated to cold than those from a warmer region. In laboratory experiments the snails are taken out of the environment and studied. This is where spatial analyses in disease modelling offer the advantage of linking the organism with the environment as they occur in reality. For instance, temperature recordings from weather stations can be used to approximate the temperature at the different localities at which the snails occur. It is also important to consider, following Brown (1994), the difficulty of assessing the direct relationship between temperature and snail mortality in the field. The reason is that large temperature gradients often occur within the snails' habitats in three-dimensional stands of vegetation for example. This is reflected in the earlier discussion on daily temperature range where it was stated that the coastal areas do not have large temperature gradients. However, an added complication is the difference in ambient and water temperatures.

Water temperature versus air temperature

The important points of discussion in this section are (1) thermal differences between large and small water bodies, (2) the effect of shade, (3) the effects of dams on rivers and (4) temperatures at different locations along a water body.

Martens (1995) added that since schistosomiasis is a water-related disease, water temperature affects the dynamics of disease transmission. Schistosome transmission typically occurs in relatively small, shaded waters such as irrigation storage dams, canals, streams, shallow rivers

and pools because those are the types of water bodies both their snail and human hosts prefer (Pitchford, 1981). The temperatures of these water bodies usually conform quite closely to air temperature. Generally there is less thermal variation in water than on land. Also the range of thermal variation is smaller and the rate of change slower in water than in air (Odum, 1983).

Unfortunately appropriate water temperature recordings may not always be available for spatial analyses. Continuous longitudinal recordings of water temperatures are tedious to record and seldom available, so one has to rely on extrapolations from air temperature recordings (Pitchford, 1981). One reason for this is that different temperatures are observed at different depths of water in one water body during the day and night. In the temporary rain pools on the coastal plain of northern KwaZulu-Natal, Hamer and Appleton (1991) found temperature differences of 9 to 10°C between the surface and substratum during the day. However, at night the temperatures were almost the same. Generally water temperature in these pools was variable, related to the time of day and the prevailing weather.

However, Pitchford (1981) stated that since the ambient air temperature controls water temperature, air temperature can be used to indirectly assess and compare the temperature of similar water bodies. Analysis of air temperatures could reveal patterns over particular areas. Martens (1995) added that the average temperature of shallow water usually approximates that of air temperature, but an important difference is that on very hot days the water temperature may in fact be cooler than ambient temperature.

Another important consideration is the effect the surrounding vegetation has on these water bodies in terms of shade they provide. The effects of shade can be large in certain microhabitats, such as those provided by growing rice plants in rice paddies. Appleton (1993) recorded temperatures in different parts of two rice paddies in Mamfene (northeastern KwaZulu-Natal) including: surface shade, surface sun, bottom shade, bottom sun and in the air about 10 cm above the water in shade. Measurable temperature differences were found between shaded and sunny areas. At midday in the flood-irrigated rice paddy scheme at Mamfene the air temperature was 33°C but a sunny area on the bottom was 28°C and a sunny area on the surface was 31°C. The mean water temperatures in the shaded and sunny areas thus varied considerably between themselves and from the air temperature. Shaded areas in the paddies had higher temperature minima and lower maxima then the surrounding natural shallow pools. Temperatures varied the most near the surface but were relatively stable in the bottom areas where *B. pfeifferi* lives, compared with the other study sites. The two surface microhabitats experienced temperatures in

excess of the optimal 45 degree hours >27°C per week that Appleton (1993) determined for *B. pfeifferi*.

Appleton ranked the different microhabitats in terms of their suitabilty for *B. pfeifferi* as follows: bottom shade > bottom sun> surface shade> surface sun where the bottom shaded areas provided the best habitat for these snails from a thermal standpoint. The picture is further complicated by the fact that above-optimal temperatures may be reached at different times in different microhabitats even though they may be within a few kilometres of each other.

There are few published studies relating host snail population dynamics and water temperature. Pitchford and Visser (1975) studied the effects of the Gariep Dam (previously called the Verwoerd Dam) on the water temperature of the perennial Gariep (Orange) River, about 4 km downstream of the dam. This is the largest dam in South Africa. River temperature recordings were taken over a period of three to four years before and after completion of the dam. There was no difference in temperature during spring and autumn but there was a rise in river temperatures during winter and a decline during summer. These authors concluded that this situation i.e. variable winter temperature would encourage the establishment of *B. pfeifferi* and the *B. africanus* group snails in the irrigation scheme fed from the river, thereby improving the chances of schistosomiasis being introduced, especially transmission in summer.

In another study Appleton (1976b) collected temperature data (expressed in degree hours per week) from four different sites on the perennial Gladdespruit stream in Mpumalanga in the mid-1970s and showed seasonal differences in the water temperatures at different points within the stream, one of which was a semi-detached pool. The temperature variations along the stream were due more to higher temperature maxima than to lower temperature minima. Therefore, Appleton (1976b) concluded that the observed different temperature tolerances of the organisms living in the stream should relate to the upper limits rather than lower limits. During spring and summer, the semi-detached pool containing *B. globosus* was warmer than the mainstream channel and this author believed that air temperature contributed to that.

Duration of temperature

The following components of the thermal regime deserve consideration when assessing the likelihood of host snails colonizing a body of water: available heat (e.g. degree hours per week), mean daily minimum and maximum temperatures and daily temperature range. The first

component is discussed here as the latter three were discussed earlier in relation to the snails' thermal tolerance limits.

Appleton and Eriksson (1984) maintain that the duration of a thermal regime is as important as the age of the snails when temperatures exceed the optimum for survival and reproduction. The duration of a particular temperature affects snail reproduction and above-optimal temperatures by impairing development of the ovotestis. Oogenesis and spermatogenesis were also inhibited at above optimal temperatures (Appleton and Eriksson, 1984).

The "degree hours" parameter was introduced in Section 2.2 and is discussed further here. Appleton (1976a) maintains that degree hours per week reflect the average temperature reached and the time for which specific temperature was maintained. However, use of the index comes with inherent biological assumptions in addition to the fact that the diurnal temperature range and variations within the seasons are overlooked.

The concept of "degree days" has three assumptions, namely (1) that a linear relationship exists between growth and temperature up to a threshold temperature, (2) that the threshold temperatures may change during the snail's or parasite's life-cycle and (3) temperatures that reach the upper threshold could impair development (Higley *et al.*, 1986). Nonetheless, Shiff and Husting (1966) found peak *r* for *B. globusus* at 4200 degree hours per week (equivalent in linear terms to a constant 25°C). For *B. pfeifferi* peak *r* extended from 3359 to 4536 degree hours per week (corresponding to the range 20°C to 27°C). This is taken as evidence that *B. globusus* is better adapted to shallow waterbodies whose temperature regimes were unstable and fluctuated greatly whereas *B. pfeifferi* was better suited to habitats with more stable temperature regimes.

The important point about these studies is the inherent variability of temperature at different sites or microhabitats. Brown (1994) concluded that spatial variation in snail populations is related to seasonal variation of both rainfall and temperature. Their dual importance is shown by considering that a species known to be poorly adapted to dry conditions (low rainfall being an indicator of dry conditions) but which has a high *r*, will not necessarily flourish in a warm and dry environment. *Bulinus globosus* on the other hand, has both good desiccation tolerance and high *r* over the temperatures found in subtropical areas.

2.3.2 Rainfall

Rainfall is a proxy indicator for the availability of waterbodies suitable for the snails and for transmission of the parasite. People must live near and use the waters supporting the snail hosts. Snails are not only found in natural water bodies but also in dams and reservoirs where people swim, play sports and fish. The availability of water is essential with respect to both snails' and parasites' life-cycles, and the various instances where water is required have been mentioned previously in Chapter 1, Section 1.4). The importance of rainfall to host snails may be explained in terms of three contributory factors: the duration of desiccation, flooding and current velocity. Although these are not dealt with further in this thesis (addressed in Chapter 1) they are included here as part of this review because they have been shown to affect snails, even if only in a minor way.

2.3.2.1 Desiccation and flooding

Rainfall is an important abiotic condition in the epidemiology of schistosomiasis as it affects the duration of desiccation (Martens, 1995) and the stability (permanance) of habitats through droughts and floods. As stated earlier in Section 2.2.5, most of South Africa experiences heavy spring and summer rainfall and certain parts are more susceptible to flooding than others. The schistosomiasis- endemic areas have more reliable rainfall patterns than areas that are disease free. The rainfall concentrations (explained in Section 2.2.5) in Limpopo and Northern Provinces are high. These provinces are therefore susceptible to flooding. Furthermore, rainfall can change the water levels in waterbodies such as rivers, streams, lakes, dams and the irrigation canals which the host snails commonly occur. Corresponding changes in current velocity can affect resident snail populations because the increased water flow facilitates their dispersal. As stated earlier Appleton (1978; 1976a) pinpointed current velocity as an important factor in determining a habitat's suitability for host snails (see following Section 2.3.2.2).

Rainfall also affects the life history of snails and their seasonal fluctuations in density. There may be intense breeding of snails at times when there is intense rainfall, but heavy rains also flush them downstream. Rollinson, Stothard and Southgate (2001) believed that gradual water level increases encourage snail breeding where there is density-dependent intra-specific competition for reproduction. A seasonal influx of water may also be positively correlated with infection rates (DeWitt, 1955) and the focality of the disease could change. For instance if schistosome-infected snails are washed from rivers into lagoons and estuaries they can still release cercariae for weeks afterwards (Appleton, 1996). Thereafter if people use the water, they are at risk of becoming infected.

During conditions of drought the snails may aestivate in the dry sediments for up to six months. In infected snails the intra-molluscan incubation periods of the parasite may be extended and only resume once the habitat re-fills (Appleton, 1996). Even if there is some rainfall in the normally dry regions, snails could be washed away to another area where the habitat is sufficiently stable for parasite development during such dry periods or where little human contact occurs (Jordan and Webbe, 1982). Usually however, when water is available after dry conditions, people tend to maximise their use of it and by so doing come into contact with high concentrations of cercariae and increase their risk of infection.

The different temperature tolerances of different snail species also affect their ability to survive dry periods (Appleton, 1975). The snails' responses to high and low temperatures are discussed in Section 2.3.1.1. Brown (1994) categorised *B. africanus*, *B. globosus* and *B. pfeifferi* as moderately successful aestivators because they live in areas with aquatic or marginal vegetation that retains a distinctive appearance during the dry season thereby providing a source of food and shade. In winter it does get dry in nearly all provinces so the shallow pools where snails normally live become dry and the water becomes colder. At high altitudes the water surfaces may freeze and as was mentioned earlier in Section 2.3.1.1, such prolonged cold temperatures do not support snail breeding, growth or survival.

Bulinus globosus and *B. africanus* live in both permanent and temporary habitats with the latter more likely to dry out during conditions of drought than more stable habitats like dams. Hence, dry conditions imply poor transmission of *S. haematobium* in South Africa. However, small partially shaded waters like irrigation dams used for storage, canals and creeks seldom dry out and make for more permanent snail habitats. In South Africa transmission is known to occur in dams and irrigations schemes (Pitchford and Visser, 1975; Pretorius, Joubert and de Kock, 1989).

In Section 2.1 the importance of rainfall to snail populations found in tropical areas was mentioned. O' Keeffe's (1985a) study in Kenya found rainfall to be the most important factor determining snail survival and his study showed reproductive peaks just after heavy rainfall in April, May, August and November. The author concluded that conditions in the area were only suitable when heavy rains fell during the cooler months of May to September. When large amounts of rain fell during these cool months snail populations increased rapidly and achieved the highest densities at this time. Hence, the best conditions were created for the snails to multiply.

2.3.2.2 Current speed

The rate of flow of water in a habitat affects host snail colonization as it affects their ability to hold onto the substratum, oviposit and feed. Most snails cannot withstand fast currents so in flood conditions they will be washed away. Studies have shown that these snails have a narrow tolerance to current velocity and cannot live in waters with flow velocities greater than $0.3ms^{-1}$ (Appleton, 1976a) which limits them to standing habitats or those where the water flow is minimal. Different areas within a river system will therefore show different suitabilities for supporting snail populations.

Current speed affects a snail's ability to become established in a habitat but is a difficult measure to take in the field due to its spatial and temporal variability. Schistosome-infected snails sometimes occur in standing (lentic) water bodies like lakes and ponds. However, non-persistant snail populations are also found in flowing or lotic waters like springs, streams and rivers. Therefore current is more of a controlling and limiting factor to these organisms in streams (Odum, 1983) than in calmer ponds for example. Appleton (1976a) suggests that in river systems, current velocity is important while in permanently lentic habitats the snail's physiological requirements for survival (such as temperature) are more important.

Geomorphology has been linked to current velocity. Appleton (1976a) studied the influence of geomorphology as a significant determinant of current speed in Mpumalanga and Swaziland and found that the distribution of hard rock (granites, quartzites and medium-hard rock) correlates with snail distribution. Uneven erosion of underlying hard bedrock produces uneven channels of water. Thus, these hard rock types allow the formation of side pools where the current is relatively stable and calm and can be colonized by snails.

Appleton and Stiles (1976) extended this and reported that in South Africa generally *B. pfeifferi* is found mainly on hard granite rock formations. In the Gladdespruit and Komati river there was a correlation between the distribution of permanent, lentic habitats on hard rock formations and that of persistent populations of *B. pfeifferi* and the *B. africanus* group snails (Appleton, 1976a). The softer bedrock at these study sites harboured non-persistent snail populations at the sides of lotic environments that were produced. This positive association between hard rock types and the country-wide snail distribution is interesting but the occurrence of these host snails is also subject to the thermal variation within the resultant micro-environments (Brown, 1994) that these pools of water represent. This association has never been quantified.

2.3.3 Summary

The influence of temperature on the population dynamics of the poikilothermic host snails is apparent in the studies mentioned in the previous sections but Joubert *et al.* (1986) also pointed out that it is important to consider the possible weakening of snails by schistosomes. Multiple factors shape the host snail-schistosome interaction. Although much work has been done on this subject (e.g. Bayne and Loker, 1987) it will not be discussed further here except to say that schistosome infection inhibits host snail fecundity and increases their mortality. From the point of view of a schistosome, its host snail is a resource to be converted into cercariae and to continue its parasitic life-cycle (Brown, 1994), but theirs is still a parasitic relationship in which the snail is harmed. Therefore, the combined effect of schistosome infection, desiccation and temperature- induced stress as discussed earlier, is detrimental to the host snails' reproduction and success in their habitat.

2.3 INTRA-MOLLUSCAN DEVELOPMENT OF THE SCHISTOSOMES

The influence of seasonality, high and low temperatures and rainfall are discussed in relation to larval schistosomes in this section.

2.4.1 The effect of temperature on cercarial shedding from infected snails

The intra-molluscan stages of schistosome development has been identified as the "weakest link" in the transmission cycle because they are the most sensitive to the effects of temperature (Standen, 1952; Stirewalt, 1954; Martens, 1995). During this phase in its life-cycle the parasite is tolerant of a smaller range of temperatures than the snail it resides in (Martens, 1995). There is firm evidence that temperature affects the length of the prepatent or incubation period (the time from penetration by the miracidium to cercarial shedding) and cercarial emergence from the host snail. Due to cercarial development being temperature-related, cercarial shedding follows a marked seasonal pattern. This evidence is discussed firstly for *S. mansoni* and then for *S. haematobium*. An important point is that human contact must also play a role on infection success.

2.4.1.1 *Schistosoma mansoni*

Brown (1994) concluded that the effect of temperature on the intra-molluscan stages of *S. mansoni* could play a part determining the parasite's distribution. Schistosome infections are regulated by the temperatures to which their host snails are subjected (van der Schalie and Berry, 1973) and DeWitt (1955) found that the optimum temperatures tolerated by strains of *S.*

mansoni were limited by the maximum temperatures that could be tolerated by their snail hosts. There is experimental evidence on the optimum temperatures for cercarial production, making it difficult to define in any better terms than "temperature tolerance ranges". This discussion on the influence of temperature on *S. mansoni* includes (1) seasonal transmission and (2) the influence of optimal, high and low temperatures on cercarial production.

Seasonal transmission

Brown (1994) remarked on the seasonal variability of *S. mansoni* transmission in subtropical southern Africa, which was established about a decade earlier by workers such as Pflüger (1981) and Pflüger *et al.* (1984). These authors reported that cercarial production and transmission of *S. mansoni* is seasonal. Pitchford and Visser (1965) had also much earlier demonstrated seasonal *S. mansoni* transmission using sentinel rodent immersion in canals in Malelane district, Mpumulanga, and considered the possibility that it may follow an annual cycle.

Pitchford and Visser (1962; 1969) carried out a detailed study of daily and seasonal periodicity of *S. mansoni* using the mouse exposure recovery technique. Transmission of South African *S. mansoni* measured by their rodent immersion studies either began or increased significantly during September (spring) (Pitchford and Visser, 1962, 1969). Transmission reached a peak in the mid-summer heat and fell in January (late summer). These authors also observed sharp peaks in the cooler months of April and May (autumn). Studies on the coastal plain of north-eastern KwaZulu-Natal found that high summer temperatures permitted intra-molluscan development of *S. mansoni* but cercarial production was short-lived (Appleton and Eriksson, 1984; Appleton, 1997).

Stirewalt (1954) observed declining *S. mansoni* infection rates during spring and summer. Neither Stirewalt (1954) nor Standen (1952) working independently, found any direct relationship between seasonal temperature changes and the susceptibility of snails to infection by Puerto Rican and Egyptian strains of *S. mansoni* respectively although temperature was clearly an influential factor.

Pitchford and Visser (1962, 1969) concluded that *S. mansoni* transmission was seasonal at endemic Nelspruit (altitude 655m) and at Coopersdal (altitude 380m) (both in Mpumalanga province) and went on to say that temperature exerted a considerable influence on the incubation period of both *S. mansoni* and *S. haematobium*. In another study, Pitchford (1981)

observed short incubation periods for both schistosomes during the warmer months at Nelspruit. However, for *S. mansoni,* overall incubation periods were shorter than those of *S. haematobium* though a similar pattern was observed i.e. a drop in *S. haematobium* cercarial production as the temperature rose.

Optimum temperatures for intra-molluscan development and cercarial shedding

Pflüger (1980) determined the developmental times (prepatent periods) of Egyptian *S. mansoni* in the snail *B. glabrata* over a spectrum of constant temperatures and quantified that relationship by the hyperbolic formula: **y = 268/(x-14.2)**, where **y** is the minimum time from miracidial infection to cercarial shedding (in days), **x** is the mean temperature value, 14.2°C is the theoretical temperature threshold (development null point) and 268 is the constant time-temperature product. This work is important as it modeled cercarial production in relation to temperature. Pflüger (1980) determined that *B. glabrata* produced *S. mansoni* cercariae within the rather broad temperature range of 16°C to 35°C.

A more refined optimal range for cercarial production (15°C to 20°C) was specified later by Pflüger, Roushdy and El-Emam (1981). They then found cercarial production to be positively correlated to temperature within the range 15°C to 20°C and went further to note that *S. mansoni* cercarial shedding stopped at 15°C or less. However, Pflüger (1981) did find some *S. mansoni* development even below the so-called developmental null point of 14.2°C when the effects of diurnally fluctuating temperatures were studied.

In South Africa, *S. mansoni* appears to be tolerant of a warm thermal range. Appleton's (1997) studies on South African *S. mansoni* in north-eastern KwaZulu-Natal showed that intra-molluscan development of *S. mansoni* occurs over the range 23°C to 36.5°C, although the high temperatures did limit cercarial production. This is a narrower temperature range than that found by Pflüger (1980) but it also shows that South African *S. mansoni* is tolerant of warmer temperatures than their Egyptian counterparts.

Intra-molluscan development at high temperatures

Pflüger's (1980) studies on *B. glabrata* showed that constant high temperatures (>35°C) resulted in low *S. mansoni* cercarial production and high snail mortality. The adverse effect of prolonged high temperatures on *B. pfeifferi* have been described earlier in Section 2.3.1.2. Pitchford and Visser (1969) reported that the number of *S. mansoni* cercariae shed increased as the temperature rose from 26°C to 32°C. When the temperature rose above 32°C cercarial

production dropped while temperatures below 26°C produced moderate numbers of cercariae. Pitchford and Visser (1969) also noted that the number of *S. mansoni* cercariae dropped following a sudden rise in the temperature under controlled conditions. Pflüger *et al.* (1984) also found the shortest *S. mansoni* prepatency at high temperatures of 30°C to 32°C and much longer prepatency at 18°C. This inverse relationship between the length of the prepatent period and temperature is well defined.

Intra-molluscan development at low temperatures

Earlier it was stated that schistosomes tolerate low temperatures poorly. It has been shown that development of miracidia to mature cercariae within the snail slows down during cool weather and cercarial shedding is subsequently reduced (Pitchford and Visser, 1969; Pitchford, 1981). If low winter and autumn temperatures are experienced, the development of the parasite larvae to the cercarial stage in the snails is prolonged (Pitchford, 1986). Stirewalt (1954) found low *S. mansoni* infection rates for snails kept at lower temperatures (23°C to 25°C) compared to those kept at higher temperatures of 26°C to 28°C. Further evidence supporting this was found by Pitchford and Visser (1969) who showed that at temperatures of about 10°C or lower, miracidial penetration of the host snail was marginal.

Appleton (1977a) agreed that the schistosomes were able to survive over an optimum range of 26°C to 28°C, while they are in the poikilothermic stages of their life-cycles. The duration of the prepatent period was extended as the snail- maintenance temperatures were lowered. The possibility also exists that snails could lose their infections after many months of exposure at low temperatures. *Biomphalaria pfeifferi* cannot survive at low temperatures (0 °C –6°C) for more than a few days as was mentioned earlier.

2.4.1.2 *Schistosoma haematobium*

Optimum temperatures for intra-molluscan development and cercarial shedding

According to Pflüger *et al.* (1984) the minimum prepatent period of *S. haematobium* in *B. truncatus* is described by the formula **y = 295/x-15.3**, where 15.3°C is the theoretical developmental null point and the other variables are as explained in Section 2.4.1.1. Pitchford and Visser (1969) showed that the prepatent periods of *S. haematobium* in South African *B. globosus* and *B. africanus* varied from one month to about four and a half months over a temperature range of 15°C to 22°C. Blankespoor (1989) stated that snails kept at warmer temperatures of 26°C -28°C produced the most infective and viable *S. haematobium* cercariae in the shortest time.

Intra-molluscan development at high temperatures

The distribution of *S. haematobium* is wider than that of *S. mansoni* in hot areas possibly because the latter species does not maintain high cercarial production at high daily maximum temperatures over 32°C (Pitchford and Visser, 1969). North West Province has the hottest mean daily maximum temperature (32°C) and here *S. haematobium* does have a much wider distribution than *S. mansoni*. The optimal temperature for the *B. africanus* group snails was 25°C and prolonged high temperatures (34°C) are indeed unsuitable for them.

Intra-molluscan development at low temperatures

Populations of host snails can live in areas that are possibly too cold for schistosome development. For instance Pitchford and Visser (1969) stated that even though the intermediate snail hosts were found in Lydenburg, no schistosomiasis was found there. Blankespoor and Blankespoor (1989) found no evidence of *S. haematobium* infection at a low temperature of 12°C. Pitchford and Visser (1969) found a drop in the number of *S. haematobium* cercariae shed with a sudden drop in the temperature but this increased again as the temperature rose.

As with *S. mansoni*, during the cooler months there is little or no *S. haematobium* development and also little or no cercarial shedding. For Egyptian *B. truncatus*, Pflüger *et al.* (1984) found low cercarial shedding and transmission potential at continuous low temperatures of 16°C to 19°C despite normal intra-molluscan development of the parasite.

Pitchford (1981) observed long incubation periods (up to 30 weeks) for *S. haematobium* during the cool autumn and winter months in the endemic area of Nelspruit in Mpumalanga, South Africa. Stirewalt (1954) also observed an inverse relationship between the prepatent period and snail maintenance temperature (23°C to 38°C) of *B. glabrata*. She found many snails lost their infections within months of exposure to low temperatures, although this loss of infection (spontaneous cures) did not occur at high temperatures.

The differences in cercarial shedding patterns of *S. haematobium* and *S. mansoni* are related to how their host snails respond to thermal variations in Fig. 2.6. Some anomalies are observed. Fewer snails develop cercariae in temperatures that are either too hot or too cold. For instance in Fig. 2.6 many more snails produced *S. haematobium* cercariae during spring and summer compared with the number of snails that developed cercariae during autumn and winter (Pitchford, 1981). This was expected since *S. haematobium* has long incubation periods during

the cooler autumn and winter months (Pitchford, 1981) when *B. globosus* and *B. africanus* respond to the cooler weather.

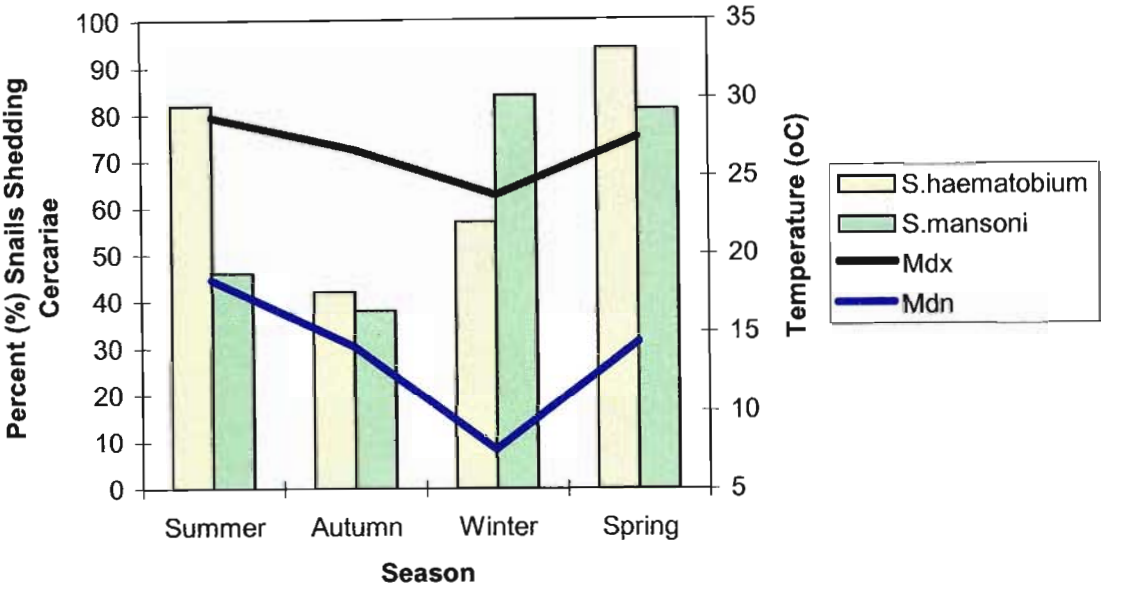

Figure 2.6: Data adapted from Pitchford (1981) relating cercarial shedding by different proportions of snails exposed seasonally to Mdx and Mdn at Nelspruit (altitude 655m)

Mdx = mean daily maximum temperatures Mdn = mean daily minimum temperatures

This was not the case for *S. mansoni* because Fig. 2.6 shows that more snails developed cercariae after exposure during winter and spring in the endemic area. During winter the Mdx was 23.8°C and the Mdn was 7.7 °C. Hence, the Mdn was 16.1°C colder than the Mdx. De Kock and van Eeden's (1986) life table studies on *B. pfeifferi* showed that a 10°C daily temperature fluctuation was the most suitable. Although more snails shed *S. mansoni* cercariae it may not have been in sufficient amounts to allow even a few to survive the cold water temperatures during winter. Nevertheless the difference between the host snail shedding behaviour is clearly evident in this figure.

To summarise, temperature is one variable that influences the timing of cercarial shedding and the number of cercariae that are shed. Generally during winter there is minimal or no cercarial shedding of *S. mansoni* and *S. haematobium*. More cercariae are shed at higher temperatures and fewer at lower temperatures. In Pitchford's (1986) study, all test snails produced cercariae

during late September and early October. Thereafter transmission continued throughout summer and declined in autumn (Pitchford, 1986).

2.4.2 The role of water in parasite development and transmission

A few points in relation to water are discussed here: (1) correlations between cercarial shedding and people's water contact patterns, (2) schistosome egg transmission and (3) the salt content of the water bodies in which schistosomes are transmitted.

As mentioned earlier, if the urine or faeces of an infected person come into contact with water, they become diluted and expose the parasite eggs. The eggs of *S. haematobium* hatch on contact with water and release miracidia but those of *S. mansoni* display delayed hatching mechanisms (Pitchford and Visser, 1972). In either case however, a miracidium must be able to survive in water until it penetrates a snail host. Miracidia become activated and then break through the egg shell by the combined effects of decreasing osmotic pressure and larval activity. Light and temperatures ranging between 10°C and 30°C assist the hatching process.

2.4.2.1 Cercarial shedding

Cercarial emergence is rhythmic. There is a correlation between peak shedding periods and peoples' water contact patterns. Pitchford *et al.* (1969) found that most *S. haematobium* and *S. mansoni* cercariae were shed during late morning and early afternoon (11h00 and 14h00) during the hot summer months. During these times of day the temperature rises and may peak. This is also the most likely time when people make contact with infected water for swimming or washing, weather permitting. From the work of Kvalsvig and Schutte (1986), it seems that peak water usage is between 9h00 and 12h00. The warm weather of South Africa encourages water contact and even during weekends, the frequency of water contact increases (Kvalsvig and Schutte, 1986), thereby enhancing the chances of transmission.

2.4.2.2 Transmission of eggs to water

Rainfall assists in washing eggs from one area to another especially in the case of *S. mansoni*. Since *S. mansoni* eggs are passed in faecal matter (usually on dry ground), they need fairly heavy rainfall to be transported. Since not every rain shower will be "heavy" their ability to survive in faecal matter is of epidemiological importance. Porter (1938) found that the maximum egg survival time in faeces was three days while Pitchford and Visser (1972) found it to be six days. No eggs survived beyond a week (Porter, 1938). Generally, *S. haematobium* eggs are excreted via urination directly into water. However if the urine is passed on land the eggs

will die as the urine dries. Urine tends to dry far more quickly than faecal matter, so the *S. mansoni* eggs will remain moist for longer than the *S. haematobium* eggs. Porter (1938) found that fewer *S. haematobium* eggs survived in urine compared to the number of *S. mansoni* eggs that survived in faeces over a period of 8 days. No eggs survived after eight days. These subtleties of transmission are relevant when there is a change in the seasons.

Pitchford and Visser (1965) considered the part played by rainfall to be less important in influencing seasonal *S. haematobium* transmission and more important for seasonal *S. mansoni* transmission. In Pitchford and Visser's (1965) three- year study at ten different sites, they found consistently longer intra- molluscan development periods for *S. haematobium* than for *S. mansoni.* They observed short *S. haematobium* incubation periods during summer (5 to 6 weeks) but longer periods during winter (24 to 25 weeks). Peak *S. haematobium* transmission occurs from December to January because people increase their contact with infected water from October onwards when the weather is warm.

Peoples' water contact behaviour probably plays a more important role in urinary schistosomiasis transmission than rainfall, e.g. washing clothes or swimming increases the risk of exposure to infection. Saathof *et al.* (2002) found a positive association between washing clothes in natural waterbodies and *S. haematobium* infection but this was not the case for swimming. The authors attributed this anomaly to their study being conducted during the cool winter months when the frequency of water contact decreases as Kvalsvig and Schutte (1986) found. Hence, little *S. haematobium* transmission from people to snails would be expected after summer in endemic areas, in spite of good rainfall.

Snails can be exposed to *S. mansoni* parasites at almost any time of the year. Snails infected in winter incubate until spring, which is the rainy season in South Africa. Hence, a rise in *S. mansoni* transmission would be expected in spring while *S. haematobium* transmission rises in summer.

Once in the waterbody, *S. mansoni* cercariae cannot swim in current velocities faster than $0.05ms^{-1}$ (Rowan, 1965). Rowan (1965) studied the movement of *S. mansoni* cercariae under field conditions in Puerto Rico and found them at depths of up to 50cm in streams with flow velocities ranging from 0.1 to $0.5ms^{-1}$. Hence, cercariae seem to tolerate a range of relatively fast flow velocities while their snail hosts have a remarkably narrow tolerance range to current velocities up to $0.3ms^{-1}$.

2.4.2.3 Intolerance to high salt content

Rainfall contributes to fluctuations and variation in the physico-chemical conditions of the aquatic habitat. The South African schistosomes' cercariae are able to tolerate a varying range of salinities. Transmisson is known to occur in freshwater where salinities are less than 0.5 parts per thousand (Odum, 1983). The young stages of parasite development, i.e. the ova and miracidia, are affected by salinity. At salinities greater than 3.5 parts per thousand (^{0}/00) hatching of ova was impaired and complete inhibition of hatching occurred at >14 ^{0}/00 (Donnelly, Appleton and Schutte, 1984b). Miracidial mortality was high at salinities ≥ 7 ^{0}/00 while those less than 3.5 ^{0}/00 appeared to be suitable for both egg hatching and miracidial survival.

Donnelly, Appleton and Schutte (1984a) also found the longevity of cercariae in the lowest salinities (0 to 5.2^0/00) to be better than in freshwater. These authors also found that miracidial surivival was better at 1.7 ^{0}/00 and 3.5 ^{0}/00 compared to their freshwater controls (Donnelly *et al.*, 1984b). Generally these authors found a decrease in longevity as the salinity increased. However *S. mattheei*, a parasite of ungulates, could tolerate the experimental salinity range (1.75 to 3.5 ^{0}/00) better than *S. haematobium* or *S. mansoni.*

Another point to note is that the free-living stages of the schistosomes could tolerate salinities up to 7% better than their snail hosts (Donnelly *et al.*, 1983,1984a, 1984b). Donnelly *et al.* (1983) showed that adult South African *B. africanus* could tolerate salinities up to 3.5 ^{0}/00 in the laboratory. There are also differences in salinity tolerance between the younger stages of the snails life and their adult stages. The work of Donnelly *et al.* (1983) showed that as salinity increased from 1.0 ^{0}/00 to 7.0^0/00, the rate of snail hatching was greatly reduced. Importantly, uninfected *B. africanus* kept at the same salinity ranges survived better than the hatchlings and their infected counterparts.

Both *B. africanus*, and *B. globosus* as well as *B. pfeifferi* can tolerate freshwater but the relatively high salinities (>3.5 ^{0}/00) found in brackish waters like estuaries and lagoons are unsuitable for their survival. The planorbids' ability to survive in brackish water is an important aspect of their population dynamics. Although Donnelly *et al.* (1984c) did not discount the potential for infected snails to survive in the lagoons and estuaries of the KwaZulu-Natal coast, they are not known to reproduce successfully there. These host snails have probably been dislodged and flushed downstream from their more suitable freshwater habitats upstream after rain.

2.5 SUMMARY

A spatial analysis of schistosomiasis in South Africa requires consideration of how the main abiotic conditions (temperature, rainfall) affect the presence and success of snail hosts, the intra-molluscan development of the schistosomes and their free-living stages. The reason is that the environment provides a consistent set of suitable conditions for both organisms. Much of the host snails and schistosomes distribution covers the warmer rain-fed ecological zones in the eastern parts of the country. The evidence showing that South African *B. globosus, B. africanus* and *B. pfeifferi* can tolerate high temperatures confirms their tolerance of tropical climates. However, the snails' vulnerability to limiting factors, such as extremely high or low temperatures outside their tolerance ranges, contributes to the patchy spatial distribution of both urinary and intestinal schistosomiasis. It is also clear that while a large amount of evidence exists relating schistosomiasis to temperature, not as much relates it to rainfall.

CHAPTER THREE

Building a Disease Model

3.1 INTRODUCTION

This focus of this chapter is development of a disease model using the principles of epidemiology and GIS. In Chapter 2 the climatic and ecological characteristics of a place determine the flora and fauna that can live in that environment (McMahon and Pugh, 1970). Susser (1973) expanded the frame of reference in the schistosomiasis transmission cycle to include this influence of the environment on the snail hosts and schistosomes. The interactions Susser described are simplified and adapted to the South African context in this section. Following this, schistosomiasis transmission can be considered in terms of the following three levels:

1. The parasites, *S. haematobium* and *S. mansoni,* as discussed in Chapter 1.
2. The host snails, viz., the South African *B. africanus* group and *B. pfeifferi*, also described in Chapter 1.

2.1 The parasites and host's reaction in response to each other.

3. The climatic factors including temperature and rainfall discussed in Chapter 2 that affect the parasite's survival and are determinants of the snail hosts' behaviour and distribution.

The preceding chapters described the elements of schistosomiasis transmission and some of the causal factors that assist or inhibit the transmission process. The most important of these are temperature and rainfall (see Chapter 1, Section 1.7 and Chapter 2, Section 2.5). These factors influence the geographical distribution of intestinal and urinary schistosomiasis. The varying rainfall and temperature at different locations were shown in Chapter 2. These factors influence disease patterns with respect to (1) providing temperature and other conditions which allow the survival of the parasite's eggs, miracidia and cercariae and (2) providing suitable habitat conditions for the survival and fitness of the snail. This theoretical biological framework forms the basis for the present chapter which describes the process of disease model building within a GIS. The GIS allows many climate indices to be meaningfully combined with the disease data. In the following sections of this chapter, relevant theoretical aspects of GIS and epidemiology are discussed within the framework of building a model. These include hypothesis generation, using statistics, map output, spatial autocorrelation, epidemiological risk, components of the

GIS and common GIS operations. Examples of other studies that have used GIS to study schistosomiasis are also discussed.

3.2 CONSTRUCTING A DISEASE MODEL

The epidemiologist seeks to know where in geographical space certain health problems exist and to establish ecological associations describing disease patterns (Matthews, 1990). These descriptions are often based on descriptive, inferential, multivariate and spatial statistics. In 1915 Ronald Ross (loc cit Susser, 1973) stated the following: "all epidemiology, concerned as it is with the variation of disease from time to time or from place to place, must be considered mathematically, however many variables are implicated, if it is to be considered scientifically at all. To say that a disease depends upon certain factors is not to say much, until we can also form estimates as to how largely each factor influences the whole result. And the mathematical method of treatment is really nothing but the application of careful reasoning to the problem at issue." Hence Ross recognized long ago the need for quantifying the effects of individual causal factors on disease transmission. Systematic data processing is required to do this properly.

Ross was ahead of his time since about a century later Elliot *et al.* (1996) defined geographical epidemiology as the description of spatial patterns of disease. It is a part of descriptive epidemiology, which describes the occurrence of disease with respect to the following three characteristics: (1) person - age, gender, (2) time (day, season, degree-day) and (3) place-geographic location (Katzenellenbogen, Gear and Tollman, 1999). So the next step is to ask how? How can disease information and causative factors be brought together to increase our understanding of the process of transmission and further to support decisions related to the control of diseases? We know what causes the disease, where the disease presents, and what conditions are conducive to disease transmission, but it is difficult to make efficient use of such comprehensive information if they are not available in a systematic manner. A management information system facilitates systematic data collection.

The development of a model of a disease through the use of computer technology and software, allows such data to be processed systematically. Geographic Information Systems (GIS) are useful tools for disease modelling as they can be used to convert maps and images from paper to digital format for database management, map display and spatial and statistical analyses (Maguire, 1991, Appendix A). All these system components offer a digital (Appendix A) mechanism to manage data and to construct disease models, based on a geographic or spatial

platform. What differentiates GIS from other research tools is that data within the system are geo-referenced within a co-ordinate system. Therefore, simply put, it is the attachment of a spatial dimension to data (Boelaert, Arbyn and Van der Stufyt, 1998). For South Africa generally the longitude/latitude system of projection is used.

Four specific generic functions that a GIS offers are (1) data input (2) data storage and retrieval (3) data manipulation and analyses and finally (4) data output (Spear *et al.*, 1995; Maguire and Dangermond, 1991). Therefore, within a GIS different datasets such as disease observations, other attribute data like census databases and climatological data all have a latitude and longitude. Generally the relationship between exposure to a disease and the location it occurs in is indirect. Therefore, one can use the prevailing conditions at a place, such as temperature and rainfall as surrogates for "exposure." The validity of the disease model is then dependent on how well the surrogate indicator (e.g. temperature or rainfall) measures the actual exposure.

GIS is driven both by technology and science. Consequently, many theoretical principles and practical application issues deserve consideration and have been given due attention in the literature. For the purpose of this thesis, emphasis is placed on the use of GIS in disease model development and theoretical features related to this are considered. Three aspects are discussed in the following sections: (1) spatial analysis (2) specific methods related to constructing a disease model and (3) examples of the use of GIS for schistosomiasis as a framework for the methods used in this thesis.

3.2.1 Spatial Analysis

Biological systems consist of variables that vary in geographical space. The recognition of a spatial dimension for analysing disease data yields different results with possibly more meaning to them than analyses that do not consider the place where the disease presents. The origins of spatial analysis lie within quantitative and statistical geography, which later expanded to include mathematical modelling and operational research methods (Openshaw, 1991). Spatial analysis is defined as the geographical manipulation and transformation of data (Briggs and Elliot, 1995).

Spatial analysis in the context of this work is therefore the quantitative study of the location of schistosomiasis, the exploration of patterns and relationships within the disease and climate data, and the search for explanations of such patterns and relationships (Bailey and Gatrell, 1995). Longley, Batty and Batty (1997) add that spatial analysis encompasses a cluster of techniques and models to apply structures to systems in nature. These techniques Bailey and

Gatrell (1995) list as visualization, exploratory data analysis and model building. Hence "model building" in a GIS context is part of spatial analysis. According to Clarke, McLafferty and Tempalski (1996) modelling involves the integration of GIS with standard statistical and epidemiological methods. The "disease model" is a central theme of this chapter and it needs to be differentiated from the model defined as a spatial analysis task. These GIS models may be thought of as sub-models that eventually lead to the final disease model. It is possible to use a GIS in all steps of model building. The first step is to generate a hypothesis, which in turn can serve as the basis for developing predictions.

3.2.1.1 Hypothesis generation

A GIS can be used to formulate a hypothesis based on the patterns or visualizations that occur on a map (Clarke *et al.*, 1996; Matthews, 1990; Vine, Degnan and Hanchette, 1997). From an epidemiological perspective the first step towards analysing data spatially is to develop hypotheses that explain disease patterns in terms of specific human observations, experiences and experimental biological evidence (Metcalf and Coetzee, 1999). The next step is to test the hypotheses by formulating models to integrate the causal factors and disease observations (Clarke *et al.*, 1996). These models are derived from methods that describe or explain the disease transmission process. The disease "outcome" will vary depending on the influence of the various causal factors. The relationships between the causal factors and disease outcomes can then be quantified using statistics.

3.2.1.2 Statistics

Statistical models describe the relationship between causal factors and disease by reducing them to variables and by offering methodologies for current epidemiological analyses (Breslow, 2000). Joubert (1999a) defines a "statistic" as a characteristic of a sample of a population and the measured statistic is an estimate of the corresponding parameter in the population. For example an independent variable is one that is not influenced by the dependent variable within the defined area of study. This study assesses the effects of temperature on schistosomiasis prevalence but temperature is independent of the disease although it does cause or contribute to the variation in disease observations.

Matthews (1990) added that a GIS and rigorous statistical modelling are mandatory for much epidemiological research. Therefore, the best way to construct a disease model is to use maps to support and sometimes drive statistical analyses (Appendix A). While the majority of such disease models do have a statistical component, there are also non-statistical GIS methods for

spatial data analyses, such as fuzzy logic models and neural network analyses (Thompson and Connor, 2000). Neural networks have become an expanding and interdisciplinary field bringing together the varied disciplines of biology, computer science, statistics and mathematical modelling.

Neural networks use the underlying principles of brain function to make decisions. Openshaw (1991) stated that fuzzy analysis is useful as it provides a means of dealing with all types of data uncertainty (the extent to which a condition exists). The main difference between fuzzy logic and boolean (standard) logic is that possible values range from 0.0 to 1.0 (inclusive) not just 0s and 1s when reasoning about data. The use of fuzzy logic takes into account the fact that biological systems are complex and often decisions cannot be "all or nothing." Fuzzy models are already being applied in medicine and healthcare for decision-making (Linkens, Abbod and Mahfouf, 2000). While statistics are not always required to construct a disease model it is important to note that aspatial statistical analyses do not take into account spatial dependence and heterogeneity of a study area (Moore and Carpenter, 1999; McMahon and Pugh, 1970) and in order to do this efficiently a GIS is required (Coppock and Rhind, 1991).

It is simple enough to identify factors that can be statistically associated with disease observations even if the association is illogical. Statistical models assist in hypothesis testing and for estimations using the experimental evidence. The extent and form of relationships are also determined by such models (Bailey and Gatrell, 1995) that in turn are subject to uncertainty and governed by the laws of probability depending on the tests that are used. Communicable diseases are complex and it is necessary to consider expert opinion and experience to make the disease model more realistic. Furthermore, the results from the disease model must be interpreted in the context of the problem under consideration (Gettinby, Revie and Forsyth, undated). The outputs of statistical models are tables that have the advantage of presenting summarized data. However the disadvantages of such tables are that patterns do not show up easily, subtle patterns are lost, large tabular outputs are often incomprehensible and inaccessible and spatial relationships cannot be accounted for automatically. Hence other visual aids such as maps become necessary.

3.2.1.3 Maps

There is a need to know where disease occurs in order to learn about causal mechanisms as described above, to explain local disease occurrence, to describe the natural history of disease and provide guidance in administration of health services. Prior to GIS advancements, the

geographic distribution of disease relied on the observations of medical practitioners (Moore and Carpenter, 1999; McMahon and Pugh, 1970). For instance Porter's (1938) work on schistosomiasis in South Africa provided an excellent definitive illustration of the two forms of the disease in the country. However, the fact that her maps are only available in a book, in paper format limits their accessibility and use. Improved data accessibility, is a distinct advantage of incorporating such data into a GIS.

Another primary advantage of using a GIS is the ability to produce map outputs as a product of research. Many maps are aimed merely at illustrating distributions in space, to provide a succinct summary of data, to contextualise the study area and highlight important features to supplement hypotheses, descriptions and reports of disease. Low- end mapping packages are suitable for this purpose.

More advanced applications of GIS offer analytical operations so that maps are used as research tools for recording observations, analysing spatial variation in disease rates and in assisting hypothesis generation as mentioned earlier, e.g. formulating hypotheses about the cause of a disease by considering the spatial variation in environmental factors. Further, maps can stimulate ideas and are a way of communicating research findings. High-end mapping packages have full integration of all tools in a system and can handle both vector and raster information (explained later) to perform spatial analysis (Scholten and de Lepper, 1991). Low-end GIS software packages have only part of this functionality. These applications require more powerful software packages that have built-in statistical modules. They use more formal statistical data manipulation to build models and estimate parameters. Usually there is a close interaction between the simple mapping procedures and the more advanced methods to produce a disease model.

3.2.1.4 Spatial autocorrelation

It was only during the 1980s that spatial statistics and computer mapping were successfully coupled within a GIS. Statistical analyses are useful, but they are more powerful if they are used with a spatial component. This is another advantage of a GIS but consideration of the spatial component requires data to be manipulated in ways that consider the effect of geographical space.

For instance some GIS packages contain modules that calculate the effects of spatial dependence. Spatial dependence means that what is observed at one place depends on events in

nearby places and is based on the principle that nearby observations are more related than distant observations (Moore and Carpenter, 1999). The subsequent pattern of map objects and attributes is termed spatial autocorrelation (Appendix A, Gatrell, 1991). For instance if high temperatures are seen to cluster in one region and low temperatures in another region on a map it is said to exhibit positive spatial autocorrelation (Gatrell, 1991). However, if high and low temperature values appear randomly on a map it suggests the absence of autocorrelation. In fact, this spatial association between nearby entities in geographical space violates the statistical assumption of independence in most epidemiological studies (Vine *et al.*, 1997). Therefore, where possible one should attempt to account for spatial autocorrelation in GIS- based epidemiological studies.

According to Glass (2000), spatial autocorrelation of infectious disease cases can commonly occur due to these diseases being contagious. People may become infected due to a single time and place of exposure. Consideration of spatial dependence is useful in disease modelling as it allows the researcher to make inferences from data that are available to support data deficits in other areas. Measures of autocorrelation provide a useful summary description of data on a map. The measurement allows a quantitative assessment of whether what is displayed on the map is any more than would be expected by chance.

3.2.1.5 GIS as a Health Research Tool

The aims in using a GIS to construct a disease model are manifold but six of these relevant to this work are listed below:

a. **To understand the distribution of the disease (s) in South Africa.**

Such models serve a representational function, by showing existing or hypothetical relationships between the disease occurrence and causal factors in simplified form (Susser, 1973). First there are a few assumptions that need to be made and these are driven by the nature of the data. Maps are used to visualise the data being analysed even if they are exploratory analyses. Joubert (1999b) describes exploratory data analysis as an exploration of data through graphical display that allows the researcher to become familiar with the data. This requires some data manipulation to summarise and investigate the patterns and relationships on a map. A good description of data can be used to generate a hypothesis.

b. **To predict disease frequency in areas where disease observations have not been made**

As is the case with schistosomiasis in South Africa, comprehensive prevalence data are either unavailable or it is impossible to map the distribution adequately due to data deficits. This issue of the schistosomiasis data deficit was discussed in Chapter 1. Hence, all available and relevant disease survey information should be used to extrapolate to areas where there are little or no data. A prediction or representational disease model helps to develop and clarify historical statements relating to the causal relationships associated with the disease transmission (Susser, 1973).

c. **To generate output such as maps for use in the health care system.**

Samples of disease observations permit the overall picture to be inferred. As described in Chapter 1, Primary Health Care workers should know the endemic areas for schistosomiasis (Anon, 2002b). Once this information is readily available they can give correct health education information to patients, for instance the types of worm infections they are vulnerable to and preventative measures they can take to avoid becoming infected.

d. **To generate population estimates that are useful to identify factors related to the course of a disease.**

People who live in schistosomiasis endemic areas may be classified into groups according to aetiological factors, differences in age and sex and in geographic location. From a control point of view, there is a need to know the risk of people becoming infected with the disease if they live in an area where schistosomiasis is known to occur. This risk may be determined by assessing how many people live in the area and how many of them are infected. Briggs and Elliot (1995) state that it is of limited use to only map case data without appropriate population data.

Risk

"Risk" may be defined as the "probability of harm," (McMahon and Pugh, 1970) and the 'population at risk' is the group of healthy or sick people. People would be counted as positive cases if they had the disease being studied (Coggon, Rose and Barker, 1997). For instance if a clinic nurse wanted to record the number of children treated for schistosomiasis, the population at risk would comprise those children who might come to the clinic with urine in their blood (Red Urine Study Group, 1995). Children who subsequently move to another area would no longer attend that clinic and would then not belong to the population at risk. Consideration of the population at risk is important to determine which segments of the population are more at

risk than others. In the case of schistosomiasis it has been determined that school-aged children between 5 and 14 years are most likely to become infected (Schutte, Fripp and Evans, 1995).

Identifying the relative frequencies of schistosomiasis in population sub-groups such as school-age children is useful. It enables health intervention studies and health promotion programmes to be directed towards the children in areas where the greatest concentrations of the diseases present. Health facilities and resources are generally limited in South Africa and this epidemiological information could be effectively used to target control programmes. Planning clinical, therapeutic or preventative research requires knowledge of how many cases of a particular disease are likely to be found in a given population during a given period and under different scenarios (Dilraj and Abdool Karim, 1999). This is achieved by different methods of surveillance such as routine or sentinel surveillance. Dilraj and Abdool Karim (1999) state that poor planning, unnecessary illness, mortality and higher economic costs contribute to the lack of accurate and timely surveillance data. To this end, Beck, Wood and Dister (1995) pointed out the advantages of GIS as an innovative set of tools for disease surveillance at a variety of scales and over large areas.

Risk assessment, rates, incidence and prevalence

Risk assessment is a scientific approach used to estimate the probability and impacts that result from exposures such as contact with certain substances, people and activities (McMahon and Pugh, 1970; Joubert, 1999a). There are two common measures of association between exposure to a factor and risk of a certain outcome. First, Relative Risk (RR) is the ratio of those people exposed to the disease to the rate among those not exposed (Joubert, 1999a; McMahon and Pugh, 1970). Attributable Risk (AR) indicates the proportion by which the rate of the disease will be reduced if the exposure were eliminated (Joubert, 1999a). It considers the relative risk and how common the risk factor is in the study population. An important point to consider is that these traditional measures of risk may sometimes be inappropriate for small spatial units (Matthews, 1990) within the GIS model.

Epidemiological studies generally relate disease observations to population data by rate, incidence and/or prevalence. These can be defined as follows (McMahon and Pugh, 1970; Joubert, 1999b):

(1) *rates* describe the frequency of a disease expressed per unit of size of the population in which it is observed.

(2) *incidence* is the number of new cases of the disease which arise during a certain period of time.

(3) *prevalence* may be expressed as point prevalence or period prevalence. Point prevalence is a census type of measure that records what prevails or exists and is defined as the frequency of the disease at a designated point in time. It indicates the number of cases existing at the beginning of the designated time period. Period prevalence expresses the total number of cases of a disease known to have existed at some time during a specified period. For schistosomiasis studies, prevalence is sometimes used to indicate the potential level of contamination of the environment with schistosome eggs (Jordan and Webbe, 1982).

The choice of disease measurement will impact on the strengths and limitations of the disease model.

e. **To understand the causes of excessive prevalence of schistosomiasis (outbreaks) or re - emergence of the disease where there previously was none or very little.**

Epidemiologists may not be concerned with seeking new knowledge about the origins of a disease such as schistosomiasis because this is well known. They will however, want to understand the predisposing factors in communities where the disease presents and represent them in appropriate descriptive terms such as epidemics, outbreaks or point epidemics.

Epidemics are assessed by comparing disease frequency in different places, following the frequency over time and comparing one subgroup of the population with another (McMahon and Pugh, 1970). According to Robinson (1985) an *epidemic* is any substantial increase in the number of cases of a disease above the level to be normally expected in that population, but an *outbreak* generally refers to an epidemic that affects fewer people, is of shorter duration and is localized within a specific geographic area (Metcalf and Coetzee, 1999). This is a better term to refer to schistosomiasis because the disease's profile fulfills these criteria. Point epidemics occur mainly when people are exposed to a source of infection or contamination almost simultaneously (McMahon and Pugh, 1970).

McMahon and Pugh (1970) state that sharp increases in disease frequency in a relatively short period of time are associated with sudden encounters with organisms via water, air, food or by contact with the skin. This is of relevance to schistosomiasis. In Chapter 1 Swimmer's Itch was described as affecting people who have not developed immunity against cercariae. These non-

immune people may be migrants or tourists who come into contact with infected water for the first time.

f. **To generate output under different causal factor scenarios such as the effects of increasing temperature due to climate change predictions.**

This involves two important components namely, prediction from the present to the future and scenario- testing. Most biological systems change with time, but the rate of change differs. The occurrence of a disease in a certain place is generally characteristic of a certain time. When large temporal or geographic units are analysed, small- scale variation may be overlooked and the overall change in distribution may be small. An example of this was described with the rainfall data in Chapter 2 and Brown (1994), also highlighted the importance of considering the effect of large and small- scale variations of abiotic conditions on host snail distribution. One goal of such a model is to find out if suitable climate conditions also tend to occur in the same geographic area over a particular time frame.

The model begins with the known relationships between variables through the passage of time, from the present to the past. For instance there is a linear relationship between cercarial emergence and temperature increases up to a certain temperature peak. From these trends and relationships, future trends are extrapolated and predicted within margins of error. For instance, if the temperature increase remained constant, the outcome on cercarial emergence will be projected based on the statistical relationship between temperature and cercarial emergence. The assumption here is that the relationships will remain constant through the passage of time (Susser, 1973). For instance with population models, predictions of future population estimates differ according to the initial assumption regarding the trend of the variables used. Sometimes adjustments may need to be made to account for realistic change, for instance the starting population estimates can be increased by a statistically valid population growth rate. For the South African situation some studies even take into account growth and death rates related to the impact of HIV/AIDS related deaths. The r for 1996-2001 was estimated at 0.019841 for men and 0.019738 for women in South Africa after factoring in the HIV/AIDS statistics (Statistics, SA, 2001).

Scenario testing sub-models allow data to be organised and analysed in a way that shows commonalities and differences (Susser, 1973). The organisation of data involves synthesising related factors into coherent forms. By putting data in the same format, apparent commonalities

and disparities are highlighted. When analysing data in this way, gaps in existing knowledge can also become apparent.

3.2.2 Constructing a GIS disease model

GIS has emerged as a discipline in itself, and there are many theoretical aspects that drive its application in a study. Three relevant aspects are briefly discussed here to build the framework for the disease model. These include data acquisition, data processing and integration and types of methodologies using vector and raster data formats.

3.2.2.1 Data acquisition

Firstly, hardware and software have to be sourced (Jackson and Woodsford, 1991). This process can be expensive and labour intensive, and for many projects staff are employed simply to acquire and maintain geo-referenced data. Two processes will be briefly discussed here, viz. digitizing and obtaining co-ordinates using a global positioning system.

Digitising

If the data are in paper format they will have to be digitized (Appendix A). Digitising is a process of encoding features in digital form as x/y coordinates. A digitiser is used to convert the map positions of features to a series of x/y coordinates which are then stored in computer files. Pushing a digitiser button records an x/y coordinate for a point on a map.

Global Positioning System (GPS)

Alternatively a Global Positioning System (GPS) may be used. This is a receiver that records the longitude (x), latitude (y) and altitude (z) of a point on the Earth's surface (Thompson and Connor, 2000). The technology relies on 24 satellites that are managed by the United States Department of Defence (Thomspon and Connor, 2000). The satellites transmit radio signals to the GPS receiver, which relays its distance from the satellites. The receiver tracks four satellite signals and then mathematically triangulates the data to fix the location.

This technology is powerful as the exact location of any point on Earth can be made available for any purpose, including hostile ones. Hence, some degree of random positional error is intentionally introduced in the data obtained by the receiver. This is called Selective Availability. In addition, errors are introduced by atmospheric conditions. Thompson and Connor (2000) report that most GPS receivers indicate less than 100m accuracy 95% of the time

(Appendix A). For large- scale GIS studies this level of accuracy is satisfactory, but not for smaller scale point to point disease observations for instance. In the latter case the data require some correction to represent reality accurately. This is achieved by using Differential GPS, which compares field data against those from a known geo-referenced point. The next step after acquiring the dataset is to process and integrate it within a GIS.

3.2.2.2 Data processing and integration

The database management system offered by many GIS software packages offers the ability to both import and export data and then re-project from one co-ordinate system to another. This process requires considerable effort. Shepard (1991) defines "information integration" as the synthesis of geographical information in a computer system by linking and matching spatial and attribute data consistently from various sources within a coherent data model. This allows the data to become interchangeable. For instance remotely sensed environmental data obtained by aerial or digital photography and/or digital satellite imagery are large datasets which require much processing before the climate information is used.

The file types are different for the different GIS software used in this thesis. Mapinfo Professional® (Mapinfo Corporation, UK) uses tabular files (eg. town.tab) and workspaces (eg. KZN. Wor) while the Idrisi®for Windows software package (Clarklabs, Worcester, MA) uses raster files (eg. Tmin.rst) formats which store data in ASCII (American Standard Code for Information Interchange), binary or packed binary files. The latter saves memory space. While the file type is different, all files have an associated documentation file (town.dat and tmin.rdc) which describe the reference system, reference units, and co-ordinates of the bounding corners of the image (Thompson and Connor, 2000). The reference units and map projection allow interchangeability of file types between software packages. Furthermore, the integration of data from different sources relies on using a common file format, mapping projection and scale (Thompson and Connor, 2000).

The issue of different datasets having different scales or simply whether or not to use a particular scale in disease modelling often presents difficulties. Muller (1991) discussed the advantages of scale- independent databases but pointed out that the data will only be as good as their source. However if one were to link school-based screening surveys with census-type information like sanitation, both data layers would have to be analysed at the same scale to detect meaningful patterns. Tanser (2000) maintains that correlations at one scale can be different at other scales, creating confusion. Most times it is necessary to make do with what

data are available and adjust the scales appropriately. This is due to the high cost of datasets like satellite imagery. Very small scales could also obscure patterns by considering unnecessarily small- scale variation. Schistosomiasis is a focal disease. Therefore, data at small scales like district level are useful for spatial analyses (Saathof, *et al.*, 2002). However this type of spatial analysis is sometimes difficult to perform due to the complexity of the variables involved in transmission.

Earlier it was stated that GIS software allows the integration (Flowerdew, 1991) of different types of data, viz. climatological, census and disease observations, to illustrate the geographic distribution of the disease. These data are in the form of layers (Frank and Mark, 1991) within the GIS which can be overlayed on one another and analysed separately or together. The use of layers is a way of separating complex datasets for disease model building. Each variable in the model can be reduced to a single layer of information, which in turn can be further broken down into other layers to show different data types.

3.2.2.3 Type of methodology

Within a GIS environment there are different methodologies available to construct the disease model depending on what output is required. These methods differ by virtue of the way they handle different types of data. Data may be vector (arc-based, and not to be confused with the biological 'vector'), and raster (grid-based). Raster and vector based models each have their advantages and limitations. The GIS user will decide which format is relevant to the type of modelling involved. Features of raster and vector models and the common methods of map overlay and neighbourhood construction are discussed here.

Vector models

Vectors are entities that have both magnitude and direction and hence they are described by absolute co-ordinates. These types of data are based on analytical geometry and can be points (e.g. disease observations), lines (e.g. rivers) or polygons (e.g. districts). Polygons are described by boundary lines, which are connected by a series of points (Chrisman, 1997).

Raster models

Whereas the vector data model is constructed from points, lines and polygons as its logical structure, the raster model has close links to the physical layout of computer hardware graphics (Appendix A, Chrisman, 1997). Raster derives from a word used in mechanical engineering for a tool that advances in a back and forth sweep (Appendix A, Chrisman, 1997). In the raster

format a region (e.g. weather station data) is divided into small uniform cells (pixels) to make up a grid (Appendix A). Each cell contains a data value, e.g. disease presence or absence. These images are geo-referenced using the boundaries of the image. A key issue with a raster system is the size of the cells. Smaller cells permit the raster to approximate the flexibility of the vector system, but this takes up hardware space.

3.2.2.4 Development of map overlay

This was mentioned earlier in this Chapter as a powerful way to integrate different types of geographic information from different sources (Vine *et al.*, 1991). One of these applications, called site suitability, played a role in developing the overlay technique (Chrisman, 1997; Clarke *et al.*, 1996). The site suitability application uses data as layers to examine social, economic, physical, biological, and other criteria to locate potential study sites (Chrisman, 1997). Such data include presence or absence of disease, climate data, census data such as population estimates and administrative or district boundaries to drive the decision-making process. Any of these datasets can be either historical or present-day information.

Raster implementations of overlay

Two maps in the same grid system share the cell as the base object, and this common factor can be used to translate the data from the two reference maps into a third map. The computation of an overlay result translates into boolean (zeros and ones) or arithmetic operations on a cell-by-cell basis (Chrisman, 1997). Idrisi® (Clarklabs, Worcester, MA) has a function called *Overlay* which performs this operation automatically. What the function actually does is compare one image against another and the output is the result of the comparison between the two. If rainfall for January and December are compared with each other and any area shows the same rainfall for both months, the cells within that area can be given a value of 1. Areas that have experienced different rainfall in those months will be given a value of 0. The final image will consist of a map of zeros and ones.

Data processing might include a threshold that classifies the original measurements into two categories, such as suitable and unsuitable. The 1s can indicate suitable rainfall and the 0s represent unsuitable rainfall in a disease model. Likewise, the temperature tolerance ranges of the schistosomes and snails as discussed in Chapter 2 can be translated into maps using the binary classification. The binary maps can then be combined with boolean operators, such as AND (set intersection) and OR (set union). The process of *resampling* an image may be

necessary for *overlay* to ensure that the two images are the same size and resolution (Appendix A).

3.2.2.5 Neighbourhood construction

"Neighbourhood" is a criterion in spatial decision-making. Chrisman (1997) lists two ways to define the nearest neighbour in spatial analysis:

(1) on the basis of Euclidean distance (as the crow flies), e.g. to find the perimeter and area of a district.

(2) in terms of the connection between objects and not their size, for instance this method can be used to study the proximity of clinics and homesteads to eachother. In addition rivers grouped together at a particular level of typing hierarchy are more similar to one another than to rivers in other groups.

The vector and raster formats described earlier handle neighbourhood construction differently. Storage of data in raster format offers a more flexible implementation of near neighbour operators than data in vector format, as the objects are connected on a cell-by-cell basis. Neighbourhoods are inherent features of the raster grid.

Vector neighbours are derived in terms of distance or connections, such as adjacent polygons. If one wanted to know how many waterbodies exist within a 5km radius of a school, one would select a distance search radius (buffer, Appendix A) of 5km and increase the radius by any size if larger distances are required. Buffers around vector data are not limited by the grid spacing as with raster data. To reproduce the same result with raster data requires a raster algorithm, in a vector-based system. The schools constitute one data layer and the waterbodies another layer. The buffers would be contructed around the school and this will be stored in an additional layer that will be superimposed over the school and waterbodies. In vector data format, any number of water bodies can be accounted for within the search radius, while the same data in raster format are limited by the number of cells within the 5 km radius.

These are some important considerations related to the use of GIS as a research tool. An understanding of the theory behind the utilities offered by GIS software packages drives the decision- making process when constructing a GIS- based disease model. The power of the selected software is such that data can be manipulated in almost any way. Therefore, the quality of the output is directly dependent not only on the data that are fed into the model, but also on how the data are manipulated. Additionally, what is sometimes overlooked, is the availability of

appropriate software and computer hardware necessary to perform the intensive operations that some GIS applications require. The next section discusses a few of the relevant GIS methodologies that have been applied to schistosomiasis research such as small area analysis and climate scenario modelling.

3.2.3 Examples of the use of GIS in schistosomiasis modelling

Computer-based GIS systems have been used since the 1960s according to Coppock and Rhind's (1991) history of GIS, by users from different fields who initially did not have the forum to communicate and discuss their work together. Such was the case for health researchers using GIS. Vine *et al.*, (1997) listed the following three measures to improve communication among GIS researchers in the different fields: (1) health studies involving GIS should be published in journals read by epidemiologists, environmental scientists and biostatisticians, (2) include GIS as a subject heading in ``Medline" (Pubmed, National Library of Medicine, 2002) and (3) researchers should attend discussions on GIS applications in health research. GIS applications for disease modelling and in particular, schistosomiasis, are now gaining momentum although the first relevant work was published about 18 years ago.

Table 3.1 provides comparisons among the amount of published work on (1) schistosomiasis worldwide, (2) schistosomiasis in South Africa, (3) GIS worldwide and (4) GIS in South Africa using the Pubmed (Pubmed, National Library of Medicine, 2002) search engine. It is clearly evident from Table 3.1 that no work is available on Pubmed relating GIS, schistosomiasis and South Africa despite the advantages discussed previously.

Table 3.1: Pubmed (Pubmed, National Library of Medicine 2002)
Search showing articles on Schistosomiasis

Query Term(s)	Number of Articles
Schistosomiasis	13731
Schistosomiasis and South Africa	96
GIS	588
GIS and South Africa	15
GIS and Schistosomiasis	20
GIS and Schistosomiasis and South Africa	0

Generally, the objective of such GIS studies is to link the variables related to schistosomiasis transmission with spatial parameters. Some examples are provided below and are ranked in order of most recent to earliest published work.

Multivariable analysis is a statistical method of determining how well several causal variables explain the variation in a single outcome variable (Jekel, Elmore and Katz, 1996). The causal variables can act independently or together. Matthews (1990) stated that multivariate techniques are useful when applied to complex disease causation and suitability mapping. This usefulness was illustrated by Saathof *et al.* (2002) who used multivariate analyses to assess whether environmental factors (elevation, slope, distance to water and vegetation cover) could be used to predict small-scale infection patterns of urinary schistosomiasis in northern KwaZulu-Natal, South Africa. This type of study had not been done before in South Africa. Despite some of the factors such as altitude being strongly correlated with urinary schistosomiasis, they concluded that at sub-district level these environmental factors inadequately explained the spatial pattern of infection. Rainfall and temperature were not used for the study as the necessary data for that spatial resolution were not available and the variation within such a small area would have been small anyway.

Brooker (2002) provided examples of the schistosomiasis risk models done in Egypt, Cameroon and Tanzania and emphasized the need to develop separate models for each snail-schistosome system due to their different habitat types and environmental requirements. Remotely sensed satellite and climate data (land surface temperature, rainfall, and NDVI) were used to predict the distribution of urinary schistososomiasis in Tanzania and the results were compared to maps delineating the ecological zones where hosts snail are commonly found (Brooker *et al.*, 2001). High prevalence rates of urinary schistosomiasis were found within the same ecological zones, in contrast to the low prevalence rates found in different ecological zones where different snail species occurred. These authors illustrated how remotely sensed data could be used to predict schistosomiasis occurrence in Tanzania. Brooker *et al.* (2002b) and Beasley *et al.* (2002) used remotely sensed data again to define seven ecological zones, which in turn were used to guide an epidemiological survey of helminths in school-going children in Chad. Brooker *et al.* (2002b) found a close association among the defined ecological zones, environmental data (land surface temperature and rainfall) and *S. haematobium* and *S. mansoni* prevalence rates. Multivariable analysis was also used in this study.

Brooker *et al.* (2000) have also used GIS to collate data for an Atlas of Human Helminth Infection in sub-Saharan Africa. The aim of this atlas is to provide detailed spatial information on helminth infections in these areas where systematic information is lacking for geographically targeted control programmes. The database is made up of published information sourced from international literature as well as some unpublished data from the 39 countries themselves. Data for South Africa were excluded because the authors accepted that the information was being worked on by South African researchers.

Bavia *et al.* (1999) used a GIS to study the spatial and temporal dynamics of intestinal schistosomiasis and to identify the environmental factors that affect its distribution in Bahia, Brazil. Climate data included maximum rainfall, mean rainfall in three consecutive months, maximum and minimum temperature, change in diurnal temperature (ΔT) and duration of dry months. Their results showed that population density and the duration of the annual dry period were the most significant variables that determined the probability of intestinal schistosomiasis occurring in their study area.

Malone *et al.* (1997) used satellite data to develop schistosomiasis prediction and control models for the Nile Delta, Egypt. The diurnal temperature difference (ΔT) was used to reflect moisture domains, which in turn affected the relative risk of schistosomiasis. Regions that had low ΔT corresponded with higher intestinal schistosomiasis risk. The results of Spearman Rank Correlations showed that permanent hydrologically related features such as the water table had a greater impact on disease patterns than vegetation or climate. In another earlier study, Malone *et al.* (1994) described the use of temperature indices related to intestinal and urinary schistosomiasis risk. Two sets of historical prevalence data (1935 and 1983) for *S. mansoni* and *S. haematobium* in the Nile Delta and Nile River basin were used. The temperature indices were derived from polar orbiting environmental satellites. The outcome of the study was an inverse relationship between the ΔT and *S. mansoni* prevalence surveys for 1935 and 1983. An inverse relationship also existed between *S. haematobium* and ΔT for 1983 but there was no correlation with the 1935 survey.

Cross and Bailey (1984a) identified the need for a system to use available data to predict the occurrence of disease in areas where there are no disease information. They used step-wise discriminant analyses to select climate variables from their dataset, which could then be used to predict the presence/absence of disease in a specific area. In the Caribbean and Philippines there are areas where schistosomiasis is known to occur and others where it is observed to be absent.

Twenty-three independent seasonal variables were identified for use including mean annual precipitation, mean annual temperature, the annual variance of the monthly temperature, twelve lagged covariances and twelve lagged autocovariances for temperature and precipitation. The latter two variables were outputs from the discriminant analysis procedure, which was performed to reduce the number of variables that could be used to obtain the discriminant equation. For *S. mansoni* in the Phillipines, four of these these variables were used in the discriminant equation to calculate the probability of the presence or absence of disease. These included the covariance lag eleven months, the mean annual precipitation, the covariance lag eight months and the autocovariance for precipitation lag 6 months. These variables produced a discriminant function which allows 93.2% of the observations to be classified correctly. In the Caribbean, the covariance lag nine months, the mean annual precipitation, the variance in precipitation and the covariance lag three months were used. The resulting discriminant function identified 87.1% of the observations correctly for the Caribbean islands.

A follow- up study to the one above rectified some of the shortcomings encountered due to data problems (Cross and Bailey, 1984b) related to the geographical linking of disease observations to weather station data. The detail of the weather station data were insufficient to accurately correlate with disease observations. Therefore, the authors interpolated the weather station data to obtain temperature and precipitation data at the actual disease sites. A Landsat database also provided remotely sensed data for combination with the weather station data in the geographic database, and to improve the models prediction capabilities. The discriminant analysis model was used to determine the probability of disease occurrence at any site. The result was a disease distribution map that illustrated the statistical correlation between the probability of disease occurrence and the climate data.

3.3 CONCLUSION

The above studies use statistics, spatial analyses and satellite data to model schistosomiasis at both small and large scales. Fortunately, very detailed GIS- based weather station data and other climate data do exist in South Africa which can be used for disease modelling. However as can be seen from this Chapter very little work has been published on the application of GIS to schistosmiasis in this country. As the technology becomes more and more accessible, this is likely to change. Exploratory analyses such as that done by Saathof *et al.* (2002) are useful to expand our effective use of GIS for schistosomiasis studies. However Mathews (1990) and Richards *et al.* (1999) cautioned against neglecting epidemiological research study design,

statistical issues, data reliability issues and mapping issues when using GIS to formulate study questions and to test hypotheses about causal relationships. The next chapter shows how these GIS methodologies and epidemiological principles were used to construct disease models for *S. haematobium* and *S. mansoni* in South Africa.

CHAPTER FOUR

Methods used to Construct the Disease Models

4.1 INTRODUCTION AND AIM OF THE STUDY

The aim of this study was to construct models that relate the occurrence of urinary and intestinal schistosomiasis in South Africa to two environmental variables, temperature and rainfall (see Chapter 1, Section 1.7 and Chapter 2, Section 2.1) using a geographic information system. These climate variables provide measures of the likelihood of the presence or absence of each of the two forms of the disease. The output of the model would illustrate the environment where these occur in South Africa. The methods are described in terms of the study design, necessary elements for building the disease model and post model processing.

4.2 STUDY DESIGN

This is a retrospective study using historical urinary and intestinal schistosomiasis prevalence data and historical climate data with a geographic information system as the research tool.

4.3 RATIONALE FOR USING A GIS

The reasons for considering the incorporation of the available schistosomiasis data within a GIS were firstly that the data were georeferenced. Secondly, this would render the disease datasets more accessible and manipulable than they were in their current hardcopy format (Appendix A). Thirdly, the datasets could be used in new ways for different types of visual data analyses. For instance, the data could be combined with causal factors to build a schistosomiasis model for South Africa. The patchy occurrence of the disease in different areas within the country would be difficult to describe on a purely mathematical basis.

4.4 PRELIMINARY PREPARATIONS FOR MODEL BUILDING

The GIS had to be set up and the conceptual framework for the model had to be constructed before undertaking any analyses. The following specific objectives were needed to meet the basic requirements for deriving the disease model:

1. Point prevalence data for intestinal and urinary schistosomiasis from the Atlas of Bilharzia in South Africa (Gear *et al.*, 1980) were digitised.
2. Descriptive statistics for the disease data were generated using CrimeStat ® (Levine, 2000).
3. The data were imported into Mapinfo Professional® (vector-based GIS package, Appendix A) (Mapinfo Corporation, UK) and the distribution patterns of urinary and intestinal schistosomiasis were displayed.
4. The published literature was surveyed to identify the abiotic factors that affect the occurrence of the host snails and the disease. Where possible specific limiting levels of these variables were noted.
5. The necessary climate surfaces were obtained in raster format for use in the raster-based software package, Idrisi® (Clarklabs, Worcester, MA).

4.5 DERIVING THE DISEASE MODELS

4.5.1 Hypothesis

Evidence to confirm seasonal transmission was described in Chapter 2 but a few noteworthy studies are mentioned again here to support the hypothesis. Pitchford and Visser (1962, 1969) found positive correlations with spring and summer temperatures. Summer has been described as the middle of the transmission season (Pitchford, 1981) due to Pitchford and Visser's (1962) early rodent immersion study that concluded that mid-summer was a well- defined transmission period for *S. mansoni.* During the cooler autumn months intra-molluscan development is prolonged (Pitchford, 1986). These studies also show no transmission during winter (Pitchford, 1962) because cercarial shedding ceased (Pitchford, 1986).

Therefore the hypothesis for this work was that spring and summer temperatures correlate positively with both urinary and intestinal schistosomiasis transmission while there is a negative correlation with winter and autumn temperatures. Moderately warmer temperatures are expected to favour parasite growth and development, but it would be too cold during winter and autumn. Since the host snails cannot tolerate very high temperatures, while both *S. haematobium* and *S. mansoni* cannot tolerate too low temperatures some anomalies in the relationship between

climate variables and each disease's occurrence were expected. The association between both of the rainfall variables (annual rainfall and average monthly rainfall) and disease occurrence was also tested and a positive association was expected with one or both variables based on the discussion in sections 2.3.2, 2.4.2.2 and 2.5 where the lack of literature relating schistosomiasis transmission to rainfall was highlighted. Vector- and raster-based GIS software were used for model development. The methods were constructed to test:

(1) whether the areas that were found to be suitable with respect to temperature follow the occurrence of each disease;

(2) the relationship between temperature and rainfall and the urinary and intestinal schistosomiasis observations.

The available software allows data to be analysed at different spatial and temporal scales. Spatial modelling based on actual disease data allows for realistic predictions of the occurrence of schistosomiasis at different point localities.

4.5.2 Post model processing

1. Derive population estimates based on each disease model.
2. Compare the results obtained from Hutchinson *et al.* (1995) and Schulze (1997) climate datasets which are described in section 4.6.3.

4.6 DATA

4.6.1 Disease data

Data were digitised from the Atlas of Bilharzia for South Africa (Gear *et al.*, 1980) and imported into Mapinfo Professional® (Mapinfo Corporation, UK). The database consisted of prevalence categories for *S. haematobium*, and presence and absence data for its host snails, *B. globosus* and *B. africanus*. Data for the intestinal parasite *S. mansoni* and its host snails *B. pfeifferi* are presented in the Atlas in the same way. There are a total of 48 maps (Fig 4.1) in the Atlas depicting the distribution of schistosomiasis nationally according to magisterial district. The data are based on primary school surveys and represented on a 1:250000 scale.

Figure 4.1: Picture of Atlas of Bilharzia (Gear *et al.*, 1980)

These maps were based on survey data collected over a period of about 20 years (from approximately 1960 to 1980) by the following collaborating teams (Gear *et al.*, 1980):

1. The Medical Ecology Centre; a unit of the State Health Department but housed at the South African Institute for Medical Research in Johannesburg. The Medical Ecology Centre's team made a preliminary visit of the area to be surveyed. During this time they noted the features of the streams and dams to facilitate sampling for snails. The principals of the selected schools were contacted so the team could obtain parental consent to obtain blood from a sample of children. Two immunological tests were performed. Firstly, the sera were tested with the bilharzia complement-fixation test using three antigens from cercariae, schistosomes and *S. mansoni* ova. Secondly the sera were also tested using an indirect fluorescent antibody test for antibodies, where the antigen was a cercarial suspension. However most of the diagnoses were done using urine and stool samples. They found a close correlation between the tests for antibodies in the blood and the urine and stool sample analyses.
2. Regional Offices of the State Health Department of the former Northern Transvaal (now Limpopo Province) and Natal (now KwaZulu-Natal).
3. The Bilharzia Research Unit of the South African Institute for Medical Research (SAIMR), Johannesburg.
4. The Bilharzia Field Research Unit of the Medical Research Council, Nelspruit.
5. The Snail Research Unit of the Medical Research Council in the Department of Zoology, University of Potchefstroom.

The Bilharzia Research Unit of the SAIMR and Medical Ecology Centre collected snails from the streams and other waters in the area. The snails were identified on site and these identifications were confirmed later. Wherever possible samples or a subset of samples,

depending on the number of snails, were placed singly in test tubes with water and observed for 1 to 24 hours for the shedding of cercariae. The snails were then preserved so they could be sent to the Snail Research Unit in Potchefstroom. Here the final identifications were made.

If cercariae were shed and identified as mammalian type schistosomes, then in selected cases, rodents, either white mice, laboratory bred *Praomys (Mastomys) natalensis* or *Saccostomus campestris,* were exposed to the cercariae. Parasite identifications were done 6 to 8 weeks later, after sacrifice.

The other research teams collected urine, faeces, some rectal biopsy material and blood from a representative sample (about 100) of the children attending school in the vicinity of the snail collection sites. After collection, the urines were examined microscopically for ova. The rectal biopsies were examined microscopically on site in the field. Faecal samples were collected in bottles and fixed by the addition of 10% formalin for later examination in the laboratory for the presence of schistosomiasis and other ova. The bloods were taken back to the laboratory for serum separation. However, if more than 48 hours were to elapse before the bloods could be received at the laboratory, the serum was separated the day after collection and stored under refrigeration until they could be delivered to the laboratory. The sera were used for immunological diagnostic tests.

The results of the diagnostic tests, snail data and other incidentally collected samples were collated and plotted on large scale maps and then transferred to the maps constituting the Atlas of Bilharzia. The disease data are presented in the form of seven prevalence categories, which were already quantified as percentages (Table 4.1).

Table 4.1: Prevalence Categories used by Gear *et al.* (1980)

No.	Category
1	0%
2	1-5%
3	6-10%
4	11-25%
5	26-50%
6	51-70%
7	71-100%

4.6.2 Population data

In Chapter 3, the usefulness of mapping appropriate population data with case data was mentioned (Briggs and Elliot, 1995). For that reason population data were used in this study. These data came from two sources listed below:

(1) An African Population Database (Deichman, 1995), which was derived from about 4700 African administrative units, and interpolated from existing data sources in raster format. The data sources for South Africa were the South African Central Statistical Service, 1991 Population Census and 1996 Population Census Atlas of South Africa (Census South Africa, 1998). Deichman (1995) adds that South Africa's changed district boundaries after 1994 made it difficult to estimate the population data consistently.

(2) Geo-referenced census data from the 1996 census conducted in South Africa (Statistics SA, 2001) - these are the most representative of the country to date. The lowest level of data is "placenames." These data could be imported seamlessly into Mapinfo Professional® (Mapinfo Corporation, UK) then Idrisi® (Clarklabs, MA) for raster analysis.

4.6.3 Climate data

Two climate datasets were used and reference to climate data in this work is made through their respective main authors, i.e Hutchinson *et al.* (1995) and Schulze, (1997). The differences between the two are described below.

Climate Dataset 1: Hutchinson *et al.* (1995)

Monthly mean minimum and maximum temperatures, and monthly mean rainfall for Africa were obtained from a topographic and climatic database produced by the Centre for Resource and Environmental Studies (CRES) at the Australian National University (Hutchinson *et al.*, 1995). The dataset consisted of grid values of temperature and precipitation obtained from source, point and line data. Eventually 1500 temperature data points and 6000 precipitation data points based on data from international collections and 13 national meteorological services were used. The authors made use of all available years of records between about 1920 and 1980 for temperature and rainfall. This includes the time period during which all the disease data were collected for the Atlas of Bilharzia (Gear *et al.*, 1980). Rainfall averages were for a minimum of five years of record with the standard errors of the rainfall grids ranging between about 5% to 15%. These errors were partially due to the density of the data and spatial variability of the actual monthly mean rainfall (Hutchinson *et al.*, 1995). The standard errors for temperature

were about 0.5°C. The climate grid files were created using spatial analysis and interpolation techniques and were at a spatial resolution of 5 x 5 km (Hutchinson *et al.*, 1995).

Climate dataset 2: Schulze (1997)

The second climate dataset included minimum and maximum temperature, temperature range, altitude, heat units, and mean monthly rainfall. This dataset is available digitally and in hardcopy format as The South African Atlas of Agrohydrology and Climatology (Schulze, 1997). The Atlas illustrates the climate in southern Africa and gives sufficient detail to be used at a regional level. However, the author cautions against using it to get exact locational parameters because values at a particular point were obtained by regression analysis or by other simulation models. Therefore there may have been some smoothening effects on the final climate dataset.

The data contained in this Atlas were obtained from various sources but were specifically applicable to southern Africa (defined as the geographical entity covered by South Africa and the Kingdoms of Swaziland and Lesotho). A one minute by one minute of a degree latitude and longitude grid of altitudes containing 440 000 points for South Africa was used. Each grid was spaced at 1.6 km x 1.6 km. Precipitation, temperature and potential evaporation were then mapped. South Africa was delineated, using statistics, into 712 zones which were further divided into subzones of greater than average, average and less than average. This division created 2136 zone, and each was assigned a climate station between 30 to 100 years of climate variables. The climate data were converted from one software package (ArcInfo®, Esri International, USA) into another (Mapinfo Professional®, Mapinfo Corporation, UK) for the purpose of this study.

4.7 GENERATING SUMMARY STATISTICS

Summary statistical analysis was performed using software called Crimestat® (Levine, 2002) . CrimeStat® (Levine, 2002) is a spatial statistical package that works within the Microsoft Windows® environment. It is designed to read 'dbf', 'shp', 'dat' and ASCII files, which are database and mapping file formats and can write selected graphical objects to MapInfo Professional® (Mapinfo Corporation, UK). The following measurements were obtained for each of the seven prevalence categories (Table 4.1): sample size, nearest neighbour distances and average density (points per square metre). Some summary statistics can be generated in Mapinfo Professional® (Mapinfo Corporation, UK) but not neighbour distances.

4.8 GIS SOFTWARE

Mapinfo Professional® (Mapinfo Corporation, UK) offers a vector GIS capability which was discussed in Chapter 3. Idrisi version 32® (Clarklabs, MA) offers the raster GIS capability discussed in Chapter 3.

4.8.1 Putting Data into GIS Software

Once digitised, the point data from the Atlas of Bilharzia (Gear *et al.*, 1980) were put into digital format in Mapinfo Professional® (Mapinfo Corporation, UK) and then imported for use in Idrisi® (Clarklabs, MA). Each prevalence category was stored in a separate layer as a separate file. The relevant climate data were also imported into Idrisi® (Clarklabs, MA). Rainfall and temperature data for each month were stored as separate files and layers. This system facilitated the merging of each disease dataset with the climate information.

4.9 DERIVING THE DISEASE MODELS

A literature search revealed the many field studies that have been conducted on schistosomiasis in South Africa. Two models could be constructed using some of the available literature as a framework. The first was based on suitability mapping for urinary and intestinal schistosomiasis using temperature. The second used regression analysis to assess the relationship between temperature, rainfall and the presence of schistosomiasis.

4.9.1 Model One: Temperature- suitability models

This model used experimental evidence identifying which temperatures were suitable or unsuitable for urinary and intestinal schistosomiasis transmission to create suitability maps. Mean monthly minimum and maximum temperatures were taken from the Hutchinson *et al.* (1995) climate database. Digital data from Schulze's (1997) Atlas only became available towards the end of this study and hence could not be used for the model development.

Deriving the temperature- suitability model

A definitive work published by Pitchford (1981) of the Medical Research Council's Bilharzia Field Research Unit was used. Pitchford saw the need to study the relationship between the parasites and temperature since most of the available studies focused on the snails' responses to temperature. The intention of Pitchford's work was to address the lack of data on schistosome distribution and field water temperature regimes. Pitchford also recognised the difficulty of

extrapolating the results of laboratory-based studies to field situations, which was discussed in Chapter 2 and he designed his study with that in mind.

Pitchford (1981) classified air temperatures according to their suitability for the transmission of *S. mansoni* and *S. haematobium* based on experimental evidence. He based his results on outdoor field experiments at twenty-three study sites in both endemic and non-endemic areas. Cercarial shedding patterns were obtained from batches of snails exposed to *S. haematobium* and *S. mansoni* miracidia every two weeks for periods ranging from one to twenty years, depending on the site.

Field transmission data were obtained from infections acquired by sentinel rodents immersed in waters in two endemic areas. Batches of snails were also exposed to each species' miracidia every fortnight over a period of up to 20 years and the life-cycle findings (especially the prepatent period) were observed. Thereafter the local air temperature requirements of the two parasites were related to the observed field transmission data and the prepatent periods. The temperature recordings were obtained from about 620 weather stations across the country.

This work represents an early initiative in establishing the geography of schistosomiasis in relation to temperature. Pitchford mapped temperature and his data on schistosome transmission using 1/16° squares. This allowed the spatial definition of minimum and maximum temperature cut-offs for both *S. mansoni* and *S. haematobium* in this model. Pitchford used three indices of temperature: monthly mean of the daily maximum (Mdx), monthly mean of the daily minimum (Mdn) and monthly temperature range (R) to define temperature regimes in relation to schistosome transmission. For purposes of the present work these were further classified into three categories: (1) suitable regimes, (2) unsuitable regimes and (3) marginally suitable regimes.

This classification, derived from Pitchford's (1981) descriptive statements (such as Mdn 1°C or lower for 1 month or more), (Table 4.2) was translated into mask map layers in Idrisi® (Clarklabs, MA) using the climate data of Hutchinson *et al.* (Appendix B). A mask layer is a layer of data that has some or all of the data required for the final map output. In this case all the areas where the minimum temperatures were 1°C or lower for each of the 12 months of the year, were selected out and stored in a separate data layer. Any temperature measurement that did not satisfy this requirement was excluded or masked out. Each of Pitchford's (1981) temperature regimes was translated into suitability mask layers. Hence, Pitchford's results were

integrated into a GIS using the best climate data available. These maps could then be compared to the disease observations obtained from Gear *et al.* (1980), the hypothesis being that areas with suitable temperature regimes cited by Pitchford (1981) should match the areas where either urinary or intestinal schistosomiasis actually occurred.

Idrisi's® boolean logic was used to define areas that were suitable and unsuitable for urinary and intestinal schistosomiasis transmission (Clarklabs, MA). If an area on the map had both the temperature measurement and occurrence of any one of the seven categories of disease prevalence listed in Table 4.1, the area was designated as a "1", and conversely if either condition existed individually, the area on the map was designated as "0". This was done by looking at the map outputs. On this basis, some temperature regimes were excluded and some included to finally select the input variables for each disease model. The resulting optimal suitability maps for urinary and intestinal schistosomiasis were derived from a combination of suitability maps or scenarios from Pitchford's (1981) work. It is appropriate to combine these maps because in nature the parasite would be subjected to the cumulative effects of both suitable and unsuitable temperature conditions over time. The combinations that best visually corresponded to each disease distribution were selected.

The temperature regimes that were excluded from the model and the reasons for their exclusion are shown in Table 4.2. Table 4.3 lists those regimes that were included. For *S. haematobium* the optimal mask was created using the following three temperature cut-offs:

1. minimum temperature of 1°C or less for one month or more;
2. temperature range of 14°C or more during December and January (mid- transmission season);
3. minimum temperature of 14.5°C or more for four months or more.

The optimal mask for *S. mansoni* (Table 4.3) was obtained using the following temperature parameters:

1. minimum temperature of 3°C or less for one month or more;
2. temperature range of 14°C or more during December and January (mid- transmission season);
3. minimum temperature of 16°C or more for two months or more.

The results of the model were tested against the known distribution of *S. mansoni* and *S. haematobium* from the Atlas of Bilharzia (Gear *et al.*, 1980). The precision and accuracy of the map outputs were determined.

Table 4.2: Temperature regimes from Pitchford (1981) that are excluded in the model
* The temperature regimes in column 1 were abbreviated for ease of use for model building.

Excluded temperature regimes	Disease occurrence – expected/observed	Abbreviated temperature regime*
Minimum temperatures of 5°C or less for one month or more.	Too cold for *S. haematobium* and *S. mansoni.* Included too many areas in the western regions of the country where disease is absent. See Fig. 4.2 as an example.	Mdn ≤ 5°C for ≥1 month
1. Minimum temperatures of 17°C or more for seven months or more. 2. Maximum temperatures of 30°C for three months or more.	Allowed little or no transmission of *S. mansoni.* The minimum temperature covered virtually the whole country with the exception of the coastal strip of KwaZulu-Natal. The maximum temperature did not extend to parts of the western regions of the country. Neither did it fit well in Limpopo Province nor in the eastern part of Mpumalanga.	Mdn ≤ 17°C for ≥ 7 months. Mdx ≥ 30°C for ≥ 3 months.
Maximum temperatures of 27°C for four months or more.	Suitable for *S. haematobium.* Limited in the Eastern Cape, but fits relatively well in the Limpopo Province, Mpumalanga and KwaZulu-Natal. Bad fit west of the Free State where areas that do not have the disease were selected by this temperature regime.	Mdx ≥ 27°C for ≥ 4 months.
1. Maximum temperatures of 27°C for three months or more, combined with minimum temperatures of 17°C for one month or more. 2. Maximum temperatures of 27°C. 3. Minimum temperatures of 16°C for nine months or more. 4. Minimum temperatures of 17°C for nine months or more.	Suitable for *S. mansoni.* The 27°C for 3 months mask covered a larger area than the 27°C for four months mask. The nine-month regimes did not fit well against the disease because they excluded some endemic areas.	1.Mdx ≥ 27°C for ≥ 3 months + Mdn=17°C for ≥ 1 months. 2. Mdx= 27°C. 3. Mdn = 16°C for ≥ 9 months. 4. Mdn = 17°C for ≥ 9 months.

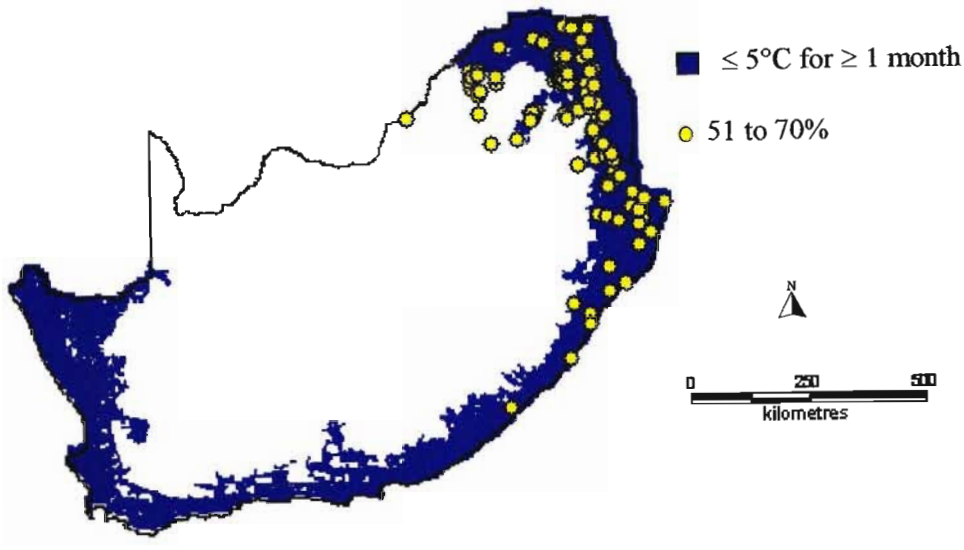

Figure 4.2: Map showing excluded minimum temperature regime of 5°C or less for one month or more and *S. haematobium* prevalence 51 to 70%

Table 4.3: Temperature regimes used by Pitchford (1981) that were included in the present study

Included temperature regimes	Effect on parasite occurrence	Abbreviated temperature regime*
Minimum temperatures of 1°C or less for one month or more.	Unsuitable for *S. haematobium* and *S. mansoni.*	Mdn ≤ 1°C for ≥ 1 month.
Temperature range of 14.5°C during the mid-transmission season (December and January).	Unsuitable for both *S. haematobium* and *S. mansoni.*	Trange=14.5°C in (01+12) months.
Minimum temperatures of 14.5°C or more for four months or more.	Suitable for *S. haematobium.*	Mdn ≥ 14.5°C for ≥ 4 months.
Minimum temperatures of 3°C or less for one month or more.	Unsuitable for *S. mansoni.*	Mdn ≤ 3°C for ≥ 1 month.
Minimum temperatures of 16°C or more for two months or more.	Suitable for *S. mansoni.*	Mdn ≥ 16°C for ≥ 2 months.

4.9.2 Model Two: Regression model

Clark, McLafferty and Tempalski (1996) stated that regression analysis can be used to find the linear combination of factors to explain the spatial variation typical of disease prevalence. After consulting a biostatistican, ordered regression analysis was selected to determine the association between each of the disease observations and temperature and rainfall. The results of the

regression analysis (weights) could then be used to interpolate the probability of schistosomiasis occurring where there were gaps in the distribution map. The resulting map could be used as a composite of schistosomiasis risk. Mean monthly minimum and maximum temperatures and mean monthly rainfall were the variables selected from the climate database to derive this model.

Deriving the regression model

Each disease data layer was overlaid on monthly minimum temperatures (Tmin), monthly maximum temperatures (Tmax) and monthly rainfall respectively. Idrisi's® *Extract* function was used to select the climate parameters underlying each disease observation (Clarklabs, MA). The monthly data were combined into four sets of three months each representing the seasons as described earlier in Chapter 2, Section 2.2 (Appendix C).

The temperature data were grouped in quarters to reflect the seasons as follows:

(1) hottest three months during which time relatively stable, high temperatures are experienced (December to February - summer),

(2) when rapidly increasing temperatures are experienced (September to November - spring).

(3) when rapidly falling temperatures are experienced (March to May - autumn).

Spring and autumn temperatures show more variability than summer and winter temperatures. Also, Figures 2.2 and 2.4 in Chapter 2 illustrate how the autumn and spring temperatures in KwaZulu-Natal, Eastern Cape and Western Cape approximate one another. The autumn temperatures in the Western Cape are actually higher than the spring temperatures experienced in that province.

(4) the coldest three months when there are relatively stable, low temperatures (June to August - winter).

The annual rainfall variable was derived by adding the monthly rainfall figures at each disease data point. The result was a database consisting of each disease data point and it's associated Tmin, Tmax and rainfall. There were thus ten variables in total, viz. Tmax1, Tmax2, Tmax3, Tmax4, Tmin1, Tmin2, Tmin3, Tmin4, annual rainfall, average rainfall per month (annual rain/12).

Ordered logistic regression analysis with a 95% confidence interval was performed on the resulting database for each parasite species using Stata® software (Stata, 2001). This type of statistical analysis makes few assumptions regarding the data and is an extension of binary logistic regression. Unfortunately the categorised prevalence data obtained from the Atlas of

Bilharzia (Gear *et al.*, 1980) limited the spatial and statistical analysis that could be performed due to the lack of information on the sample sizes. The actual prevalence rates for each site were also unavailable (K.N. de Kock, Potchefstroom University, pers comm[2]).

Deriving the prediction equation from the regression model

To map the probability of each cell (pixel) occurring in each schistosomiasis prevalence category the regression output was used. The equations were fed back into the model to produce a map showing the disease category having the highest probability (maximum likelihood) of occurring in each cell with the associated climate variables. The map would show the prevalence category that would most likely occur given the climate estimates used. Appendix C contains the generic formulae and procedures used to derive the models for urinary and intestinal schistosomiasis.

The following equations were used for the different urinary schistosomiasis (*S. haematobium*) categories:

1. Category 0%: $P_0 = 1/1 + e^{s - 9.98656}$
2. Category 1-5%: $P_1 = 1/1 + e^{s - 10.80347} - 1/1 + e^{s - 9.98656}$
3. Category 6-10%: $P_2 = 1/1 + e^{s - 11.52915} - 1/1 + e^{s - 10.80347}$
4. Category 11-25%: $P_3 = 1/1 + e^{s - 12.42612} - 1/1 + e^{s - 11.52915}$
5. Category 26-50%: $P_4 = 1/1 + e^{s - 13.804767} - 1/1 + e^{s - 12.42612}$
6. Category 51-70%: $P_5 = 1/1 + e^{s - 14.24769} - 1/1 + e^{s - 13.804767}$
7. Category 71-100%: $P_6 = 1/1 + e^{s - 14.24769}$

where S = 0.0033635 x annual rainfall - 1.27823 x tmax1 + 0.7063469 x tmax2 - 0.7712254 x tmax3 + 1.664342 tmax4 -2.958864 x tmin1 + 3.678978 tmin2 -1.461983 x tmin3 + 1.00727 x tmin4.

tmax1 = maximum temperatures for December, January and February,

tmax2 = maximum temperatures for March, April and May,

tmax3 = maximum temperatures for Jun, July and August,

tmax4 = maximum temperatures September, October and November, and similarly for minimum temperatures (tmin1 to tmin4).

Annual rainfall = sum of mean monthly rainfall

[2] Prof. K.N. de Kock, School of Environmental Sciences and Development, Potchefstroom University for CHE, Private Bag X6001, Potchefstroom 2520

The following equations were used for the different intestinal schistosomiasis (*S. mansoni*) categories:

1. Category 0%: $P_0 = 1/1 + e^{s - 14.15619}$
2. Category 1-5%: $P_1 = 1/1 + e^{s - 14.94952} - 1/1 + e^{s - 14.15619}$
3. Category 6-10%: $P_2 = 1/1 + e^{s - 15.60341} - 1/1 + e^{s - 14.94952}$
4. Category 11-25%: $P_3 = 1/1 + e^{s - 16.30314} - 1/1 + e^{s - 15.60341}$
5. Category 26-50%: $P_4 = 1/1 + e^{s - 17.22045} - 1/1 + e^{s - 16.30314}$
6. Category 51-70%: $P_5 = 1/1 + e^{s - 17.83996} - 1/1 + e^{s - 17.22045}$
7. Category 71-100%: $P_6 = 1/1 + e^{s - 17.83996}$

where S = 0.00389559 x mean monthly rainfall - 1.689384 x tmax1 - 2.303627 x tmin3 + 5.10582 x tmin2 + 1.907905 X tmax4 -2.465768 x tmin1.

4.10 POST MODEL DERIVATION PROCESSING

4.10.1 Population estimates

The aim was to generate population estimates using the maps derived from the disease models as representations of areas at risk for schistosomiasis. As mentioned in Chapter 3, school-age children are most at risk of becoming infected with schistosomiasis (Schutte *et al.*, 1995). For that reason population data for this age group (5-14 years) were taken from the two population datasets (Deichman, 1995 and Census South Africa, 1998). The Deichman (1995) dataset was already in raster format, but the 1996 Census data (Census South Africa, 1998) had to be converted for use in Mapinfo Professional® (Mapinfo Corporation, UK) and then imported into Idrisi® (Clarklabs, MA) raster format to query against the disease models. The maps derived from the descriptive and statistical models were then used as mask layers to obtain the numbers of children living in the areas delineated by the models' outputs. Idrisi's® *extract* function was used to do this. Thereafter both models for each parasite species were tested against the climate data of Hutchinson *et al.* (1995) and Schulze (1997) for purposes of comparing the ouput from the two climate datasets (Clarklabs, MA).

4.10.2 Hutchinson *et al.* (1995) versus Schulze (1997): Comparison of outputs

This was a two-step process. First two climate datasets were compared with each other. Secondly the *S. haematobium* map outputs were compared. These were obtained by running the models using the different climate datasets.

Cross-classification involves multiple overlay operations. The result is a new image that shows the locations of all combinations of the categories in the original images. The categories of one image (Hutchinson *et al.*, 1995) are compared with those of a second image (Schulze, 1997) and a tabulation of the number of cells in each combination is kept. The result of this operation is a measure of association between the images. Since the two resulting images have exactly the same number of categories, the Kappa measure of association can be used. This index may only be used if the categories on the two maps depict the same kind of data with the same data classes, which was the case here.

4.11 CONCLUSION

Although the two disease models for *S. haematobium* and *S. mansoni* were based on different methodologies they were created using the raster and vector capabilities offered by the two available GIS software packages. The results were in the form of statistical tables and map outputs.

CHAPTER FIVE

Results

5.1 INTRODUCTION

Two patterns of representation were developed to explain the occurrence of *S. haematobium* and *S. mansoni* in South Africa. The subsequent results are presented here in the form of maps. The following list summarises the decision- making steps that were used in the process of building a disease model for schistosomiasis:

1. Establishing schistosomiasis transmission constraints

What is available in the literature?

Which temperatures are suitable or unsuitable?

What role does water (rainfall being the surrogate indicator) play?

2. Data

What disease data are available?

What climate data are available?

What population data should be used?

3. GIS

Selection of appropriate software.

Are the data georeferenced?

What type of analysis - vector and/or raster?

4. Outputs

Model #1

Temperature-suitability map for *S. haematobium* based on translating literature findings into a disease model.

Temperature-suitability map for *S. mansoni* based on translating literature findings into a disease model.

Model #2

Regression analysis and prediction for *S. haematobium.*

Regression analysis and prediction for *S. mansoni.*

5. Model Applications

Determine the population at risk using the model outputs.

Compare the output maps from Hutchinson *et al.* (1995) data against Schulze's (1997) climate data.

Figure 5.1 shows the major components of the disease models described in the methods in Chapter 4. The logical flow in their development is indicated by arrows. Figure 5.1 lists the two GIS-based disease models for both for *S. haematobium* and *S. mansoni*. Two climate datasets and two population datasets were used. First summary statistics are presented followed by two maps showing the distribution of *S. haematobium* and *S. mansoni* in the country. Thereafter the results of both models are presented.

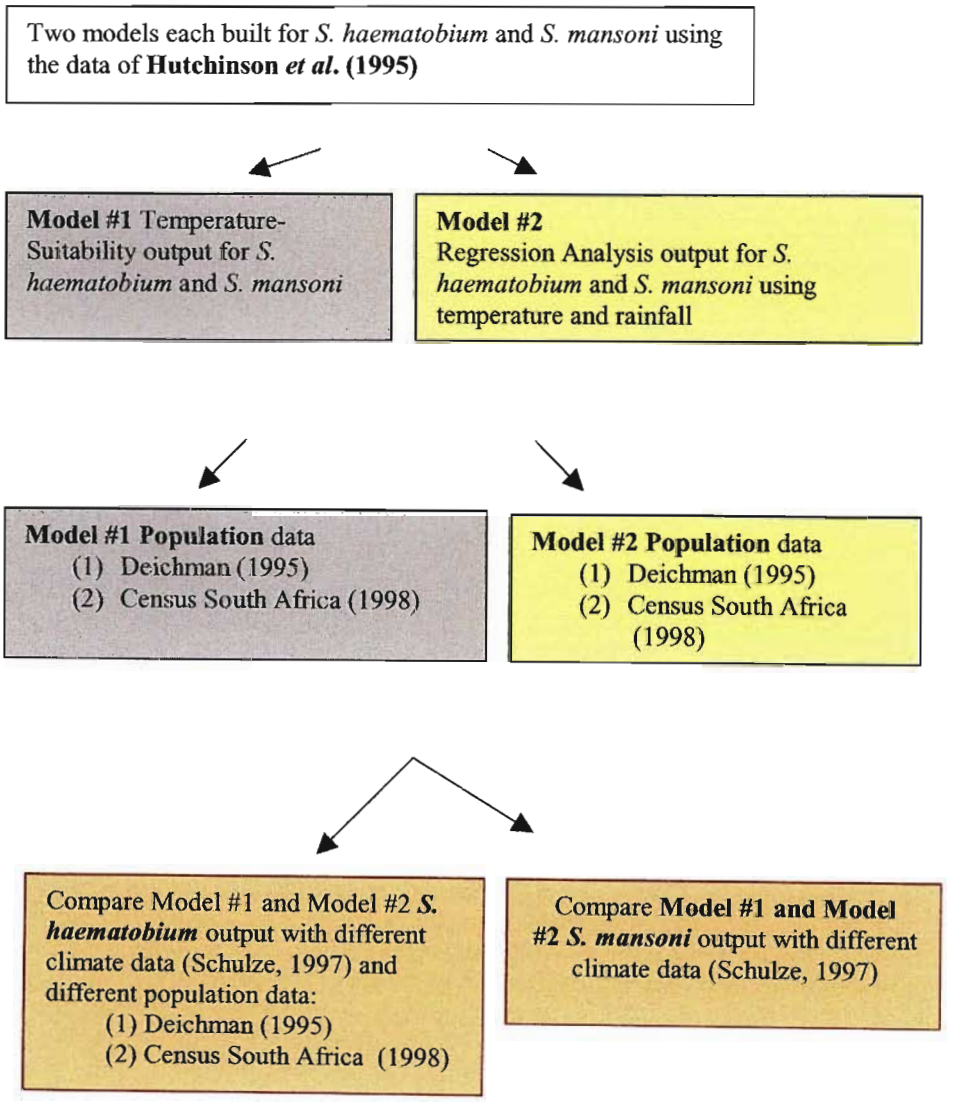

Figure 5.1: Summary Diagram showing disease model components

5.2 SUMMARY STATISTICS FOR PREVALENCE DATA

Tables 5.1 and 5.2 show the sample size, mean nearest neighbour distance and average density that were generated for the seven prevalence categories, using Crimestat® (described in Chapter 4, Section 4.7). The mean distances between points show how far apart each disease observation is from the next one in the same prevalence category. The density shows the number of disease observations for each prevalence category per square metre distance.

Table 5.1: Summary statistics for each of the seven prevalence categories for *S. haematobium*

	0%	1-5%	6-10%	11-25%	26-50%	51-70%	71-100%
Sample Size	453	209	226	302	405	99	285
Mean nearest neighbour distance (metre)	0.11	0.15	0.12	0.11	0.08	0.2	0.1
Average Density (points per square metre)	6	4	4	5	8	2	7

Table 5.2: Summary statistics for each of the seven prevalence categories for *S. mansoni*

	0%	1-5%	6-10%	11-25%	26-50%	51-70%	71-100%
Sample Size	665	129	101	90	81	34	48
Mean nearest neighbour distance (metre)	0.09	0.14	0.17	0.17	0.15	0.25	0.14
Average Density (points per square metre)	10	3	2	2	2	2	6

The sample sizes are in fact the number of prevalence points collected at each site and not the actual number of children involved in the study. The database consisted of more surveys for *S. haematobium* than for *S. mansoni*. Furthermore, the *S. haematobium* prevalence data were more dense than those for *S. mansoni*. These summary statistics confirm that *S. haematobium* has a wider distribution than *S. mansoni*. This can also be seen in Figures 5.2 and 5.3 where all the prevalence categories are mapped for both diseases. The maps give an indication of the spread of urinary and intestinal schistosomiasis in the country.

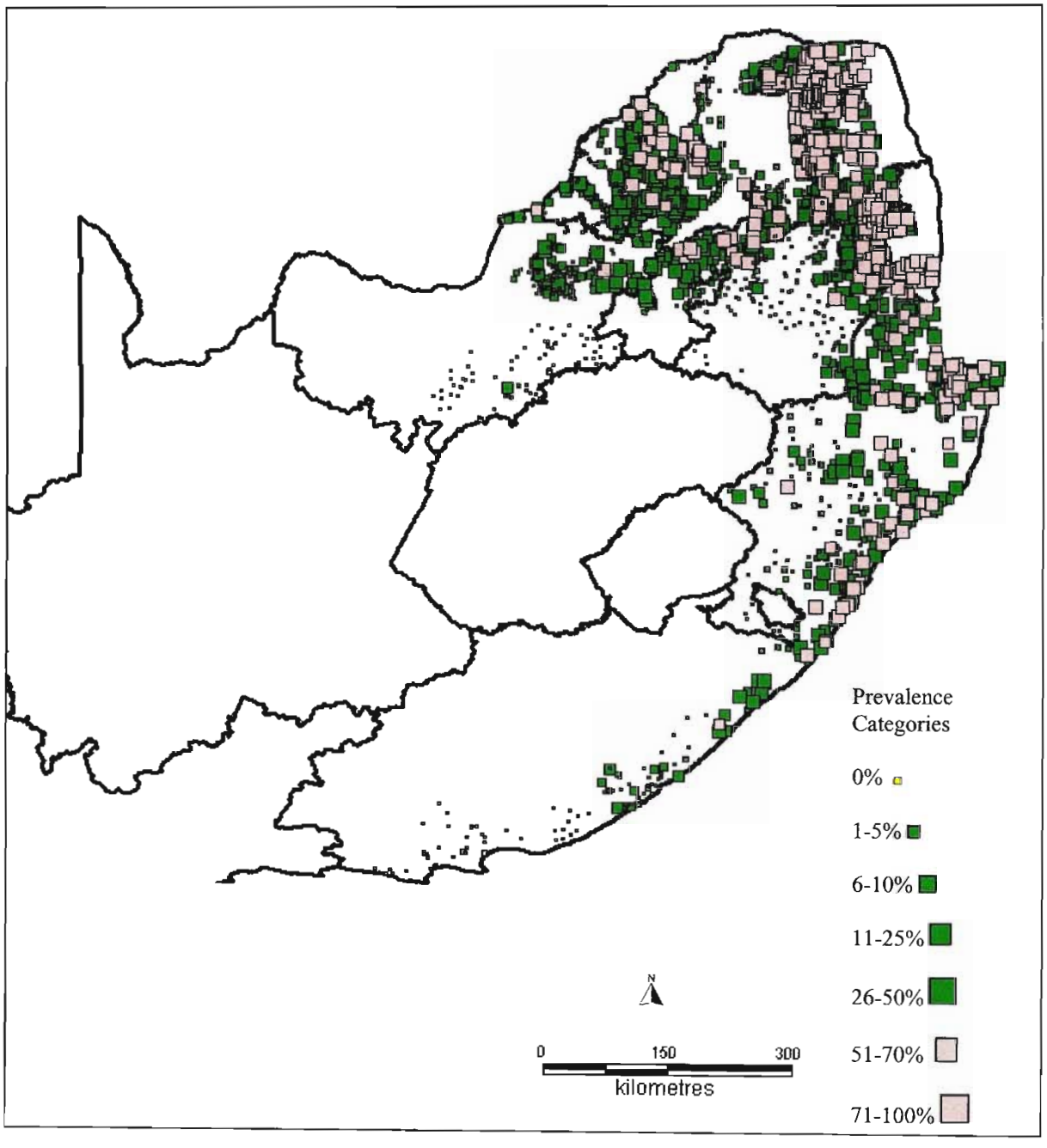

Figure 5.2: Distribution of *S. haematobium*. Adapted from Gear *et al*. (1980)

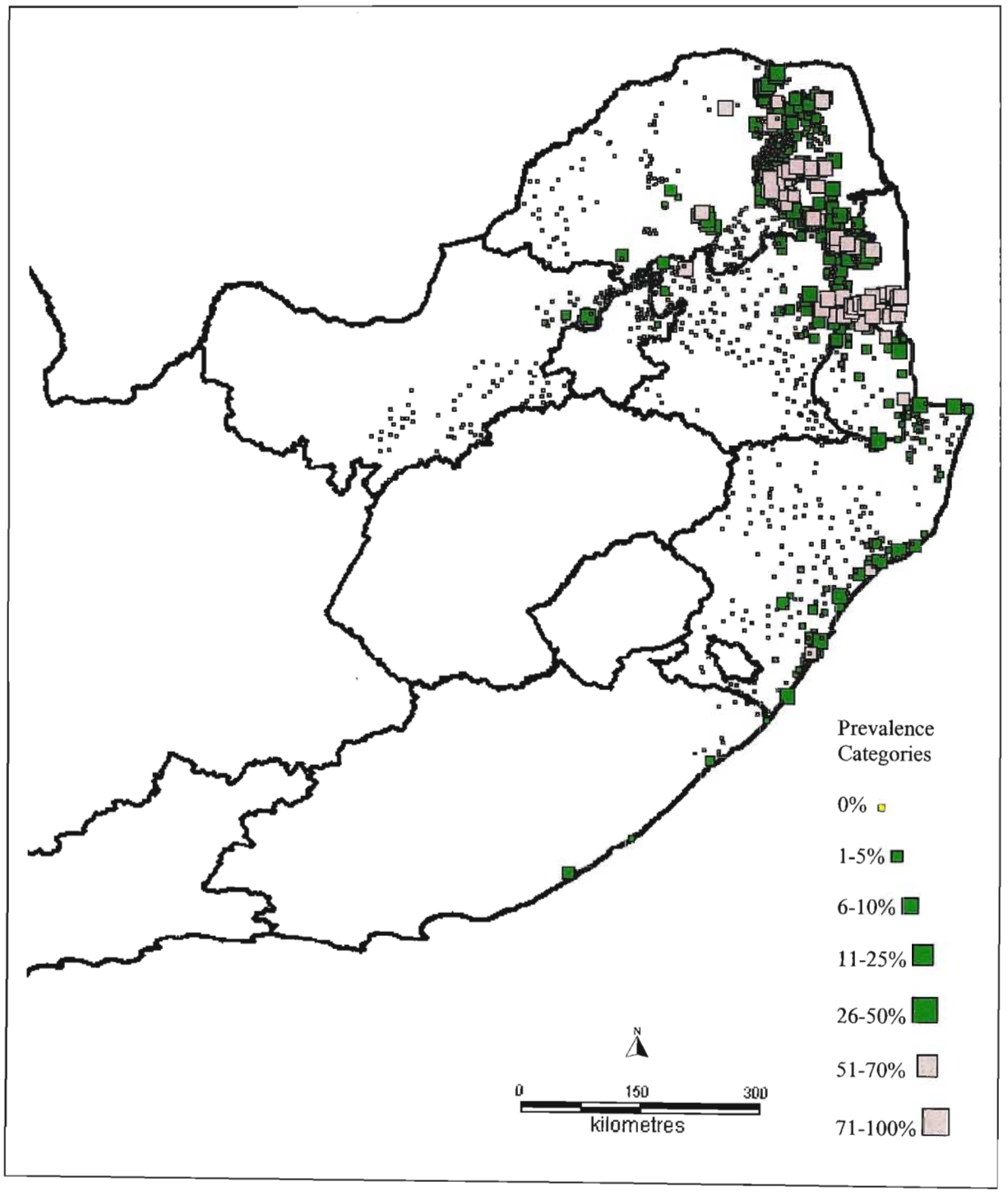

Figure 5.3: Distribution of *S. mansoni.* Adapted from Gear *et al.* (1980)

5.3 RESULTS OF MODEL ONE: SUITABLE TEMPERATURES

This section shows the findings in relation to the temperature-suitability maps for *S. haematobium* and *S. mansoni*. The disease data for each parasite were overlaid on each of the masks to determine the combination of temperature cut-offs that explained the distribution of the disease best.

Map scanned from Pitchford's (1981) attempt at relating temperature regimes and schistosomiasis on maps formed the basis for the temperature-suitability maps presented here. Figure 5.4 is an example of one of the 10 maps from Pitchford's (1981) work. The red South African boundary was superimposed on the map in Mapinfo Professional® (Mapinfo Corporation, UK) for orientation purposes.

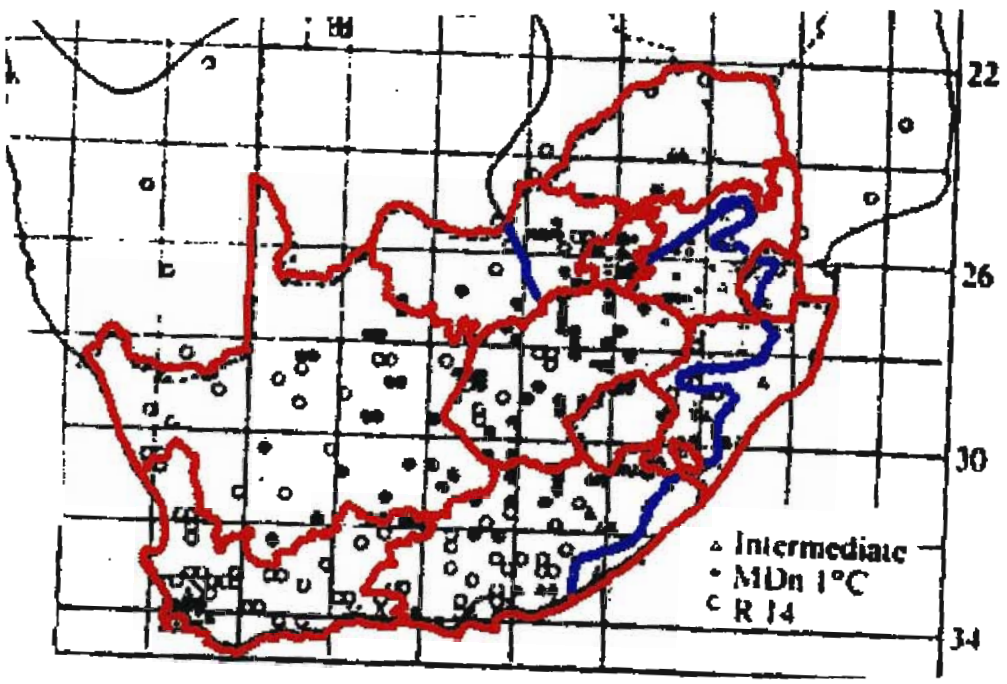

Figure: 5.4: Map adapted from Pitchford (1981), showing unsuitable temperature regimes for *S. haematobium* and *S. mansoni*

The contour (blue) demarcates the limits of marginally suitable and suitable *S. mattheei* temperature regimes. The data are presented in point form in black and white, making it difficult to detect patterns. The importance of this map is that it intends to show the following temperature regime: minimum temperature of 1°C, temperature range being unsuitable for *S. haematobium* and *S. mansoni*. Pitchford used his map illustrations as aids to convey his experimental results but their true value in explaining his research was limited at the time. The

reason for that was the lack of a tool to integrate the spatial component which he considered useful, with his experimental findings. Pitchford's (1981) work is ideally suited to the applications offered by a GIS. The contrast between Pitchford's maps and the present work is evident when the maps are compared. Figures 5.5 and 5.7 depict the temperature- suitability maps for *S. haematobium* and *S. mansoni*.

5.3.1 *Schistosoma haematobium* temperature- suitability map

Pitchford (1981) found suitable regimes for *S. haematobium* at 12 sites where the minimum requirements were Mdx 25°C - 27°C, Mdn 14.5°C for at least seven months, Mdx 27°C for two to three months and Mdn 14.5°C for five months. The abbreviations used here are explained in Chapter 4, Table 4.3. These conditions were suitable for both snail survival and completion of the schistosome's intra-molluscan development and cercarial shedding.

However these suitable regimes did not visually correspond with the disease data used in the present study. Therefore, of these only the last parameter (Mdn 14.5°C for five months) was selected for the suitability map for *S. haematobium*. Fig. 5.5 includes minimum temperatures of 1°C and colder for a minimum of one month and 14.5°C or more for a minimum of four months. If the difference between Tmax and Tmin during December and January was 14°C or more it was included.

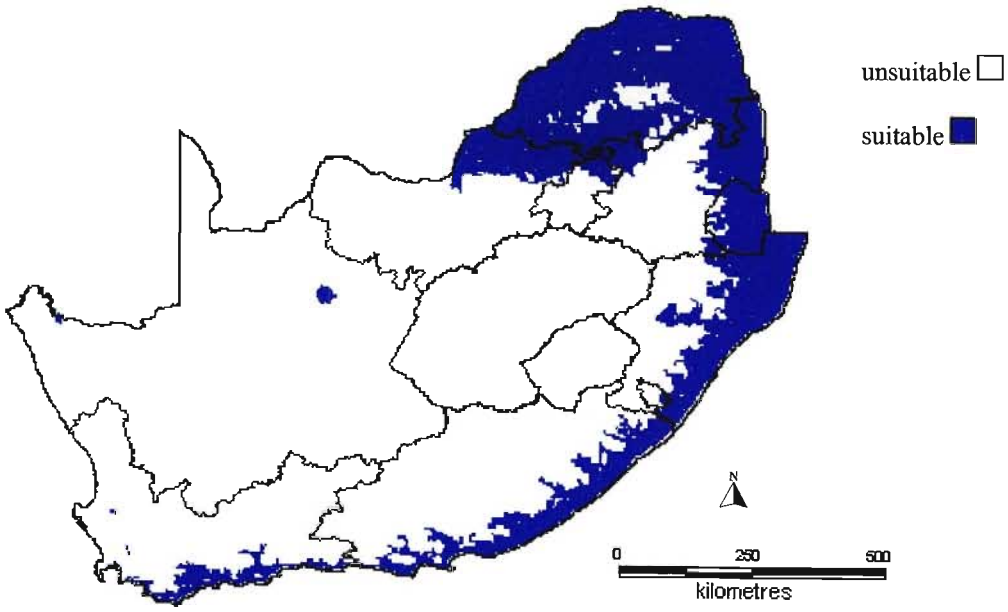

Figure 5.5: Temperature-suitability map for *S. haematobium* derived from temperature regimes listed in Table 4.3

The other temperature regimes, Mdn 1°C or less and the temperature range of 14°C in mid summer were used even though Pitchford (1981) found these to be unsuitable for transmission. Pitchford (1981) found that snails exposed to miracidia from autumn (March) to winter (July and August) died before cercarial shedding as it was too cold for too long. He concluded that the spread of *S. haematobium* into areas with Mdn 1°C was unlikely because of snail mortality and long parasite incubation periods at these low temperatures. Snails are also sensitive to the effects of long-term warm temperature ranges during December and January. The unfavourable responses of snails to too high temperatures were noted in Chapter 2.

Pitchford (1981) observed that these unsuitable conditions were found in a large portion of south-central South Africa and included Gauteng and KwaZulu-Natal provinces. However, Pitchford (1981) also noted that these unsuitable temperature regimes did overlap with the suitable regimes, which justifies their use in this model, and explains the patchiness of urinary schistosomiasis in certain areas. Small-scale spatial analyses would be required to test this.

The specificity and sensitivity of the models for *S. haematobium* and *S. mansoni* were calculated and shown in Tables 5.3 and 5.4 respectively. These are two important measures of the model function. The sensitivity refers to the ability of the model to detect schistosomiasis when it is present. The specificity refers to the model's ability to detect no schistosomiasis when the disease is not present.

Table 5.3: Validation of model for *S. haematobium* based on Pitchford's (1981) data

Temperature mask	**Survey Results**	
	Disease present	**Disease absent**
Number of disease data points in **suitable zone**	1530	231
Number of disease data points in **unsuitable zone**	213	256
Total	**1743**	**487**

These values were obtained using the prevalence data presented in Figure 5.2. The sensitivity of the *S. haematobium* temperature model was found to be 87.78% (Table 5.3), with a standard error (S.E) of 0.0078 and the 95% confidence interval for the presence of schistosomiasis was 0.86 to 0.89. This indicates that 87.78% of the positive disease data points were correctly

identified in the temperature suitable zone. The false-negative error rate is 12.22% indicating the rate at which the model fails to account for schistosomiasis in areas that have suitable temperatures (Jekel *et al.* 1996).

The proportion of true negatives that were correctly identified as negatives by the temperature mask was found to be 52.57% using Table 5.3, but the estimate was not very precise (S.E = 0.023, and 95% confidence interval of 0.48 - 0.57). The false positive error rate was 47.43%. Thus, the suitability map for *S. haematobium* had a high sensitivity but low specificity. This infers that a small change in temperature would produce a large change in disease occurrence. However the relatively low specificity implies that the map inadequately accounted for "disease absent" observations. Hence, the map was better in accounting for disease presence than it was in explaining disease absence.

5.3.2 *Schistosoma mansoni* temperature-suitability map

Figure 5.6 includes minimum temperatures below and including 3°C for a minimum of 1 month and 16°C or more for a minimum of two months. In addition, if the difference in Tmax and Tmin during December and January was 14°C or more it was included in the model.

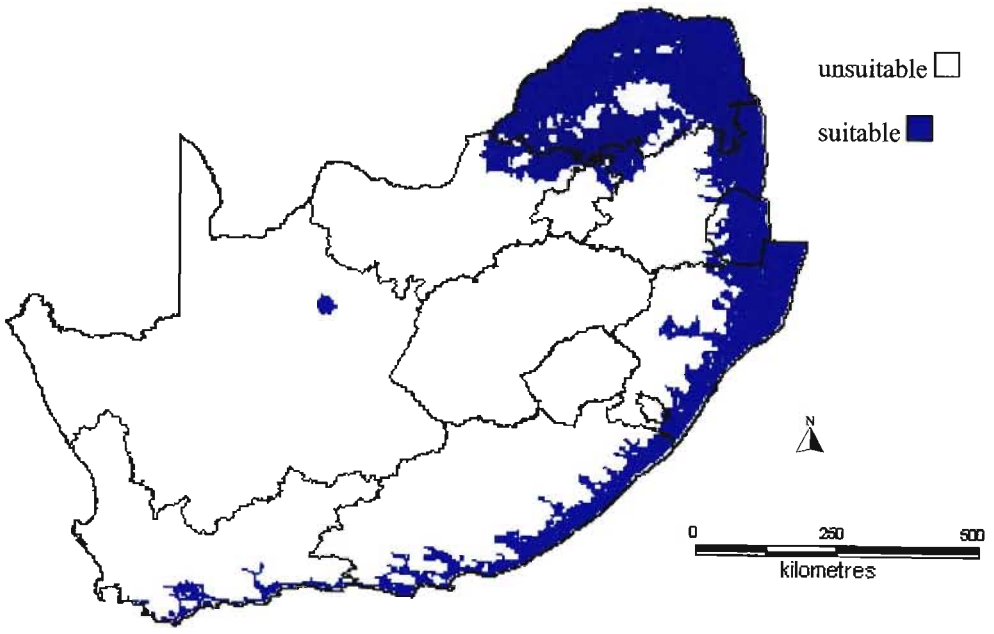

Figure 5.6: Temperature-suitability map for *S.mansoni* derived from temperature regimes listed in Table 4.3

Pitchford (1981) believed that winter Mdn 3°C was unsuitable for *B. pfeifferi* as the infected snails died at these temperatures. Again, high temperature ranges were unsuitable for *S. mansoni.* Both these regimes were used in building the model. The Eastern Cape province experiences a MDn of 1°C and temperature range of 14°C. Both parasite species may be found in this region although *S. mansoni* is very rare there.

A MDn of 3°C has a westerly distribution inland, while the unsuitable MDn 17 °C for seven months is found east of 31°E according to Pitchford (1981). This latter temperature regime is in fact uncommon in South Africa and is observed sporadically in a narrow coastal belt from Durban northwards through northern KwaZulu-Natal and into Mozambique. The regime appears to be absent between 18°S and 20°S and is suitable for *S. mansoni* survival. Pitchford (1981) noted the anomalies existing between *S. mansoni* occurrence and unsuitable regimes in what is now Gauteng. *Schistosoma mansoni* is more sensitive to daily fluctuations in temperature than *S. haematobium* and this also limits its distribution.

The model for *S. mansoni* had a low specificity as only 44.60% of the true negative data points were correctly found in the unsuitable temperature zone, (S.E = 0.019 and 95% confidence interval of 0.41 to 0.48, Table 5.4). The false positive error rate was 55.4%. The sensitivity was 93.10% (S.E 0.011, and 95% confidence interval of 0.91 to 0.95) and the false negative error rate was 6.9%. Figure 5.3 was used for these calculations. Thus the *S. mansoni* model was highly sensitive but not as specific as that for *S. haematobium.*

Table 5.4: Validation of model for *S. mansoni* based on Pitchford's (1981) data

Temperature mask	**Survey Results**	
	Disease present	**Disease absent**
Number of disease data points in **suitable zone**	499	400
Number of disease data points in **unsuitable zone**	37	322
Total	**536**	**722**

The optimal maps for each parasite species were derived using only minimum temperature regimes. Since these temperature regimes are not strictly conformed to in nature, these may be

said to represent the minimum temperature requirements for parasite transmission. For instance, an Mdn of 16°C or more only excluded all minimum temperatures below 16°C. Higher specificity could be obtained with consideration of other variables such as rainfall.

5.4 RESULTS OF MODEL TWO: ORDERED LOGISTICAL REGRESSION ANALYSIS

The data for the second model were derived by extracting the temperature and rainfall regimes that occurred at each prevalence location on the map. Section 4.9.2.1 in Chapter 4 explains how this was done. Summaries of the extracted seasonal temperature minima and maxima for *S. haematobium* and *S. mansoni* are shown in Figures 5.7 and 5.8 respectively. These temperature values were extracted from the climate database of Hutchinson *et al.* (1995) and summarized by season (Section 4.9.2.2) for statistical analysis.

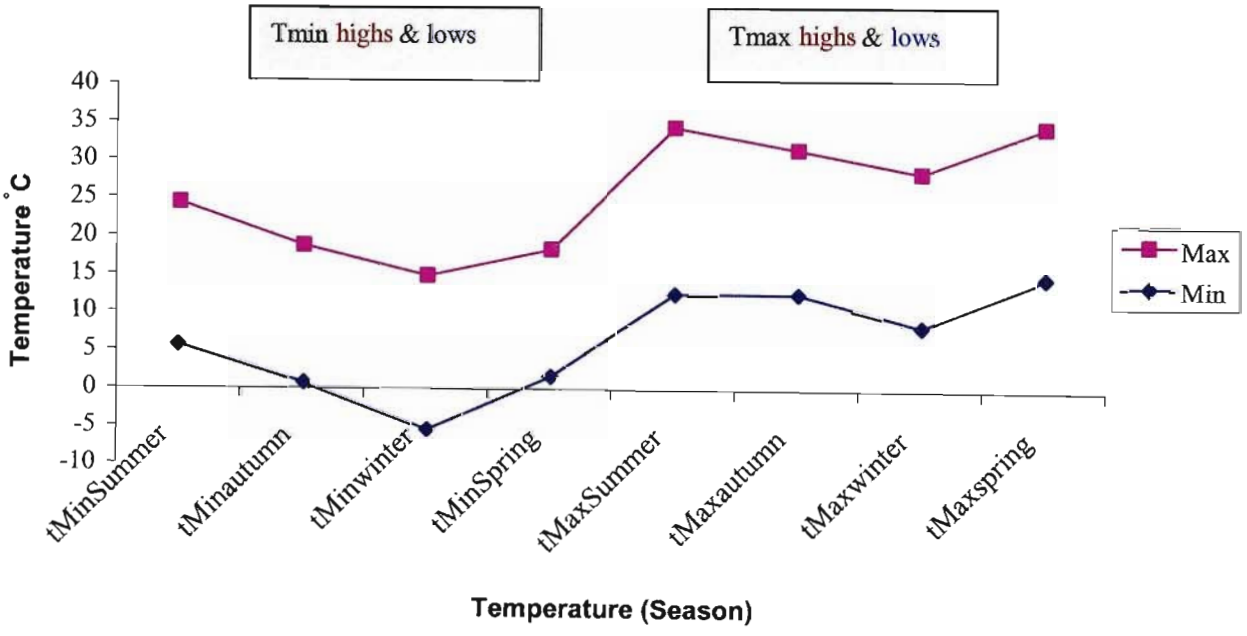

Figure 5.7: Extracted temperature variables for each *S. haematobium* point on the map

The graphs show the highs and lows of both maximum (Tmax) and minimum (Tmin) temperatures for each season and give an indication of the temperature variation (range) that occur in areas where both schistosomes are prevalent. For instance, the variable "tminsummer" in Figs. 5.7 and 5.8 refers to the minimum temperatures observed in summer.

During winter, where *S. haematobium* occurred, the lowest overall minimum temperatures were observed. The Tmin highs and lows approximated each other during autumn and spring. Summer had the highest Tmin minima and maxima. The results for Tmax did not show the same trend. The Tmax spring and summer highs and the Tmax summer and autumn lows approximated each other. However the lowest temperatures were observed during winter again. For *S. mansoni* a similar pattern for Tmax and Tmin were observed (Fig. 5.8). An important difference between Figs. 5.7 and 5.8 is that all the Tmin values were above zero for *S. mansoni* but this was not the case with the Tmin values for *S. haematobium* because sub-zero temperatures were obtained.

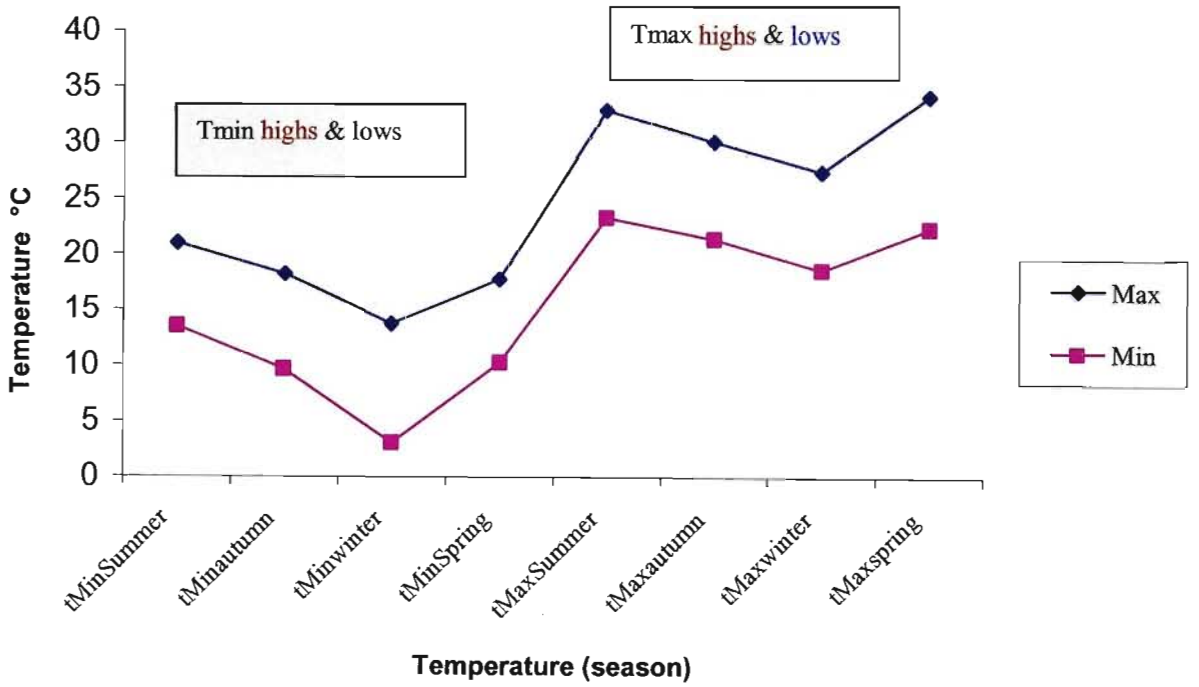

Figure 5.8: Extracted temperature variables lying under each *S.mansoni* point on the map

5.4.1 Ordered logistical regression analysis for *S. haematobium*

All of the eight temperature variables, and one of the two rainfall variables contributed significantly to describing the occurrence of schistosomiasis. The average monthly rainfall variable was excluded while annual rainfall was included. The log likelihood was -3106.82 for 1979 *S. haematobium* observations and $p < 0.1$. The $LRChi^2$ (9) was 1160.8. This ($LRChi^2$) is a test where the coefficients (probabilities) are zero (Jekel *et al.*, 1996).

There are seven prevalence categories and without doing any spatial statistics, the chances of any disease observation being one of these seven categories can be shown as 1/7 = 0.14. The model states that on average, for each disease observation the probability of being observed

under these climate conditions is exp(-3106.8216/1979) = 0.208. Since this figure is much larger than 0.14 but is still considerably less than 1, the model has sufficient explanatory power (after Gould, 2002).

Positive coefficients were obtained with the following five variables:
1. annual rainfall = sum of mean monthly rainfall,
2. maximum temperatures in Autumn (March, April and May = tmax2),
3. maximum temperatures in Spring (September, October and November = tmax4),
4. minimum temperatures in Autumn (March, April and May = tmin2) and
5. minimum temperatures in Spring (September, October and November = tmin4).

From this it can be inferred that an increase in the annual rainfall, both maximum and minimum autumn temperatures and maximum and minimum spring temperatures predicted an increase in the prevalence of *S. haematobium.* These variables can be said to increase the chances that the higher prevalence categories will occur rather than the lower prevalence categories (after Gould, 2002).

Negative coefficients were obtained with the remaining four variables:
1. summer maximum temperatures (December, January and February = tmax1),
2. winter maximum temperatures (June, July and August = tmax3),
3. summer minimum temperatures (December, January and February = tmin1) and
4. winter minimum temperatures (June, July and August = tmin3).

Increasing summer and winter minimum and maximum temperatures decreased the chances that *S. haematobium* transmisson will occur. Therefore these climate variables increased the chances that lower prevalence rates will occur.

5.4.2 Ordered logistical regression analysis for *S. mansoni*

The regression analysis included the following five out of the nine temperature variables in the model: tmin1, tmin2, tmin3, tmax1 and tmax4. Average annual rainfall was included but total annual rainfall was excluded.

The log likelihood was -1299.09 for 1148 *S. mansoni* observations and $p < 0.05$. The LR(chi^2 (9) was 614.8 with all probabilities zero. Based on this model probability of each disease observation being on observed under these climate conditions is exp(-1299.0955/1148) = 0.323.

Since this figure is larger than 0.14 (1/7) and below one, the model has sufficient explanatory power (after Gould, 2002).

Positive correlations with disease observations were obtained with the following three variables:
1. average monthly rainfall (annual rainfall/12),
2. autumn minimum temperatures (March, April and May = tmin2) and
3. spring maximum temperatures (September, October and November = tmax4).
Thus, increases in average annual rainfall, minimum autumn temperatures and maximum spring temperatures favoured the chances of *S. mansoni* transmission. This means that autumn and spring temperatures were suitable for transmission and increased the chances of high prevalence rates.

Negative correlations with disease observations were obtained with the following three variables:
1. summer maximum temperatures (December, January and February = tmax1),
2. summer minimum temperatures (December, January and February = tmin1) and
3. winter minimum temperatures (June, July and August = tmin3).

Maximum and minimum summer temperatures and minimum winter temperatures decreased the chances of *S. mansoni* occurring. The model predicted that stable high temperatures were unsuitable for intestinal schistosomiasis transmission. Also, minimum temperatures in winter were too cold for transmission. These variables increased the chances of low prevalence rates.

These logistic equations for each disease model were used to interpolate the significant climate variables to obtain prediction maps. Autocorrelation was not performed for reasons given in Section 5.5.2 and in Chapter 6, Section 6.3.

5.5 PREDICTING SCHISTOSOMIASIS OCCURRENCE USING THE CLIMATE DATA OF HUTCHINSON *ET AL.* (1995)

By feeding back the derived models for *S. haematobium* and *S.mansoni,* into the climate data the probability of a cell in each image belonging to any one of the prevalence categories from 0 to 6 (Table 4.1) was determined. More importantly, it allowed the prediction of the prevalence of schistosomiasis where no disease data are available, taking into account the temperature and rainfall parameters used in this study. The results are depicted in map format (Figs. 5.9 and

5.10). There are seven outcome categories (Table 4.1) and the model predicted which category would occupy a cell in the climate images representing the model variables.

5.5.1 Predicted prevalence categories for urinary schistosomiasis

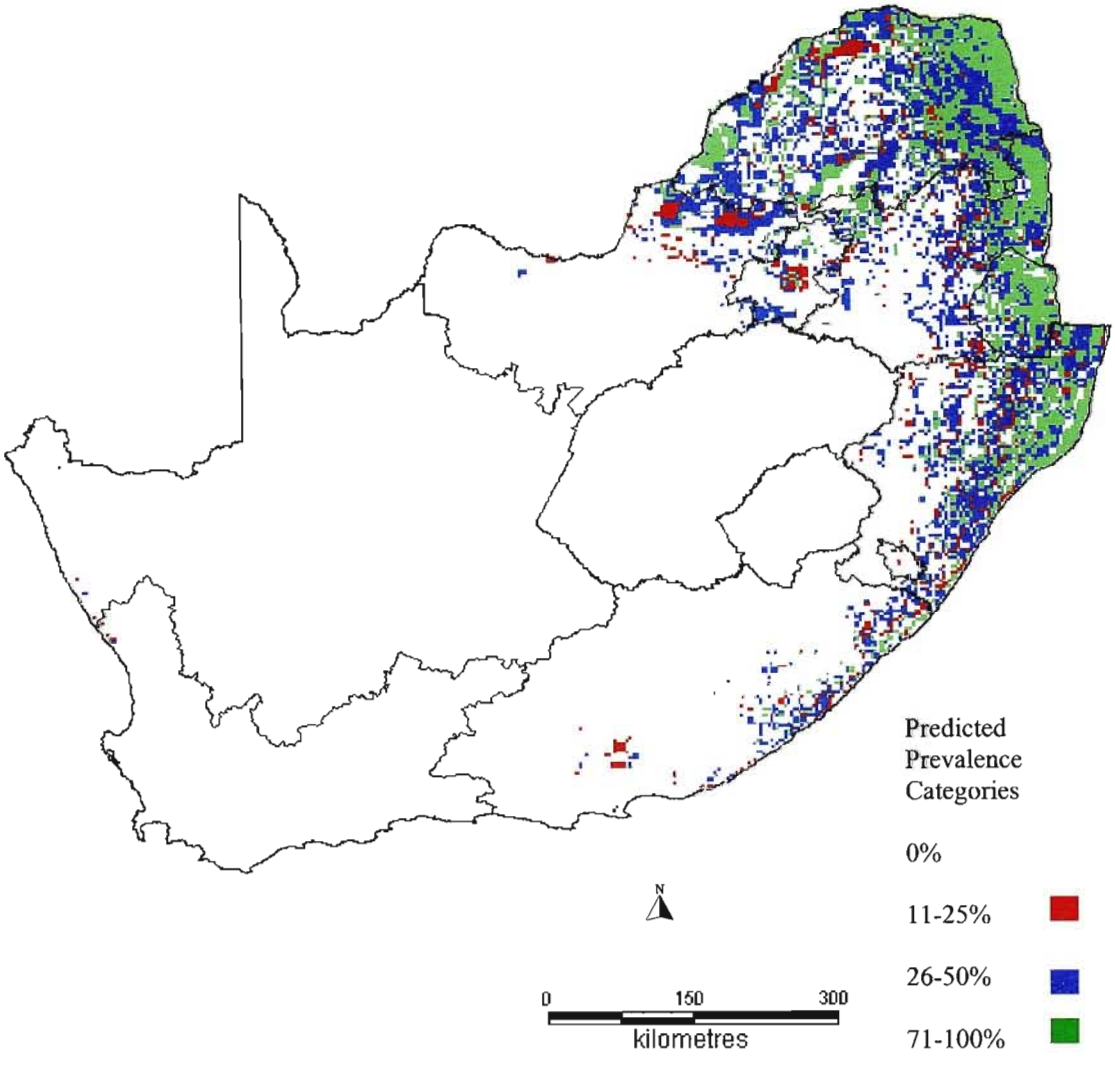

Figure 5.9: Predicted prevalence rates for *S. haematobium*

Four of the seven disease categories were included in the model as follows: 0%, 11-25%, 26-50% and 71 - 100% (Figure 5.9). The lower prevalence categories (below 10%) were excluded. High prevalence categories were predicted in the Limpopo Province, Mpumalanga, Gauteng, North-West Province, KwaZulu-Natal and Eastern Cape. The Free State was disease-free, while prevalence rates in the remaining Northern Cape and Western Cape Provinces were negligible.

5.5.2 Predicted prevalence categories for intestinal schistosomiasis

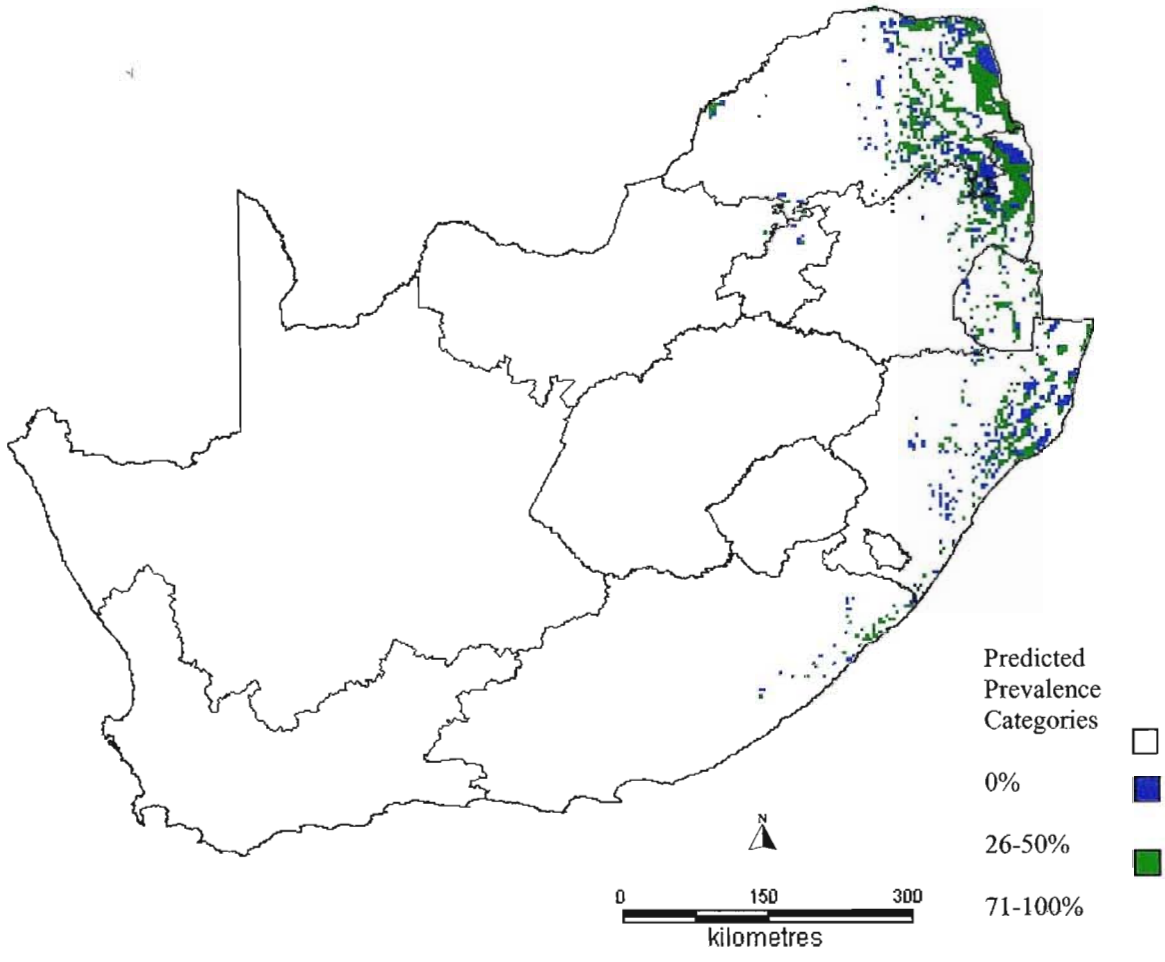

Figure 5.10: Predicted prevalence rates for *S. mansoni*

Three of the seven categories were included in the model, namely 0%, 26-50% and 71 -100% (Figure 5.10). The overall image for this species predicts that the greatest proportion of the country is not endemic for schistosomiasis given the prevailing temperature and rainfall patterns. The *S. mansoni* model predicted zero prevalence rates in Western Cape, Northern Cape, Free State, North -West province. Some areas within Gauteng and the Eastern Cape were also predicted to have schistosomiasis. Intestinal schistosomiasis was thus predicted mainly in Limpopo Province, Mpumalanga, Eastern Cape and KwaZulu-Natal.

The results for the statistical model were unexpected since only three and four out of seven prevalence categories were predicted for *S. mansoni* and *S. haematobium* respectively. These categories are also the ones with the greatest ranges, which explains to some extent why they were predicted so frequently.

It is emphasized that the ordered logistic regression model did not account for spatial correlations. This does not invalidate the model for prediction purposes, but caution should always be exercised when involving predictions outside the range of the data from which the model was derived.

It is important to note that these models utilise historical disease and climate data and as a result may differ from the present schistosomiasis situation. The models are conservative in that they take into account only temperature and rainfall. Nevertheless, the models developed for the purpose of this study represent a novel approach to studying the epidemiology of schistosomiasis in South Africa. They may also be applied over space (the whole country) and time (future scenarios). Thus, the results of this study provide a partial explanation for the occurrence of schistosomiasis within the country. Future work could include factors such as the availability of suitable water bodies, geomorphology, certain aspects of water chemistry, other temperatures variates like frost and chill units and normalised differentiation vegetation indices (NDVI, Appendix A).

5.6 COMPARISON OF OUTPUTS FOR *S. HAEMATOBIUM* USING CLIMATE DATA FROM HUTCHINSON *ET AL.* (1995) AND SCHULZE (1997)

S.mansoni is the more thermally sensitive of the two parasites, thus its occurrence is more difficult to predict than *S. haematobium*. For these reasons the *S. mansoni* model was excluded from the finer resolution Schulze (1997) dataset. The differences in the distributions of urinary and intestinal schistosomiasis were described in Chapter 2. Figure 5.11 illustrates the output after running the *S. haematobium* model using Schulze's (1997) data.

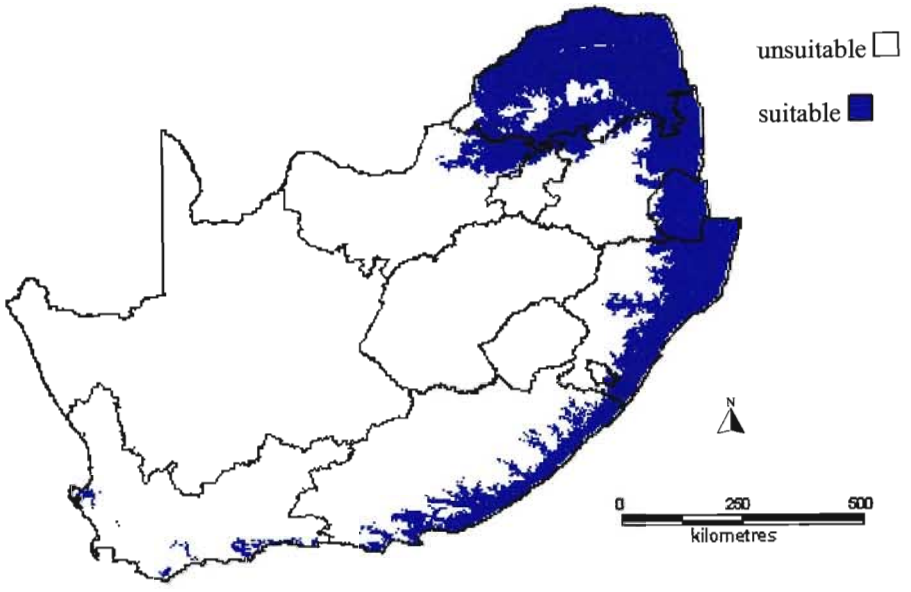

Figure 5.11: Output from running the *S. haematobium* temperature-suitability model listed in Table 4.3, with Schulze's (1997) climate dataset

5.6.1 Comparison of Hutchinson *et al.* (1995) and Schulze's (1995) Data

Cross- classification of these two climate datasets shows a 0.81 overall Kappa, indicating a close correlation but with differences observed in the North-west Province and Limpopo Province border (Figure 5.12). Idrisi®-based (Clarklabs, Worcester, MA) cross- classification of the maps derived from the *S. haematobium* model was then done and this produced a 0.84 Kappa ratio, which indicated a close correlation between the two climate datasets. Jekel, Elmore and Katz (1996) stated that a Kappa ratio over 80% indicates excellent agreement between the two datasets.

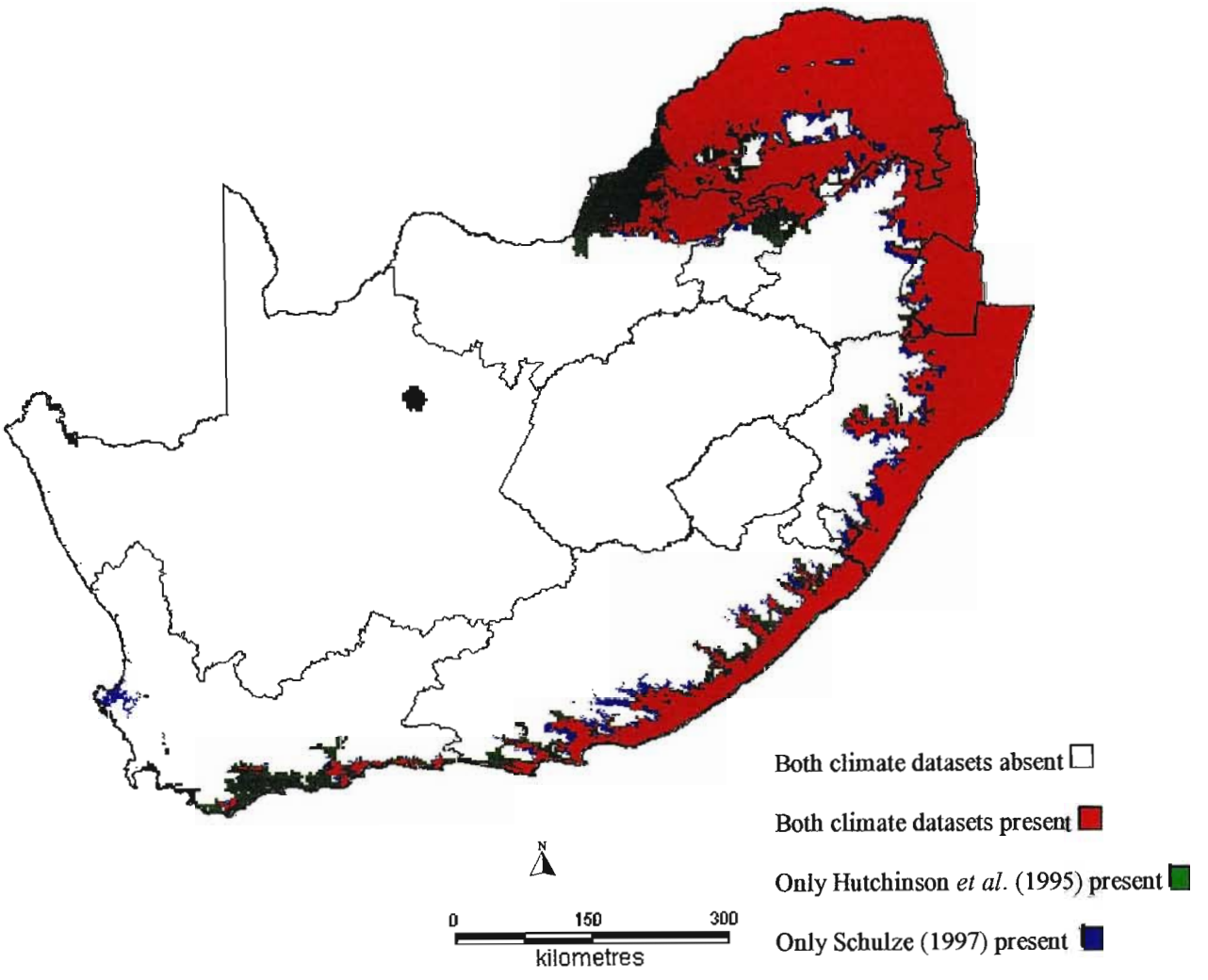

Figure 5.12: Comparison of Schulze's (1997) and Hutchinson *et al.* (1995) output from the temperature-suitability model for *S. haematobium*

5.6.2 Output from applying a predictive function to the regression analysis output using the Schulze (1997) dataset

The Schulze (1997) dataset predicted three disease categories, namely 0%, 11-25% and 26-50% (Figure 5.13), for *S. haematobium*. Using the Hutchinson *et al.* (1995) data included the category 71-100% in the prediction. Limpopo Province, North-West Province, Mpumalanga and KwaZulu-Natal could all expect prevalence rates of between 11 - 50%. The rest of the country was disease free. This shows the difference in running the model on climate data of different

spatial resolutions. It should be noted again that the models were constructed using the Hutchinson *et al.* (1997) dataset as reference climate data.

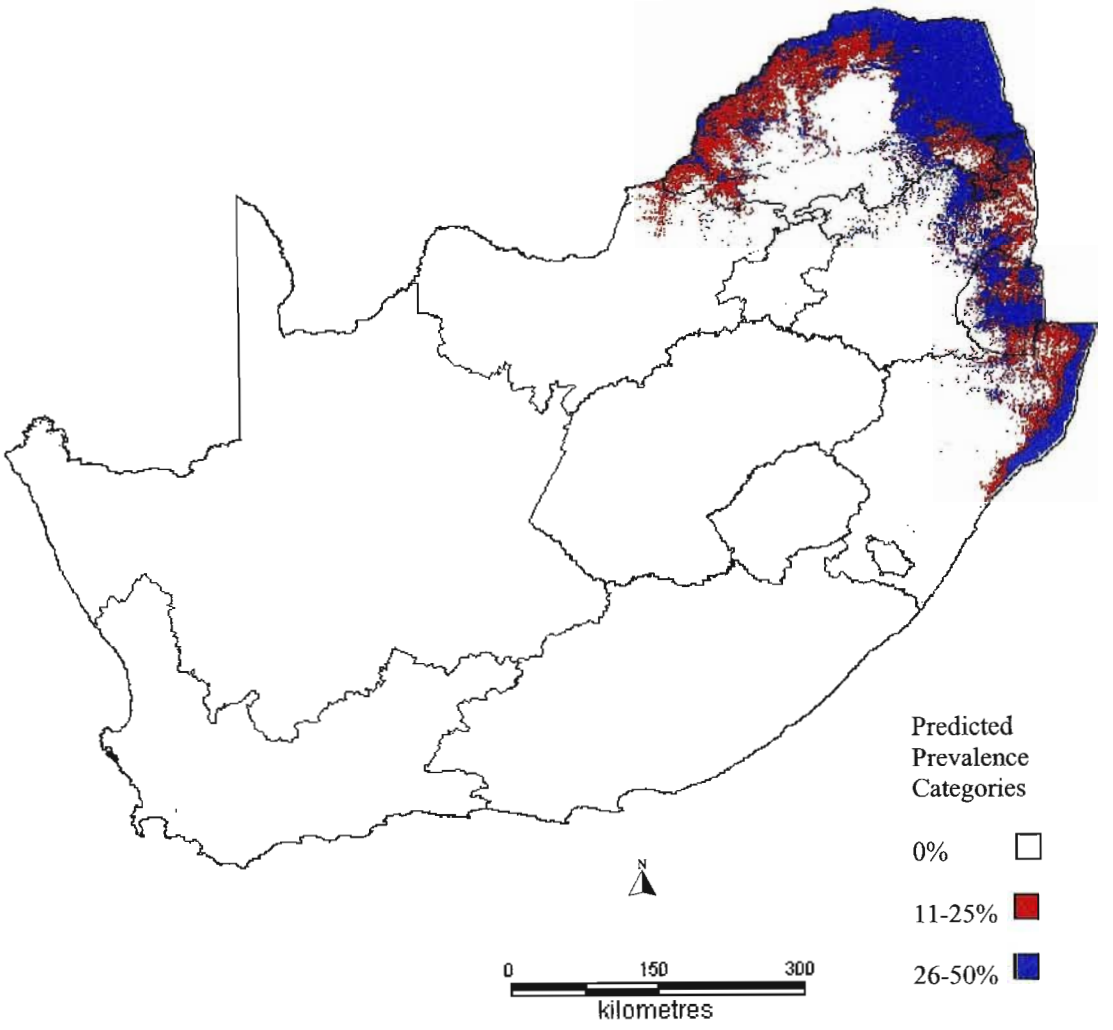

Figure 5.13: Output from running prediction model for *S. haematobium* using Schulze (1997) dataset

5.7 POPULATION ESTIMATES

The importance of obtaining meaningful population estimates for schistosomiasis was highlighted in Chapters 1 and 3 for two reasons. Firstly, mapping appropriate population data improves the value of the disease model to support the second reason, which is the lack of schistosomiasis data in the country. Population estimates were extracted from each of the two models for *S. haematobium.* Since the distribution of *S. mansoni* lies entirely within that of *S. haematobium* (compare Figs. 5.2 and 5.3), population estimates were extracted from the two

models developed for the latter disease (Figs. 5.5 and 5.9). These estimates are given in Tables 5.5 and 5.6.

The figures in Table 5.5 were generated by overlaying the two different population datasets with the two temperature-suitability models for *S. haematobium* derived from (1) Hutchinson *et al.* (1995) climate dataset (Fig. 5.5) and (2) the Schulze (1997) dataset (Fig. 5.11). Hence there were four permutations using the two different climate datasets and two different population datasets.

Table 5.5: Estimated numbers of school-age children living in temperature-suitable zone for *S. haematobium*

Source of Climate Data	Source of Population Data	
	Deichman (1995)	Census South Africa (1998)
Hutchinson *et al.* (1995)	4,102334	4,379079
Schulze (1997)	3,903734	4,258475

The figures in Table 5.6 were generated in the same way as Table 5.5 above but using the predictive model for S. *haematobium*. There were also four permutations using the two different climate and population datasets but for each of the predicted prevalence categories.

Table 5.6: Estimated numbers of school-age children living in areas where *S. haematobium* prevalence rates were predicted

Source of Climate Data	Disease Category (Gear *et al.*, 1980)	Source of Population Data	
		Deichman (1995)	**Census South Africa (1998)**
Hutchinson *et al.* (1995)	0%	7,133081	6,082782
	11-25%	540712	450960
	26-50%	1,878690	1,762356
	71-100%	983313	1,016863
Schulze (1997)	0%	9498609	8061849
	11-25%	347557	341476
	26-50%	660979	876927
	71-100%	28651	32710

5.8 CONCLUSION

The methods used in the present study allowed the spatial distribution of urinary and intestinal schistosomiasis to be defined in terms of temperature and rainfall in a disease model. Following this, new types of data analyses were performed using the historical schistosomiasis prevalence data collected by Gear *et al.* (1980) as shown with the population data extractions. The next chapter discusses the findings of this work in the context of schistosomiasis transmission.

CHAPTER SIX

General Discussion

6.1 INTRODUCTION

Schistosomiasis is an appropriate disease for which to develop spatial models because its transmission is closely linked with the environment. As discussed in Chapter 2, schistosomiasis transmission can only occur in places where suitable environmental conditions prevail.

Intra-molluscan parasite development and infection of the final human host continue through different seasons of the year but rates of transmission vary depending on these external environmental conditions. In Chapter 2 the importance of temperature and rainfall was highlighted in relation to those conditions that are either suitable or unsuitable for the growth and survival of both host snails and schistosomes. Both organisms exhibit varying degrees of tolerance for these variables but the levels that are suitable or unsuitable for their growth and reproduction can then be used as indicators of parasite occurrence and by inference, schistosomiasis transmission. Climate variables were used to establish indices for different geographical areas within the country, and consequently were particularly well-suited for computer mapping.

This work exploits the close environment–disease relationship to build the first GIS-based schistosomiasis model using national survey data in South Africa. The primary goal of using a GIS in this study was to develop methods for defining the spatial distribution of urinary and intestinal schistosomiasis in South Africa using climate variables. In spite of the prevalence data limitations discussed in Chapter 4, the available schistosomiasis dataset did lend itself to mathematical and spatial modelling. The process of disease modelling discussed in Chapter 3 is an iterative process. The model outputs in the present work provide new data and knowledge to formulate other models. During this process some decisions and choices have to be made about how the data will be manipulated, the type of spatial analysis to be used and the conclusions that need to be drawn from the results. Chapters 5 and 6 described the methods used including the decisions that were made and showed how the data were manipulated to formulate the models for *S. haematobium* and *S. mansoni*. Models such as this extend beyond the necessary exploratory analyses. The output can be used to inform decision makers for whom information

is limited due to schistosomiasis not being on the list of notifiable diseases in the country. The outputs are specific to the variables that were used in this work. The research results are discussed in this chapter.

6.2 SUMMARY OF RESEARCH RESULTS

6.2.1 Significance of the temperature- suitability maps

Pitchford's (1981) data had to be summarised into a logical format of conditional statements. Some difficulty was experienced in translating Pitchford's (1981) descriptions of the temperature parameters because they were not always clearly defined. It would therefore have been more useful if the data were presented in the form of a disease model with a conditional statement for each temperature regime. Nevertheless, this comprehensive published work provided a unique opportunity to use expert knowledge on the disease for deriving the temperature-suitability maps within a GIS. In addition, the work expressed the temperature and time relationship in the form of temperature regimes. Such temperature-time combinations are particularly relevant to biological processes as described in other GIS work done by Malone *et al.* (1997) and Bavia *et al.*, (1999) using ΔT. These studies were described in Chapter 3, Section, 3.2.3.

The temperature-suitability model for *S. haematobium* was derived using a very low temperature regime, namely, minimum temperatures of 1°C and colder for more than one month. Similarly for *S. mansoni* minimum temperatures below and including 3°C for a minimum of one month and 16^0C or more for a minimum of two months were used.

As mentioned earlier, these optimal map parameters did not correlate with the regimes identified as suitable by Pitchford (1981). However, Pitchford (1981) did state that Mdn 14.5°C for at least seven months and Mdn 14.5°C for five months were both suitable for successful completion of the intra-molluscan development phase of both parasites life-cycles. For the model purposes, the translation of "a minimum of four months" meant that the regime included nine months of data, and so it does take into account the above-mentioned suitable regimes at 14.5°C. The same applies to the regime for *S. mansoni*, 16°C or more for a minimum of two months means that the regime could last for 11 months. Recall Fig. 2.4 where minimum temperatures in schistosomiasis-endemic KwaZulu-Natal ranged from 6.5°C to about 16°C during the year.

Using Pflüger's (1980) formula for *S. mansoni* (y= 268 (14.5°C -14.2°C)), it would take 80.4 days at this temperature for cercariae to be shed, i.e three months. In Chapter 2 it was stated that during the cooler autumn and winter months in endemic areas, long schistosome incubation periods occur and parasite development rates slow down (Pitchford, 1981).

Differences in the duration of temperature regimes also render them suitable or unsuitable for transmission as was discussed in Chapter 2. The duration of a particular temperature regime affects the temperature tolerance limits of both the snail and parasite. If extreme low temperatures are short-lived then transmission will not be drastically affected although the development of the parasite larvae to the cercarial stage in the snails could be prolonged. If the snails are exposed to months of low temperatures they might not become infected at all or they could lose their infections (Stirewalt, 1954), although the latter is quite rare according to the literature.

Joubert *et al.* (1984) noted that such low temperatures were unlikely to occur in South Africa for long periods of time and Appleton (1975) concluded that temperatures at high altitude areas (>1000m) probably do not reach the lower critical limit for long enough to affect the rate of increase of *B. pfeifferi*. In field conditions, the interior parts of the country experience sub- zero temperatures, and from just above zero up to 6°C during winter (Schulze, 1997). Overall, mean minimum temperatures range from -6.4°C to 3.3°C during this time. Even during spring minimum values of -3.2°C occur in areas in KwaZulu-Natal. The schistosomes' free-living stages can survive at low temperatures but not the snails, and if the snails die before shedding cercariae, then transmission will not occur.

Also, the "unsuitable" temperature range of 14°C or more during December and January was included in the optimal maps. Relatively low temperature ranges are experienced along the east and south coasts of the country (Schulze, 1997). The highest ranges occur in a north-west/south east alignment from December to February, which is the middle of the summer transmission season. An important consideration is that the effects of temperature range may take some time to impact on schistosomiasis transmission.

An advantage of using a GIS for this type of suitability mapping is that any permutation of any geo-referenced variable can be obtained. This is useful for combining data layers that would be difficult or impossible to do otherwise. Pitchford (1981) found some overlap between unsuitable

and suitable temperature regimes, but he could not combine the temperature regimes and disease data in sufficient detail as the GIS has done in the present work.

Pitchford's suitable regimes were expected to correspond with the disease observations of Gear *et al.*, (1980) but they did not. Hence, scenario testing was performed using Pitchford's (1981) temperature parameters and the disease data obtained from the Atlas of Bilharzia (Gear *et al.*, 1980). The optimal maps for each parasite species were derived using only minimum temperature regimes. Since these regimes are not strictly conformed to in nature they may be said to represent the minimum temperature thresholds for schistosome transmission. This model helps to illustrate the ecological zones discussed in Chapter 2, and shows where both urinary and intestinal schistosomiasis can be found on the basis of the snail hosts' and schistosomes' thermal tolerance ranges. Brooker (2002) highlighted the need to develop separate models such as these within the context of an ecological zone for each snail-schistosome system.

The models were better at accounting for the presence of disease than its absence. One problem with this type of suitability mapping is the difficulty in distinguishing the difference between meaningful relationships and coincidental relationships. Therefore there is a need to link outputs with known experimental relationships as attempted here to introduce some external validity.

6.2.2 Significance of the regression analysis ouput

The results of the ordered logistic regression analyses allowed the relationship between temperature, rainfall and schistosomiasis to be determined. From this the description of seasonal associations and transmission could be defined clearly, i.e. those climate variables that favoured transmission and either high or low prevalence rates and those that did not. Both the favourable and unfavourable variables had to have sufficient explanatory power in the model in order to use them to make conclusions that can be generalized. The hypothesis that spring and summer temperatures as well as rainfall, would favour schistosomiasis transmission and hence increase the chances of high prevalence rates was not fully supported by the regression models for *S. haematobium* and *S. mansoni*. There were different associations for the different species and these are discussed in this section.

In Chapter 2 several studies showing that cercarial shedding and transmission of schistosomiasis follows a seasonal pattern were described (Pflüger *et al.*, 1984; Pitchford, 1981, 1986; Pitchford and Visser, 1969). The regression model showed that both spring and autumn temperatures, and annual rainfall were favourable for *S. haematobium* transmission and were associated with high

prevalence rates. Summer and winter temperatures were associated with low *S. haematobium* prevalence rates. For *S. mansoni,* somewhat different results were obtained. Average monthly rainfall, autumn temperature minima and spring maxima improved the chances of *S. mansoni* infection. Although Stirewalt (1954) observed declining *S. mansoni* infection rates in spring in Puerto Rico, Pitchford and Visser (1962, 1969) found that spring temperatures improved *S. mansoni* transmission in South Africa. Pitchford (1986) observed that transmission of South African *S. mansoni* monitored by rodent immersion, either began or increased significantly during September (spring). Sharp transmission peaks were also recorded in autumn. *S. mansoni* is more sensitive to fluctuations in temperature than *S. haematobium* and this limits its distribution.

Pitchford (1981) observed that *B. africanus* group snails died before cercarial shedding after being exposed to miracidia in autumn and winter but Shiff (1964b) found *B. globosus'* survival improved as autumn approached. Pitchford (1986) found that *S. haematobium* cercariae emerged during late spring (Pitchford, 1986). The warmer spring temperatures are more suitable for transmission than the winter temperatures, which the results of the present study confirm. During winter apparently no cercarial shedding of *S. haematobium* occurred (Pitchford, 1981; 1986). Hence even if the snails survive the low winter and autumn temperatures the development of the miracidia to cercariae in the snails is prolonged during this time. Pitchford (1981) found the parasite incubation periods to be longest in April, May (autumn) and June (winter) in endemic Nelspruit. Eggs are released between November and May which corresponds to two seasons of the year namely, summer and autumn (Shiff, 1964b).

During summer transmission does occur, with December and January being the middle of the transmission season (Pitchford, 1981; 1986). However, hot temperatures are more detrimental to snails than the parasites. The optimal temperature for the *B. africanus* group snails was previously shown to be 25°C. Higher temperatures of >34°C occur in Limpopo Province (35.3°C,) in mid-summer which the snails would not be able to tolerate. KwaZulu-Natal experiences a mean maximum temperature of 27°C during summer. Where the southerly limit of the disease occurs in the Eastern Cape province, temperature in excess of 27°C are experienced although this is not common. During Summer Stirewalt (1954) observed declining *S. mansoni* infection rates in Puerto Rico, which corresponds with the present work's results that the hot South African summer temperatures contributed to low prevalence rates.

In this work negative associations were obtained for increasing summer and decreasing winter temperatures, implying that extreme cold and heat produce low prevalence rates. These results therefore imply that moderately high and moderately low temperatures are more suitable for schistosomiasis transmission than the extremely hot and cold temperatures experienced during summer and winter. These findings correspond with other authors' observations which showed that the schistosomes and snails do not tolerate extreme temperatures well (Pitchford, 1981;1986; Shiff, 1964b). In Chapter 2 it was shown that prolonged periods of low temperatures as experienced in winter do not support snail and schistosome growth and reproduction as effectively as warmer temperatures do.

Furthermore, the model supported the hypothesis that rainfall correlates positively with transmission. Specifically, increasing annual rainfall increased the likelihood of transmission of *S. haematobium* in the model while increasing the average monthly rainfall increased the likelihood of *S. mansoni* transmission. There are few published data on the effects of rainfall on schistosomiasis transmission and these are compared with the present findings.

O' Keeffe (1985a) found reproductive peaks in the *B. globosus* population just after heavy rainfall in April, August, May and November. However, large amounts of unseasonal rain that occurred during cooler months produced the best conditions for these snails to survive (O' Keeffe, 1985a), suggesting the importance of the effects of annual rainfall over seasonal rainfall. Total annual rainfall can be used as an indication of the cumulative rainfall over the course of one year. The mean annual rainfall decreases from the eastern to the western parts of the country. The eastern parts of the country where mean annual rainfall is highest, are also schistosomiasis-endemic.

In this work, average monthly rainfall was positively correlated with *S. mansoni* observations, but not total annual rainfall as with the *S. haematobium* model. In Chad, Brooker *et al.* (2002b) found that mean land surface temperature and rainfall were significantly associated with *S. haematobium* infections in school children. In Brazil, a different result was obtained for *S. mansoni* where annual dry period was used as a variable. Bavia *et al.* (1999) found that the duration of the annual dry period was a significant determinant in the prevalence of *S. mansoni* infection in Bahia. Neither maximum rainfall nor total precipitation, were significant factors in their disease model.

Biomphalaria pfeifferi occurs in stable, permanent, slow-flowing waters or standing (lentic) waters (Brown, 1994) so a steady quantity (average for the area) of rainfall over a given period would support its survival better than the cumulative effect of rainfall during this time. This supports the finding in the present work that increasing average monthly rainfall supports *S. mansoni* transmission. The influence of water and rainfall has been discussed in detail in Chapter 2, but if a snail aestivates during a dry period, it will emerge when water is available again. In drier parts of the country, small water bodies will dry up if there is little rain on a monthly basis.

Bulinus africanus colonises both stable waterbodies as well as unstable, newly formed water bodies and are hence able to survive in a relatively harsher water environment than *B. pfeifferi*. During the course of a year, an area may have heavy rains or below-average rainfall. Some provinces in South Africa experience about the same rainfall each month of the year whilst others experience heavy rains concentrated in few months and almost none in others. Limpopo Province and Northern Cape can experience concentrated rainfall in a single month. An even spread of rainfall throughout the year occurs in Eastern Cape and Western Cape. Most of the country and certainly the schistosomiasis- endemic areas experience summer rainfall except for the southern coastal areas where rain falls all year round. As was shown in Chapter 2, rainfall is more predictable in the east than it is in the west.

6.3 RECOMMENDATIONS

As stated earlier in this chapter, new models may be formulated from the experience gained through this work. Although the present findings in relation to annual rainfall and average monthly rainfall are useful, it may have been better to group the rainfall data seasonally as was done with the temperature data. This would have allowed the association between disease occurrence and seasonal rainfall variations to be examined in detail.

It is known that people's water-related activities increase during summer. This can be used as a variable that improves the chances of schistosomiasis infection. Saathof *et al.* (2002) found a positive association between the washing of clothes and respondents' water usage with *S. haematobium* infection. However, these authors found a surprising negative association between swimming and contact with water and explained that the survey was conducted in the cooler winter months, which meant that people were not swimming as much as they would have in

summer. In relation to these results, the *S. haematobium* model would be improved if these behavioural factors were included.

The disease models derived from the regression model are thus conservative because they use only two climate variables to model the disease. While this is true, it makes for a good starting point for further analyses to include the effects of sanitation, water-related activities and snail data. An additional component would be to incorporate snail data into the model, but this was beyond the scope of this project.

Another shortcoming of the ordered logistic regression model in terms of its applicability for spatial analyses is that it does not account for spatial autocorrelation. The reason for this shortcoming is that the categorical nature of the disease data, i.e. the use of prevalence categories instead of actual prevalence data by Gear *et al.* (1980) restricted the type of statistical method that could be used. Enquiries as to the availability of the sample sizes found that these data are no longer available. As mentioned in Chapter 3, spatial autocorrelation characterises the way the disease observations are distributed in space, and measures the degree of influence of one observation over its neighbours. If the positive disease observations lie adjacent to other positive disease observations on the map then the pattern would show positive spatial autocorrelation. Rainfall is an example of spatial auto-correlation as the rainfall monitored at one station is likely to be similar to that a few kilometres away, but probably less similar to the rainfall measured 500 km away.

As mentioned earlier, there are inherent limitations in the regression model due to lack of data on schistosomiasis in South Africa, as well as the available analytic software tools to appropriately handle what are available. If average prevalence rates from districts or localities are used to estimate the rates in endemic areas, the finer distribution of the data will be obscured (Utroska *et al.*, 1989). Therefore it is important to consider the focality of the disease. Another method, classification and regression analysis (CART) would have been better for categorical data analysis but this software is not freely available.

An important but often difficult part of a disease model is assessing its applicability and validity, especially if its outputs are to be used for disease control. A recent article by Brooker, *et al.* (2002a) showed that tools from ecology (e.g. receiver-operator characteristic analysis) could be used to assess the spatial limits, predictive performance and practical application of predictive disease models. For instance, data collected from sites other than those used in

disease model development are used to assess the validity of the model (Brooker *et al.*, 2002a). The type of spatial analysis described in the present study has not been done before for schistosomiasis in South Africa. This, together with the lack of updated survey data made it difficult to assess the predictive performance of the regression models and further refine them during this study.

Future work involving predictive disease modelling of schistosomiasis in South Africa should pay due attention to appropriate sampling design and spatial scales to ensure that their outputs can be applied and tested for practical control objectives (Brooker *et al.*, 2002a). However, within these limitations, the disease predictions were matched with the climate at sites where the disease is known to exist, making use of detailed and reliable meteorological images. Prevalence rates of 0% 11-25%, 26-50% and 71-100% were predicted with the highest probability according to the model for *S. haematobium.* Five provinces in the eastern parts of the country have the highest urinary schistosomiasis prevalence categories. For *S. mansoni* prevalence rates of 0%, 26-50% and 71 to 100% were predicted with the highest probability in five provinces. However, the map for *S. mansoni* shows the disease distribution to be more patchy than for *S. haematobium.*

The above discussion raises the nature of data as an important issue in the use of GIS in disease modelling. At all times the data that are used have a direct impact on the types of models that are built. In addition proper formatting of data will maintain their integrity and improve the chances of the model reflecting reality. Aside from that, GIS opens up a new world for applying epidemiological concepts but there is a need to maintain a balance between what appears on a map on screen and what makes biological sense. The GIS is simply a tool that is only as effective as the manner in which it is used for data descriptions and problem solving.

6.4 POPULATION ESTIMATES

The models were used to derive population estimates, which may be used to supplement the current schistosomiasis data deficit. A discussion of the population estimates for endemic areas of South Africa derived from the temperature-suitability model is included in Appendix D. The estimates lie between 3.9 million and 4.3 million using the different climate models and population estimates. A similar calculation for the prediction maps showed far higher estimates per *S. haematobium* prevalence category. The Hutchinson *et al.* (1995)-Deichman (1995) model estimated that just less than half a million children (983 313) live in the highest prevalence area.

The Hutchinson *et al.* (1995)-Census South Africa (1998) model estimated higher numbers of children (> 1million) for the same category. However, large differences were obtained for this category with the finer resolution (Schulze, 1997) climate data. The Schulze (1997)-Deichman (1995) model estimated that 28651 children were living where high prevalence rates, while the Schulze (1997)-Census South Africa (1998) model estimated 32710 children in these areas.

These figures illustrate the different results that may be obtained using data of different resolutions. In addition, the study used climate variables as surrogates to determine their "suitability" or "unsuitability" for transmission in an area. The study assumes that all children living in the suitable areas have the same exposure levels, when in fact the range in exposure levels could be large. Large spatial area analysis such as the one used here, makes it more difficult to apply the conclusions drawn from grouped data to each individual in the study. It is also important to consider the ecological fallacy that assumes that the exposure to disease in a group is the same as that in individuals (Joubert and Katzenellenbogen, 1999). However the nature of schistosomiasis transmission is such that groups of children are more likely to be infected than individuals in an endemic area. Thus, it is safe to assume homogenous exposure to infection.

Utroska *et al.* (1989) used the average population at risk and the average prevalence rate (17.5%) for South Africa to derive the population infected using the equation: population at risk x prevalence (%) = population infected. These authors went further to estimate the total amount of praziquantel needed to treat this number of people. That figure was calculated to be 3 150 000 tablets for 1 575 000 children under 15 years (Utroska *et al.*, 1989). The fact that the disease data used in this thesis are in prevalence categories presents difficulties in applying the formula of Utroska *et al.* (1989) to estimate the number of children infected. However, mean prevalence rates may be obtained from the prevalence categories and if one were to apply the Schulze (1997)- Census (1996) model, the result is 32710 x 85 % (mean of 71-100% expected) = 2,780 350 children infected. This figure is just less than double the estimate of Utroska *et al.* (1989) given above. An important additional point is that the population estimates do not take into account the effect of AIDS morbidity and mortality. Statistics South Africa have adjusted their mortality estimates to include the effect of HIV/AIDS in the population statistics. For instance, the total population of the country without taking HIV/AIDs- related deaths into account is 44 560 644, compared to 44 328 322 taking additional deaths due to HIV/AIDS into account (Statisitics SA, 2001). Hence the implied deaths due to HIV/AIDs is 232 321.

6.5. CONCLUSION

The population estimates indicate that schistosomiasis is very much a disease of the present, given the climate variables used in the study. The application of GIS has potential for effective use in schistosomiasis epidemiology and research to study the diseases distribution and their determinants. It is useful for planning and costing control programmes. The technology can also be used for comparative epidemiological studies with other diseases. The output can be used and made easily accessible to supply the Department of Health's Primary Health Care Norms and Standards with updated information.

To conclude this work constructed two GIS based models for schistosomiasis in South Africa and demonstrated the usefulness of spatial analysis. The first, temperature-suitability model related the distribution of urinary and intestinal schistosomiasis to temperature where they occur and the results are presented in map format. This model is currently more useful than the regression model for practical purposes. However, within its limitations, the regression model assessed the relationships between seasonal variations in temperature as well as rainfall, and the likelihood of disease occurrence.

REFERENCES

Anon. 2002a. Strategic Directions for Research. Schistosomiasis, disease burden and epidemiological trends. *The Special Programme for Research and Training in Tropical Diseases.* 6 pgs. http://www.who.int/tdr

Anon. 2002b. *The Primary Health Care Package for South Africa – a set of norms and standards*. Department of Health, Pretoria. 87 pgs.

Appleton, C.C. 1975. The influence of stream geology on the distribution of the bilharzia snails, *Biomphalaria pfeifferi* (Krauss) (Mollusca: Pulmonata). *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 71: 140-143.

Appleton, C.C. 1976a. Geographical factors that affect the distribution of schistosomiasis. In: Gear, J. H. S. [ed]. *Medicine in a Tropical Environment. Proceedings of the International Symposium, South Africa.* A. A. Balkema, Cape Town. 678-688.

Appleton, C.C. 1976b. Observations on the thermal regime of a stream in the Eastern Transvaal, with reference to certain aquatic Pulmonata. *South African Journal of Science*. 72: 20-23.

Appleton, C.C. & Stiles, G. 1976. Geology and geomorphology in relation to the distribution of snail intermediate hosts in South Africa. *Annals of Tropical Medicine and Parasitology*. 70: 190-197.

Appleton, C.C. 1977a. The influence of above-optimal constant temperatures on South African *Biomphalaria pfeifferi* (Krauss) (Mollusca: Pulmonata). *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 71: 140-143.

Appleton, C.C. 1977b. The influence of temperature on the life-cycle and distribution of *Biomphalaria pfeifferi* (Krauss, 1848) in south-eastern Africa. *International Journal for Parasitology*. 7: 335-345.

Appleton, C.C. 1978. Review of literature on abiotic factors influencing the distribution and life-cycles of bilharziasis intermediate host snails. *Malacological Review*. 11: 1-25.

Appleton, C.C. 1984. Schistosome dermatitis: an unrecognised problem in South Africa. *South African Medical Journal*. 65: 467-469.

Appleton, C.C. & Eriksson, I.M. 1984. The influence of fluctuating above-optimal temperature regimes on the fecundity of *Biomphalaria pfeifferi* (Mollusca: Planorbidae). *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 78: 49-54.

Appleton, C.C. 1985. Molluscicides in bilharziasis control - the South African experience. *South African Journal of Science*. 81: 356-360.

Appleton, C.C. 1993. Potential role for rice paddies in the introduction of *Schistosoma mansoni* to north-eastern KwaZulu-Natal, South Africa. *Unpublished data.*

Appleton, C.C. & Kvalsvig, J.D. 1994. Compiling an atlas of parasitism for Natal Province, South Africa. In: Ozcel, M.A. & Alkan, M.Z. [eds]. *Abstract of the 8th International Congress of Parasitology,* Izmir, Turkey. pg 355.

Appleton, C.C., Sharp, B.L. & Le Sueur, D. 1995. Wetlands and water-related parasitic diseases of man in southern Africa. In: Cowan, G. I. [ed]. *Wetlands of Southern Africa,* Department of Environmental Affairs and Tourism, Pretoria. 227- 246.

Appleton, C.C. 1996. *Freshwater Molluscs of Southern Africa.* University of Natal Press. Pietermaritzburg. 64 pgs.

Appleton, C.C. 1997. *Biomphalaria pfeifferi, Schistosoma mansoni* and the coastal plain of south-eastern Africa. *Unpublished data.*

Appleton, C.C. 2002. A new southern limit for *Schistosoma haematobium* in Africa. *African Snail News.* 13-14: 1.

Esri International. USA. Arcinfo.1995-2002. http:// www.esri.com

Bailey, T.C. & Gatrell, A.C.1995. *Interactive Spatial Analysis*. Longman Group Limited. Addison and Wesley, England. 413 pgs.

Bavia, M.E., Hale, L.F., Malone, J.B., Braud, D.H. & Shane, S.M. 1999. Geographic information systems and the environmental risk of schistosomiasis in Bahia, Brazil. *American Journal of Tropical Medicine and Hygiene*. 60: 566- 572.

Bayne, C.J. & Loker, E.S. 1987. Survival within the snail host. In: Rollinson, D. & Simpson, A.J.G. [eds]. *TheBiology of Schistosomes, from Genes to Latrines*. Academic Press, London. 321-339.

Beasley, M., Brooker, S., Ndinaromtan, M., Madjiouroum, E.M., Baboguel, M., Djenguinabe, E. & Bundy D.A. 2002. First nationwide survey of the health of school children in Chad. *Tropical Medicine and International Health*. 7: 625 - 630.

Beck, L.R. Wood, B.L. & Dister, S.W. 1995. Remote sensing and GIS: new tools for mapping human health. *Geographic Information Systems*. 5: 32-37.

Blankespoor, H.D.B.S.M. & Blankespoor, C.L. 1989. Influence of temperature on the development of *Schistosoma haematobium* in *Bulinus truncatus*. *Journal of Medical and Applied Malacology*. 1: 123-131.

Boelaert, M., Arbyn, M. & Van der Stuyft, P. 1998. Geographical information systems (GIS): gimmick or tool for health district management. *Tropical Medicine and International Health*. 3: 163-165.

Breslow, N.E. 2000. Statistics. *Epidemiologic Reviews*. 22: 126-130.

Briggs, D. J. & Elliott, P. 1995. The use of geographical information systems in studies on environment and health. *World Health Statistics Quarterly*. 48: 85-94.

Brooker, S., Rowlands, M., Haller, L., Savioli, L. & Bundy, D.A.P. 2000. Towards an atlas of human helminth infection in sub-Saharan Africa: the use of geographical information systems (GIS). *Parasitology Today*. 16: 303-307.

Brooker, S., Hay, S.I., Issae, W., Hall, A., Kihamia, C.M., Lwambo, N.J., Wint, W., Rogers, D. & Bundy, D.A.P. 2001. Predicting the distribution of urinary schistosomiasis in Tanzania using satellite sensor data. *Tropical Medicine and International Health*. 6: 998-1007.

Brooker, S. 2002. Schistosomes, snails and satellites. *Acta Tropica*. 82: 207-214.

Brooker, S., Hay, S.I. & Bundy, D.A.P. 2002a. Tools from ecology: useful for evaluating infection risk models? *Trends in Parasitology*. 18: 70-74.

Brooker, S., Beasley, M., Ndinaromtan, M., Madjiouroum, E.M., Baboguel, M., Djenguinabe, E., Hay, S.I. & Bundy, D.A.P. 2002b. Use of remote sensing and a geographical information system in a national helminth control programme in Chad. *Bulletin of the World Health Organisation*. 80: 783-789.

Brown, D.S. 1966. On certain morphological features of *Bulinus africanus* and *B. globosus* and the distribution of these species in south-eastern Africa. *Annals of the Natal Museum*. 18: 401-415.

Brown, D.S. 1994. *Freshwater Snails of Africa and their Medical Importance*. Taylor and Francis, London. Revised 2nd edition. 608 pgs.

Census South Africa. 1998. Statistics SA.

Chrisman, N. 1997. *Exploring Geographic Information Systems*. John Wiley and Sons, New York. 298 pgs.

Clarke, K.C., McLafferty, S.L. & Tempalski, B.J. 1996. Perspectives on epidemiology and geographic information systems: a review and discussion of future directions. *Emerging Infectious Diseases*. 2: 85-92. http://www.cdc.gov/ncidod/eid/vol2no2/clarke.htm

Clarklabs. Idrisi 32. 1999. The Idrisi Project. Worcester, MA. http://www.clarklabs.org

Coggon, D., Rose, G. & Barker, D.J.P. 1997. *Epidemiology for the Uninitiated*. 4th edition. British Medical Journal Publishing Group, London. http://bmj.com/collections/epidem/epid.shtml

Cooppan, R.M., Bhoola, K.D & Mayet, F.G. 1984. Schistosomiasis and bladder carcinoma in Natal. *South African Medical Journal*. 6: 841-843.

Coppock, J.T. & Rhind, D.W. 1991. The history of GIS. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1*: *Principles*. Longman Group, Essex. 21-43.

Cross, E.R. & Bailey, R.C. 1984a. Predicting areas endemic for schistosomiasis using weather variables and a Landsat database. *Military Medicine.* 149: 542-544.

Cross, E.R. & Bailey, R.C. 1984b. Prediction of areas endemic for schistosomiasis through use of discriminant analysis of environmental data. *Military Medicine.* 149: 28-30.

de Kock, K.N. 1973. Die bevolkingsdinamika van vyf medies en veeartsenykundig belangrike varswaterslakspesies onder toestande van beheerde temperatuur. D.Sc. thesis. Potchefstroom University vir. C.H.O, Potchefstroom, South Africa.

de Kock, K.N. & van Eeden, J.A. 1986. Effect of programmed circadian temperature fluctuations on population dynamics of *Biomphalaria pfeifferi* (Krauss). *South African Journal of Zoology.* 21: 28-32.

Deichman, U. 1995. *Africa population database*. http://grid2.cr.usgs.gov/globalpop/africa/

DeWitt, W.B. 1955. Influence of temperature on penetration of snail hosts by *Schistosoma mansoni* miracidia. *Experimental Parasitology*. 4: 271-276.

Dilraj, A. & Abdool Karim, S.S. 1999. Common approaches in epidemiology: disease surveillance. In: Katzenellenbogen, J.M., Joubert, G. & Abdool Karim, S.S. *Epidemiology. A Manual for South Africa*. Oxford University Press, Cape Town, South Africa. 140-146.

Doenhoff, M.J. 2002. Resistance of *Schistosoma mansoni* to praziquantel: is there a problem? *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 96: 465- 469.

Doherty, J.G., Moody, A.H. & Wright, S.G. 1996. Lesson of the week: Katayama fever: an acute manifestation of schistosomiasis. *British Medical Journal*. 313: 1071-1072.

Donnelly, F.A., Appleton, C.C. & Schutte, C.H.J. 1983. The influence of salinity on certain aspects of the biology of *Bulinus* (*Physopsis*) *africanus*. *International Journal for Parasitology*. 13: 539-545.

Donnelly, F.A., Appleton, C.C. & Schutte, C.H.J. 1984a. The influence of salinity on the cercariae of three species of *Schistosoma*. *International Journal for Parasitology*. 14: 3-21.

Donnelly, F.A., Appleton, C.C. & Schutte, C.H.J. 1984b. The influence of salinity on the ova and miracidia of three species of *Schistosoma*. *International Journal for Parasitology*. 14: 113-120.

Donnelly, F.A., Appleton, C.C. Begg, G.W. & Schutte, C.H.J. 1984c. Bilharzia transmission in Natal's estuaries and lagoons: fact or fiction? *South African Journal of Science*. 80: 455-460.

Doumenge, J.P., Mott, K.E., Cheung, C., Villenave, D., Chapuis,O., Perrin, M.F. & Reaud-Thomas,G. 1987. *Atlas of the Global Distribution of Schistosomiasis*. Talence, CEGET-CNRS, Geneva, OMS/WHO. 400 pgs.

Elliot, P., Cuzick, J., English, D. & Stern, R. 1996. *Geographical and Environmental Epidemiology, methods for small- area studies.* Oxford University Press, Oxford. 382 pgs.

Engels, D., Chitsulo, L., Montressor, A & Savioli, L. 2002. The global epidemiological situation of schistosomiasis and new approaches to control and research. *Acta Tropica*. 82: 139-146.

Farid, Z. 1993. Schistosomes with terminal spined eggs: pathological and clinical aspects. In: Webbe, G., Sturrock, R.F. & Jordan, P. [eds]. *Human Schistosomiasis*. CAB International, Oxon, UK. 159-194.

Fincham, J. 2001. Helminths, HIV/AIDS and Tuberculosis. *AIDS Bulletin,* 10. http://www.mrc.ac.za/aids/dec2001/helminths.htm

Flowerdew, R. 1991. Spatial Data Integration. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1*: *Principles*. Longman Group, Essex. 375-387.

Frank, G.H. 1966. The effect of temperature on the rate of development and emergence of schistosome cercariae. *Zoologica Africana*. 2: 211-221.

Frank, A.U. & Mark, D.M. 1991. Language Issues for GIS. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1: Principles*. Longman Group, Essex. 146-163.

Fripp, D.J. 1979. *An Introduction to Human Parasitology with reference to Southern Africa*. 2nd edition. Macmillan, Johannesburg, South Africa. 168 pgs.

Gettinby, G., Revie, C.W. & Forsyth, A.J. undated. Modelling: a review of systems and approaches for vector-transmitted and other parasitic diseases in developing countries. http://www.fao.org/wairdocs/ilri/x5441e/xf551e0a.htm. 39 pgs.

Gatrell, A.C. 1991. Concepts of Space and Geographical Data. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1: Principles*. Longman Group, Essex. 119-134.

Gear J.H.S. & Pitchford R.J. 1979. *Bilharzia in South Africa*. Department of Health, Pretoria, South Africa. 36 pgs.

Gear, J.H.S., Pitchford, R.J. & van Eeden, J.A. [eds]. 1980. *Atlas of Bilharzia in South Africa*. Joint publication by the South African Institute for Medical Research, South African Medical Research Council & Department of Health, Johannesburg, South Africa.

Glass, G.E. 2000. Update: spatial aspects of epidemiology: the interface with medical geography. *Epidemiologic Reviews*. 22: 136- 139.

Gould, W. 2002. Logistic regression and ologit interpretation in Stata library, StataList newsgroup. Stata Corporation. http://www.ats.ucla.edu/stat/stata/library/logit_wgould.htm

Grant, A.D. & de Cock, K.M. 2001. HIV infection and AIDS in the developing world. *British Medical Journal*. 322: 1475-1478.

Gryseels, B., Mbaye, A., De Vlas, S.J., Stelma, F.F., Guisse, F., Van Lieshout, L., Faye, D., Diop M., Ly A., Tchuem-Tchuente, L.A., Engels, D. & Polman K. 2001. Are poor responses to praziquantel for the treatment of *Schistosoma mansoni* infections in Senegal due to resistance? An overview of the evidence. *Tropical Medicine and International Health.* 6: 864-873.

Gundel, H. & Hermann, F. 2002. HIV infection and tropical parasitic diseases: deleterious interactions in both directions? *Tropical Medicine and International Health.* 7: 479-488.

Haines, A., McMichael, A.J. & Epstein, P.R. 2000. Environment and health: 2. global climate change and health. *Canadian Medical Journal.* 163: 729-734.

Hamer, M.L. and Appleton, C.C. 1991. Physical and chemical characteristics and phyllopod fauna of temporary pools in north-eastern Natal, Republic of South Africa. *Hydrobiologia.* 212: 95-104.

Higley, L.G., Pedigo, L.P. & Ostlie, K.R. 1986. DEGDAY: A program for calculating degree-days and assumptions behind the degree-day approach. *Environmental Epidemiology.* 15: 999-1017.

Hulme, M. 1996. [ed]. *Climate Change and Southern Africa*: an exploration of some potential impacts and implications in the SADC region. WWF International and Climate Research Unit, University of East Anglia, Norwich, UK. 104 pgs.

Hutchinson, M.F.H.A., Nix, H.A., McMahon, J.P. & Ord, K.D. 1995. Africa - a topographic and climatic database, CD-ROM. 1st edition. Centre for Resource and Environmental Studies, Australian National University, Canberra, ACT 0200, Australia.

Jackson, M.J. & Woodsford, P.A. 1991. GIS Data Capture Hardware and Software. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1: Principles*. Longman Group, Essex. 239-249.

Jekel, J.F., Elmore, J.G. & Katz, D.L. 1996. *Epidemiology, Biostatistics and Preventive Medicine*. W.B. Saunders Company, Philadelphia. 297 pgs.

Jones, K. & Moon, G. 1987. *Health, Disease and Society*. Routledge and Kegan Paul, London. 256 pgs.

Jordan, P. & Webbe, G. 1982. *Schistosomiasis: epidemiology, treatment and control*. William Heinemann Medical Books, London. 361 pgs.

Joubert, P.H., Pretorius, S.J., de Kock, K.N. & van Eeden, J.A. 1984. The effect of constant low temperatures on the survival of *Bulinus africanus* (Krauss), *Bulinus globosus* (Morelet) and *Biomphalaria pfeifferi* (Krauss). *South African Journal of Zoology*. 19: 314-316.

Joubert, P.H., Pretorius, S.J., de Kock, K.N. & van Eeden, J.A. 1986. Survival of *Bulinus africanus* (Krauss), *Bulinus globosus* (Morelet) and *Biomphalaria pfeifferi* (Krauss) at constant high temperatures. *South African Journal of Zoology*. 21: 85-88.

Joubert, G. & Katzennellenbogen, J. 1999. Epidemiological research methods and protocol development: study design. In: Katzenellenbogen, J.M., Joubert, G. & Abdool Karim, S.S. *Epidemiology. A manual for South Africa*. Oxford University Press, Cape Town, South Africa. 64-73.

Joubert, G. 1999a. Data presentation, analysis and interpretation: an introduction to data presentation, analysis and interpretation. In: Katzenellenbogen, J.M., Joubert, G. & Abdool Karim, S.S. *Epidemiology. A manual for South Africa*. Oxford University Press, Cape Town, South Africa. 101-123.

Joubert, G. 1999b. Contextualising epidemiology: key concepts in epidemiology. In: Katzenellenbogen, J.M., Joubert, G. & Abdool Karim, S.S. *Epidemiology. A manual for South Africa*. Oxford University Press, Cape Town, South Africa. 10-24.

Katzenellenbogen, J., Gear, J. & Tollman, S. 1999. Contextualising epidemiology: introduction. In: Katzenellenbogen, J.M., Joubert, G. and Abdool Karim, S.S. *Epidemiology. A Manual for South Africa*. Oxford University Press: South Africa. 3-9.

Kleynhans, C.J & Hill, L. 1999. *Ecoregions of South Africa – level 1. Resource directed measures for protection of water resources: river ecosystems*. Institute for Water Quality Studies. http://www.dwaf.gov.za

Kvalsvig, J.D. & Schutte, C.H.J. 1986. The role of human water contact patterns in the transmission of schistosomiasis in an informal settlement near a major industrial area. *Annals of Tropical Medicine and Parasitiology*. 80: 13-26.

Kvalsvig, J.D., Appleton, C.C., Archer, C., Mthethwa, P., Memela, C., Mpanza, J.T., Mweni, S.L., Ngcoya, M., Nkomokazi, J. & Qotyana, P. 2001. *The KwaZulu-Natal parasite control programme, 1998-2000*. Child Development Programme, Schools of Psychology and Life & Environmental Sciences, University of Natal, Durban. 41 pgs.

Lambertucci, J.R. 1993. *Schistosoma mansoni*: pathological and clinical aspects. In: Webbe, G., Sturrock, R.F. & Jordan, P. [eds]. *Human Schistosomiasis*. CAB International, Oxon, UK. 195-236.

Levine, N. 2002. *CrimeStat II: A Spatial Statistics Program for the Analysis of Crime Incident Locations.* (version 2.0). Ned Levine and Associates, Houston, TX and the National Institute of Justice, Washington, DC.

Linkens, D.A., Abbod, M.F. & Mahfouf, M. 2000. Intelligent systems in biomedicine. In: *Proceedings of the European Symposium on Intelligent Techniques*. Aachen, Germany. 46-61.

Longley, P., Batty, M. [eds]. Batty, M. [contributor]. 1997. *Spatial Analysis: modelling in a GIS environment*. John Wiley and Sons, New York. 400 pgs.

Maguire, D.J. 1991. An Overview and Definition of GIS. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1*: *Principles*. Longman Group, Essex. 9-20.

Maguire, D.J & Dangermond, J. 1991. The Functionality of GIS. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1*: *Principles*. Longman Group, Essex. 319-335.

Malone, J.B., Huh, O.B., Fehler, D.P., Wilson, P.A., Wilensky, D.E., Holmes, R.A. & Elmagdoub, A.I. 1994. Temperature data from satellite imagery and the distribution of schistosomiasis in Egypt. *American Journal of Tropical Medicine and Hygiene*. 50: 714-722.

Malone, J.B., Abdel-Rahman, M.S., El Bahy, M.M., Huh, O.K., Shafik, M. & Bavia, M. 1997. Geographic information systems and the distribution of *Schistosoma mansoni* in the Nile Delta. *Parasitology Today*. 13: 112-119.

Mapinfo Corporation. 1985- 2002. Mapinfo Professional. UK.http://www.mapinfo.com

Martens, W.J.M. 1995. *Modelling the effects of global warming on the prevalence of schistosomiasis*. Global Dynamics and Sustainable Development Programme. GLOBO Report Series, 10. University of Limburg, National Institute of Public Health and the Environment, RIVM Report No. 461502010, The Netherlands. 32 pgs.

Mathews, S.A. 1990. Epidemiology using a GIS: the need for caution. *Computational Environment and Urban Systems*. 14: 213- 221.

McMahon, B. & Pugh, T.F. 1970. *Epidemiology: principles and methods*. Little Brown, Boston. 376 pgs.

Metcalf, C. & Coetzee, N. 1999. Epidemiology applied to content areas: outbreak investigations. In: Katzenellenbogen, J.M., Joubert, G. & Abdool Karim, S.S. *Epidemiology. A manual for South Africa*. Oxford University Press, Cape Town, South Africa. 196-204.

Michelson, E.H. 1961. The effects of temperature on growth and reproduction of *Australorbis glabratus* in the laboratory. *American Journal of Hygiene*. 73: 66-74.

Moore, D.A. & Carpenter, T.E. 1999. Spatial analytical methods and geographic information systems: use in health research and epidemiology. *Epidemiologic Reviews*. 21: 143-161.

Morgan, J.A.T., Dejong, R.J., Snyder, S.D., Mkoji, G.M. & Loker, E.S. 2001. *Schistosoma mansoni* and *Biomphalaria*: past history and future trends. *Parasitology*. 123: S211-S228.

Mott, K.E. 1987. Schistosomiasis control. In: Rollinson, D. & Simpson, A.J.G. [eds]. *The Biology of Schistosomes, from Genes to Latrines*. Academic Press, London. 431-450.

Muller, J-C. 1991. Generalization of Spatial Databases. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1*: *Principles*. Longman Group, Essex. 457-475.

Murray, H.W., Pépin, J., Nutman, T.B., Hoffman, S.L. & Mahmoud, A.A.F. 2000. Recent advances: tropical medicine. *British Medical Journal*. 320: 490- 494.

Odum, E.P. 1983. *Basic Ecology*. Saunders College Publishing, Philadelphia. 613 pgs.

O'Keeffe, J.H. 1985a. Population biology of the freshwater snail *Bulinus globosus* on the Kenya coast. I- population fluctuations in relation to climate. *Journal of Applied Ecology*. 22: 73-84.

O'Keeffe, J.H. 1985b. Population biology of the freshwater snail *Bulinus globosus* on the Kenya coast. I- feeding and density effects on population parameters. *Journal of Applied Ecology*. 22: 85-90.

Openshaw, S. 1991. Developing Appropriate Spatial Analysis Methods for GIS. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1*: *Principles*. Longman Group, Essex. 389-402.

Pflüger, W. 1980. Experimental epidemiology of schistosomiasis. I: the prepatent period and cercarial production of *Schistosoma mansoni* in *Biomphalaria* snails at various constant temperatures. *Zeitschrift für Parasitenkunde*. 63: 159-169.

Pflüger, W. 1981. Experimental epidemiology of schistosomiasis. II: prepatency of *Schistosoma mansoni* in *Biomphalaria glabrata* at diurnally fluctuating temperatures. *Zeitschrift für Parasitenkunde*. 66: 221-229.

Pflüger, W., Roushdy, M. & El-Emam, M. 1981. Climate and epidemiology in schistosomiasis. *International Symposium on Schistosomiasis*. Dec 19 – 22nd. Theodor Bilharz Institute, Egypt.

Pflüger, W., Roushdy, M. & El-Emam, M. 1984. The prepatent period and cercarial production of *Schistosoma haematobium* in *Bulinus truncatus* (Egyptian field strains) at different constant temperatures. *Zeitschrift für Parasitenkunde*. 70: 95-103.

Pitchford, R.J. & Visser, P.S. 1962. Results of exposing mice to schistosomiasis by immersion in natural water. *Transactions of the Royal Society of Tropical Medicine and Hygiene.* 56: 294-301.

Pitchford, R.J. & Visser, P.S. 1965. Some further observations on schistosome transmission in the Eastern Transvaal. *Bulletin of the World Health Organisation*. 32: 83-104.

Pitchford, R.J. 1966. Some South African schistosomes: Genus: *Schistosoma. South African Journal of Science*. 62. 202-204.

Pitchford, R.J. & Visser, P.S. 1969. The use of behaviour patterns of larval schistosomes in assessing the bilharzia potential of non-endemic areas. *South African Medical Journal.* 43: 983-995.

Pitchford, R.J., Meyling, A.H., Meyling, J., Du Toit, J.F. 1969. Cercarial shedding patterns of various schistosome species under outdoor conditions in the Transvaal. *Annals of Tropical Medicine and Parasitology*. 63: 359- 371.

Pitchford, R.J. & Visser, P.S. 1972. Some observations on the hatching pattern of *Schistosoma mansoni* eggs. *Annals of Tropical Medicine and Parasitology*. 66: 399-407.

Pitchford, R.J. & Visser, P.S. 1975. The effect of large dams on river water temperature below the dams, with special reference to bilharzia and the Verwoerd Dam. *South African Journal of Science*. 71: 212-213.

Pitchford, R.J. 1976. Absence of schistosomes in potentially endemic areas in Africa. In: Gear, J.H.S. [ed]. *Medicine in a Tropical Environment. Proceedings of the International Symposium,* South Africa. A.A. Balkema, Cape Town. 667-677.

Pitchford, R.J. 1981. Temperature and schistosome distribution in South Africa. *South African Journal of Science*. 77: 252-261.

Pitchford, R.J. 1986. Some aspects of bilharzia in Southern Africa. *South African Medical Journal*. October (suppl): 80-82.

Porter, A. 1938. *The larval Trematoda found in certain South African Mollusca, with special reference to schistosomiasis (bilharziasis).* Publications of the South African Institute for Medical Research. 42: 1- 492.

Poulin, R. 1998. *Evolutionary Ecology of Parasites, from individuals to communities*. Chapman and Hall, London. 212 pgs.

Preston-Whyte, R.A & Tyson, P.D. 1988. *The Atmosphere and Weather of Southern Africa.* Oxford University Press, Cape Town. 374 pgs.

Preston-Whyte, R.A & Tyson, P.D. 2000. *The Weather and Climate of Southern Africa.* Oxford University Press. Cape Town. 391 pgs.

Pretorius, S.J., Joubert, P.H. & de Kock, K.N. 1989. A review of the schistosomiasis risk in South African dams. *Water SA*. 15:133-136.

Prinsloo, J.F. & van Eeden, J.A. 1969. Temperature and its bearing on the distribution and chemical control of freshwater snails. *South African Journal of Science*. 8: 1363-1365.

Pubmed. 2002. U.S. National Library of Medicine, Bethesda, MD. http://www.ncbi.nlm.nih.gov. Search done on 28th November 2002.

Red Urine Study Group. 1995. Identification of high-risk communities for schistosomiasis in Africa: a multi-country study. *Social and Economic Research Project Reports.* World Health Organisation. TDR/SER/PRS/15. Geneva.15.

Richards, I.D. & Baker, M.R. 1988. *The Epidemiology and Prevention of Important Diseases.* Churchill Livingston, Edinburgh. 176 pgs.

Richards, T.B., Croner, C.M., Rushton, G., Brown, C.K. & Fowler, L. 1999. Geographic information systems and public health: mapping the future. *Public Health Reports*. 114: 359-373.

Robinson, D. [ed]. 1985. *Epidemiology and the Community Control of Disease in Warm Climates*. 2nd edition. Churchill Livingstone, Edinburgh. 767 pgs.

Rollinson, D. & Southgate, V.R. 1987. The genus *Schistosoma*: a taxonomic appraisal. In: Rollinson, D. & Simpson, A.J.G. [eds]. *The Biology of Schistosomes, from Genes to Latrines*. Academic Press, London. 1-50.

Rollinson, D., Stothard, J.R., & Southgate, V.R. 2001. Interactions between intermediate snail hosts of the genus *Bulinus* and schistosomes of the *Schistosoma haematobium* group. *Parasitology*. 123: 245-260.

Ross, A.G.P., Sleigh, A.C., Li, Y., Davis, G.M., Williams, G.M., Jiang, Z., Feng, Z. & McManus, D.P. 2001. Schistosomiasis in the People's Republic of China: prospects and challenges for the 21st century. *Clinical Microbiology Reviews*. 14: 270-295.

Rowan, W.B. 1965. The ecology of schistosome transmission foci. *Bulletin of the World Health Organisation*. 33: 63-71.

Saathof, E., Olsen, A., Kristensen, T.K., Appleton, C.C., Sharp, B. & Kleinschmidt, I. 2002. Environmental factors and *S. haematobium* infection in schoolchildren from rural northern KwaZulu-Natal/South Africa. In: Saathof, E. *Geohelminth and Schistosoma haematobium infection in schoolchildren from rural northern KwaZulu-Natal/South Africa*. PhD thesis, Danish Bilharziasis Laboratory & University of Copenhagen, Charlottenlund and Copenhagen, Denmark.

Scholten, H.J. & de Lepper, M.J.C. 1991. The benefits of the application of geographical information systems in public and environmental health. *World Health Statistics Quarterly*. 44: 160- 170.

Schulze, R. E. 1997. *South African Atlas of Agrohydrology and -climatology*. Report TT82/96, Water Research Commission, Pretoria. 276 pgs.

Schutte, C.H.J., Fripp, PJ & Evans, A.C. 1995. An assessment of the schistosomiasis situation in the Republic of South Africa. *Southern African Journal of Epidemiology and Infection*. 10: 37-43.

Shepherd, I.D.H. 1991. Information Integration and GIS. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1: Principles*. Longman Group, Essex. 337-360.

Shiff, C.J. 1964a. Studies on *Bulinus* (*Physopsis*) *globosus* in Rhodesia. I- the influence of temperature on the intrinsic rate of natural increase. *Annals of Tropical Medicine and Parasitology*. 58: 94-105.

Shiff, C.J. 1964b. Studies on *Bulinus (Physopsis) globosus* in Rhodesia. III- bionomics of a natural population in a temporary habitat. *Annals of Tropical Medicine and Parasitology*. 58: 240-255.

Shiff, C.J. 1966. The influence of temperature on the vertical movement of *Bulinus (Physopsis) globosus* in the laboratory and in the field. *South African Journal of Science*. 62: 210-214.

Shiff, C.J. & Husting, E.L. 1966. An application of the concept of intrinsic rate of natural increase to studies on the ecology of freshwater snails of the genera *Biomphalaria* and *Bulinus* (*Physopsis)* in Southern Africa. *Proceedings and Transactions of the Rhodesian Scientific Association*. 51: 1-8.

Shiff, C.J. & Garnett, B. 1967. The influence of temperature on the intrinsic rate of natural increase of the freshwater snail *Biomphalaria pfeifferi* (Krauss)(Pulmonata: Planorbidae). *Archives of Hydrobiology*. 62: 429-438.

Shuhua, X., Booth, M. & Tanner, M. 2000a. The prophylactic effects of artemether against *Schistosoma japonicum* infections. *Parasitology Today*. 16: 122- 126.

Shuhua, X., Jiqing,Y., Jinying, M., Huifang, G., Peiying, J. & Tanner, M. 2000b. Effect of praziquantel together with artemether on *Schistosoma japonicum* parasites of different ages in rabbits. *Parasitology International*. 49: 25-30.

Southgate, V.R & Rollinson, D. 1987. Natural History of Transmission and Schistosome Interactions. In: Rollinson, D. & Simpson, A.J.G. [eds]. *The Biology of Schistosomes, from Genes to Latrines*. Academic Press, London. 347-378.

Spear, R.C., Zhou, Y., Maszle, D.R., Gu, X. & Gong, P. 1995. GIS and spatial analysis in schistosomiasis transmission and control. *The American Astronautical Society*. December: 6 pgs. http://ehs.sph.berkeley.edu/china/paper/ch-gis/ch-gis.htm

Standen, O. D. 1952. Experimental infection of *Australorbis glabratus* with *Schistosoma mansoni.* 1: individual and mass infection of snails and the relationship of infection to temperature and season. *Annals of Tropical Medicine and Parasitology.* 46: 48-53.

Stata. 2001. *Statistical data analysis*. STAT Corporation.Texas.

Statistics, SA. 2001. Mid -year estimates. Statistical release P0302, Pretoria. 23 pgs.

Stirewalt, M.A. 1954. Effect of snail maintenance temperatures on development of *Schistosoma mansoni. Experimental Parasitology*. 3: 504-516.

Stuckenberg, B.R. 1969. Effective temperature as an ecological factor in Southern Africa. *Zoologica Africana*. 4: 145-197.

Sturrock, R.F. 1966a. The influence of temperature on the biology of *Biomphalaria pfeifferi* (Krauss), an intermediate host of *Schistosoma mansoni. Annals of Tropical Medicine and Parasitology*. 60: 100-105.

Sturrock, M. 1966b. The influence of infection with *Schistosoma mansoni* on the growth rate and reproduction of *Biomphalaria pfeifferi. Annals of Tropical Medicine and Parasitology*. 60: 187-197.

Sturrock, R.F. & Sturrock, B.M. 1972. The influence of temperature on the biology of *Biomphalaria glabrata* (Say), intermediate host of *Schistosoma mansoni* on St. Lucia, West Indies. *Annals of Tropical Medicine and Parasitology*. 66: 385-390.

Sturrock, R.F. 1993. The parasites and their life cycles. In: Webbe, G., Sturrock, R.F. & Jordan, P. [eds]. *Human Schistosomiasis*. CAB International, Oxon, UK. 1-32.

Susser, M. 1973. Agent, host and environment as an ecological system: causal thinking in the health sciences. *Concepts and Strategies of Epidemiology*. Oxford University Press, New York. 181 pgs.

Tanser, F.C. 2000. *The application of geographical information systems to infectious diseases and health systems in Africa*. PhD Thesis. University of Natal, South Africa.

Thompson, M.C & Connor, S.J. 2000. Environmental information systems for the control of arthropod vectors and disease. *Medical and Veterinary Entomology*.14: 227-244.

Utroska, J.A., Chen, M.G., Dixon, H., Yoon, S., Helling-Borda, M., Hogerzeil, H.V. & Mott, K.E. 1989. *An estimate of global needs for praziquantel within schistosomiasis control programmes*. WHO, Geneva. Schisto/89.102. 6 pgs.

Utzinger, J., N'Goran. E.K., N'dri A., Lengeler, C., Shuhua, X. & Tanner, M. 2000. Oral artemether for prevention of *Schistosoma mansoni* infection: randomized controlled trial. *Lancet*. 355: 1320-1325.

Utzinger, J., Shuhua, X., Eliézer, K.N.G., Berquist, R. & Tanner, M. 2001. The potential of artemether for the control of schistosomiasis. *International Journal for Parasitology*. 31: 1549–1562.

van der Schalie, H. & Berry, E.G. 1973. The effects of temperature on growth and reproduction of aquatic snails. *Sterkiana*. 50: 1-92.

Van der Werf, M.J. & de Vlas, S.J. 2001. *Morbidity and infection with schistosomes or soil-transmitted helminths*. Department of Public Health, Erasmus University, Rotterdarm, The Netherlands. 103 pgs.

Vine, M.F., Degnan, D. & Hanchette, C. 1997. Geographic information systems: their use in environmental epidemiologic research. *Environmental Health Perspectives*. 105: 598–605.

von Lichtenberg, F. 1987. Consequences of Infections with Schistosomiasis. In: Rollinson, D. & Simpson, A.J.G. [eds]. *The Biology of Schistosomes, from Genes to Latrines*. Academic Press, London. 185-232.

Waner, S. 1999. Health risks of travelers in South Africa. *Journal of Travel Medicine*. 6: 199-203.

Wilson, R.A. 1987. Cercariae to Liver Worms: development and migration to the mammalian host. In: Rollinson, D. & Simpson, A.J.G. [eds]. *The Biology of Schistosomes, from Genes to Latrines*. Academic Press, London. 115-146.

Wolmarans, C. T., & de Kock, K.N. 2000. Skistosome, 'n onderskatte en verwaarloosde probleem, selfs in die endemiese gebiede van die Republiek van Suid Afrika. *Suid-Afrikaanse Tydskrif vir Natuurwetenskap en Tegnologie*. 19: 31- 36.

World Health Organisation. 1946. In: Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, 100 pgs) and entered into force on 7 April 1948. http://www.who.int/about/definition/en/

World Health Organisation. 1996. Schistosomiasis. Fact sheet 115 . http://www.who.int/inf-fs/en/fact115.html

World Health Organisation. 2002. *Prevention and control of schistosomiasis and soil-transmitted helminthiasis*. 1st Report of the Joint WHO Expert Committee, WHO Technical Report Series 912: 1-56.

World Health Report. 2002. Annex table 3. Burden of disease in DALYs by cause, sex and mortality stratum in WHO regions estimates for 2001. World Health Organisation. 3 pgs. www.who.int/whr2001/2001/main/en/pdf/annex3.en.pdf

APPENDIX A

List of Terms and Definitions

accuracy

Conformity to a standard

aetiology

A branch of medical science concerned with the causes and origins of diseases. It includes the study of factors of causation or those associated with the causation of disease or abnormal body states (Merriam-Webster Dictionary, 2002).

attribute data

Non-graphic information

autocorrelation, autocovariance

Statistical concepts expressing the degree to which the value of an attribute at spatially adjacent points covaries with the distance separating the points (GIS Combat Manual, 1988).

buffer

An area of computer storage used to accumulate plot instructions

cell

The basic element of spatial information in the raster (grid) description of spatial entities (GIS Combat Manual, 1988).

chemoprophylaxis

Drug treatment designed to prevent future occurrences of disease. Treatment may be chemotherapy as far as an individual is concerned but also chemopropylactic for the population as a whole.

condition

Abiotic factor (Odum, 1983). (Factor and condition are used interchangeably in this work)

DALYs

Disability life adjusted years.

data

The general term for numbers, letters, symbols and analog entities that are put into the computer and used for information processing. Geographic data has longitude and latitude i,e it is referenced (GIS Combat Manual, 1988).

database

A structured set of records or related subject information which can be accessed through various front-end queries (GIS Combat Manual, 1988).

definitive host

The host in which the sexual reproduction of a schistosomes occur

digital

The ability to represent data in discrete units or digits (GIS Combat Manual, 1988).

digitise

To convert analog data (maps and drawings) to digital form, to encode geographic features in digital form as x,y coordinates. The process of using a digitiser to encode the locations of geographic features by converting their map positions to a series of x,y coordinates stored in computer files. Pushing a digitiser button records an x,y coordinate. A digitised line is created by recording a series of x,y coordinates (GIS Combat Manual, 1988).

digitiser

A flat data entry device used to measure and record the plane co-ordinates of selected locations (GIS Combat Manual, 1988).

ecology

Derived from the Greek *oikos* meaning "household" and *logos* meaning study. Hence it is the study of the patterns of relations between organisms and their environment (Odum, 1983).

ecological epidemiology

A branch of epidemiology which views disease as a result of the ecological interactions between populations of hosts and parasites. In contrast, classical epidemiology describes varieties of epidemiology primarily concerned with the statistical relationships between disease agents, both

infectious and non-infectious; for example a study to establish the relative risk of lung cancer associated with smoking (Swinton, 2002).

ecological niche

Includes the physical space and functional role of an organism in its community (Odum, 1983).

ecological zone

A zone reflects the tolerance of the helminth species in question (or its intermediate host) of ecological and climate variables such as topography, soil type, altitude (temperature), rainfall or frost. The zonation may vary from one country to another (WHO, 2001).

endemic

A term to describe levels of infection which do not exhibit wide fluctuations through time in a defined place (Swinton, 2002).

Geographic Information Systems (GIS)

A computer-based tool that captures, displays and manipulates geographically referenced data. A method of using interactive computer graphics to encode, analyse and display multiple layers of data derived from many sources and presenting this information in map format. Information can be easily updated and redrafted by the computer in different scales and in different combinations of data (Maguire, 1991).

grid

Intersecting lines representing x,y co-ordinates.

hardcopy

A copy on paper or other material eg., film, picture format

immunity

1) a state in which a host is not susceptible to infection or disease, or

2) the mechanisms by which this is achieved. Immunity is achieved by an individual through one of three routes: natural or innate immunity genetically inherited or acquired through maternal antibody, acquired immunity conferred after contact with a disease, and artificial immunity after a successful vaccination (Swinton, 2002).

indirect life cycle

A life cycle which requires one or more intermediate hosts before the definitive host species is reinfected (Swinton, 2002).

layer

A logical separation of mapped information according to there. These can be viewed in single layers or any combinations of layers at a time (Frank and Mark, 1991).

map

A conventional representation, usually on a plane surface and at an established scale, of the physical features (natural, artificial, or both) of part or the whole of the Earth's surface. Features are identified by means of signs and symbols, and geographical orientation is indicated. A map may emphasise, generalise or omit the representation of certain features to satisfy specific requirements. The type of information a map is designed to show frequently appears in its title. The map projection used normally is indicated on the map.

map projection

The basic system of coordinates used todescribe the spatial distribution of elements in a GIS (GIS Combat Manual, 1988).

normalised differentiation vegetation index (NDVI)

An index derived from reflectance measurements in the red and infrared portions of the electromagnetic spectrum to describe the relative amount of green biomass from one area to the next (Clarklabs, Worcester, MA).

pixel

Short for picture element. Usually a square or rectangular cell.

polygon

A multi-sided figure representing an area on a map (GIS Combat Manual, 1988).

r

Intrinsic rate of natural increase

raster

A regular grid of cells covering in area. An array of raster cells constitute a map (Clarklabs, Worcester, MA).

raster database

A database containing all mapped, spatial information in the form of regular grid cells.

raster-to-vector

The process of converting an image made up of cells into one described by lines and polygons.

resolution

The minimum difference between two independently measured or computed values which can be distinguished by the measurement or analytical method being considered or used (GIS Combat Manual, 1988).

scale

The relationship between a distance on a map and the real world distance.

spatial resolution

The minimum distance that can be recorded and measured from cell centre to centre, produces many more grid cells with which to work (GIS Combat Manual, 1988).

sweep

the sweep technique represents an object by sweeping a defined area or volume along a defined trajectory (Raper and Kelk, 1991).

vector

A mathematical entity with both magnitude and direction.

References for List of Terms and Definitions

Clarklabs. Idrisi 32. 1999. The Idrisi Project. Worcester.MA. USA. http://www.clarklabs.org

Frank, A.U. & Mark, D.M. 1991. Language Issues for GIS. In: Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1: Principles*. Longman Group, Essex. 146-163.

Raper, J.F & Kelk, B. 1991. Three-dimensional GIS. Maguire, D.J., Goodchild, M.F. & Rhind, D.W. [eds]. *Geographical Information Systems Vol. 1: Principles*. Longman Group, Essex. 299-318.

Merriam-Webster Dictionary. 2002. http://www.m-w.com/cgi-bin/dictionary;

Odum, E.P. 1983. *Basic Ecology*. Saunders College Publishing, Philadelphia. 613 pgs.

Swinton, J. 2002. *A Dictionary of (Ecological) Epidemiology*. www.swintons.net/jonathan/Academic/glossary.html

The GIS Combat Manual. 1988. A Special Report by Venture Communications, USA.

World Health Organisation. 2002. *Prevention and control of schistosomiasis and soil-transmitted helminthiasis*. 1st Report of the Joint WHO Expert Committee, WHO Technical Report Series 912: 1-56.

APPENDIX B

Procedures used to derive the temperature-suitability maps

The format presented here is similar to that used by Tanser (2000) and the details are described in Chapter 4, Section 4.9.1.

Deriving optimal masks using the Hutchinson *et al.*, (1995) climate data.

1.1 For *Schistosoma haematobium:*
Tmin = minimum temperature

Areas where Tmin ≤ 1°C for one month or more is unsuitable
Macro Rmin1.iml
reclass x i wtmin01 rm1_01 2 1 -999 11 0 11 999 –9999
reclass x i wtmin02 rm1_02 2 1 -999 11 0 11 999 -9999
reclass x i wtmin03 rm1_03 2 1 -999 11 0 11 999 -9999
reclass x i wtmin04 rm1_04 2 1 -999 11 0 11 999 -9999
reclass x i wtmin05 rm1_05 2 1 -999 11 0 11 999 -9999
reclass x i wtmin06 rm1_06 2 1 -999 11 0 11 999 -9999
reclass x i wtmin07 rm1_07 2 1 -999 11 0 11 999 -9999
reclass x i wtmin08 rm1_08 2 1 -999 11 0 11 999 -9999
reclass x i wtmin09 rm1_09 2 1 -999 11 0 11 999 -9999
reclass x i wtmin10 rm1_10 2 1 -999 11 0 11 999 -9999
reclass x i wtmin11 rm1_11 2 1 -999 11 0 11 999 -9999
reclass x i wtmin12 rm1_12 2 1 -999 11 0 11 999 -9999

Macro rmsum1.iml
overlay x 1 rm1_01 rm1_02 sum1
overlay x 1 sum1 rm1_03 sum2
overlay x 1 sum2 rm1_04 sum3
overlay x 1 sum3 rm1_05 sum4
overlay x 1 sum4 rm1_06 sum5
overlay x 1 sum5 rm1_07 sum6
overlay x 1 sum6 rm1_08 sum7
overlay x 1 sum7 rm1_09 sum8
overlay x 1 sum8 rm1_10 sum9
overlay x 1 sum9 rm1_11 sum10
overlay x 1 sum10 rm1_12 r1mnsum

Calculate suitability:
Tmin1_1.iml
Reclass x i r1mnsum tmin1_1 2 1 12 13 1 0 1 0 1 12 -9999

Areas were temperature range (Tran) > during 14°C December and January
Tran (12- 01) > 14°C unsuitable
Tran0112.iml
overlay x 8 wtran01 wtran12 tran0112
Tran14.iml

reclass x i tran0112 tran14 2 0 140 999 1 -999 140 –9999

Final unsuitable mask:
Tmin1_1 x tran14 = unsutsh
Unsutsh x 2 = runsutsh

Suitable mask for *S.haematobium*
Areas where Tmin ≥ 14.5°C for 7 months or more = suitable
Macro rmin145.iml

```
reclass x i wtmin01 rm1401 2 0 -999 145 1 145 999 -9999
reclass x i wtmin02 rm1402 2 0 -999 145 1 145 999 -9999
reclass x i wtmin03 rm1403 2 0 -999 145 1 145 999 -9999
reclass x i wtmin04 rm1404 2 0 -999 145 1 145 999 -9999
reclass x i wtmin05 rm1405 2 0 -999 145 1 145 999 -9999
reclass x i wtmin06 rm1406 2 0 -999 145 1 145 999 -9999
reclass x i wtmin07 rm1407 2 0 -999 145 1 145 999 -9999
reclass x i wtmin08 rm1408 2 0 -999 145 1 145 999 -9999
reclass x i wtmin09 rm1409 2 0 -999 145 1 145 999 -9999
reclass x i wtmin10 rm1410 2 0 -999 145 1 145 999 -9999
reclass x i wtmin11 rm1411 2 0 -999 145 1 145 999 -9999
reclass x i wtmin12 rm1412 2 0 -999 145 1 145 999 -9999
```

Macro rmsum145.iml

```
overlay x 1 rm1401 rm1402 sum1
overlay x 1 sum1 rm1403 sum2
overlay x 1 sum2 rm1404 sum3
overlay x 1 sum3 rm1405 sum4
overlay x 1 sum4 rm1406 sum5
overlay x 1 sum5 rm1407 sum6
overlay x 1 sum6 rm1408 sum7
overlay x 1 sum7 rm1409 sum8
overlay x 1 sum8 rm1410 sum9
overlay x 1 sum9 rm1411 sum10
overlay x 1 sum10 rm1412 r14mnsum
```

tmin145.iml

Calculate suitability:

```
reclass x i r14mnsum tmin145 2 0 0 4 1 4 13 -9999
```

TOTAL MODEL

```
runsutsh + tmin145 = shmod
reclass shmod where 1 to 3 = 0
                    3 to 4 = 1 ...shmodel – final map.
```

1.2 For *Schistosoma mansoni*:

Areas where Tmin ≤ 3°C for 1 month or more is unsuitable
Macro rmin3.iml

```
reclass x i wtmin01 rm3_01 2 1 -999 31 0 31 999 -9999
reclass x i wtmin02 rm3_02 2 1 -999 31 0 31 999 -9999
reclass x i wtmin03 rm3_03 2 1 -999 31 0 31 999 -9999
reclass x i wtmin04 rm3_04 2 1 -999 31 0 31 999 -9999
reclass x i wtmin05 rm3_05 2 1 -999 31 0 31 999 -9999
reclass x i wtmin06 rm3_06 2 1 -999 31 0 31 999 -9999
reclass x i wtmin07 rm3_07 2 1 -999 31 0 31 999 -9999
reclass x i wtmin08 rm3_08 2 1 -999 31 0 31 999 -9999
reclass x i wtmin09 rm3_09 2 1 -999 31 0 31 999 -9999
reclass x i wtmin10 rm3_10 2 1 -999 31 0 31 999 -9999
reclass x i wtmin11 rm3_11 2 1 -999 31 0 31 999 -9999
reclass x i wtmin12 rm3_12 2 1 -999 31 0 31 999 -9999
```

Macro rmsum3.iml

overlay x 1 rm3_01 rm3_02 sum1
overlay x 1 sum1 rm3_03 sum2
overlay x 1 sum2 rm3_04 sum3
overlay x 1 sum3 rm3_05 sum4
overlay x 1 sum4 rm3_06 sum5
overlay x 1 sum5 rm3_07 sum6
overlay x 1 sum6 rm3_08 sum7
overlay x 1 sum7 rm3_09 sum8
overlay x 1 sum8 rm3_10 sum9
overlay x 1 sum9 rm3_11 sum10
overlay x 1 sum10 rm3_12 r3mnsum

tmin_3.iml

Calculate suitability:
reclass x i r3mnsum tmin3_1 2 1 0 2 0 2 13 -9999

tmin3_1 x tran14 = unsutsm

Suitable mask for S.*mansoni*
Areas where Tmin 16°C ≥ for ≥ 2 months.

Macro rmin16.iml
reclass x i wtmin01 rm1601 2 0 -999 160 1 160 999 -9999
reclass x i wtmin02 rm1602 2 0 -999 160 1 160 999 -9999
reclass x i wtmin03 rm1603 2 0 -999 160 1 160 999 -9999
reclass x i wtmin04 rm1604 2 0 -999 160 1 160 999 -9999
reclass x i wtmin05 rm1605 2 0 -999 160 1 160 999 -9999
reclass x i wtmin06 rm1606 2 0 -999 160 1 160 999 -9999
reclass x i wtmin07 rm1607 2 0 -999 160 1 160 999 -9999
reclass x i wtmin08 rm1608 2 0 -999 160 1 160 999 -9999
reclass x i wtmin09 rm1609 2 0 -999 160 1 160 999 -9999
reclass x i wtmin10 rm1610 2 0 -999 160 1 160 999 -9999
reclass x i wtmin11 rm1611 2 0 -999 160 1 160 999 -9999
reclass x i wtmin12 rm1612 2 0 -999 160 1 160 999 -9999

Macro rmsum16.iml
overlay x 1 rm1601 rm1602 sum1
overlay x 1 sum1 rm1603 sum2
overlay x 1 sum2 rm1604 sum3
overlay x 1 sum3 rm1605 sum4
overlay x 1 sum4 rm1606 sum5
overlay x 1 sum5 rm1607 sum6
overlay x 1 sum6 rm1608 sum7
overlay x 1 sum7 rm1609 sum8
overlay x 1 sum8 rm1610 sum9
overlay x 1 sum9 rm1611 sum10
overlay x 1 sum10 rm1612 r16mnsum

Calculate suitability:
tmin16_2.iml
reclass x i r16mnsum tmin16_2 2 0 0 2 1 2 13 -9999

total SM Model

tmin16_2 x unsutsm = smmod – final map.

APPENDIX C

Logical steps in deriving the regression model

The procedures described here relate to Chapter 4, Section 4.9.2.

Tmax = maximum temperatures
Tmin = minimum temperatures

Tmax1/tmin1 = Dec+Jan+Feb
tmax2 /tmin2 = Mar+April+May
tmax3/tmin3 = Jun+July +Aug
tmax4+tmin4 = Sept + Oct + Nov

(Satmax12 + Satmax01 + satmax02)/30= Htmax1
(Satmax03 + satmax04 + satmax05)/30= Htmax2
(Satmax06 + satmax07 + satmax08)/30 = Htmax3
(Satmax09 + satmax10 + satmax11)/30 = Htmax4

(Satmin12 + Satmin01 + satmax02)/30 = Htmax1
(Satmin03 + satmin04 + satmax05)/30= Htmin2
(Satmin06 + satmin07 + satmin08)/30= Htmin3
(Satmin09 + satmin10 + satmin11)/30= Htmin4

Saved as htmin1.exp, htmin2.exp, htmin3.exp, htmin4.exp,htmax01.exp, htmax02.exp
Htmax03.exp, htmax04.exp

1.1 For *Schistosoma haematobium*:

Raina.exp = [sarain01] + [sarain02] ……+ [sarain12]

Generic Formula:
S_sh = 0.0033635 x raina - 1.27823 x htmax1 + 0.7063469 x htmax2 - 0.7712254 x htmax3 + 1.664342 x htmax4 -2.958864 x htmin1 + 3.678978 x htmin2 -1.461983 x htmin3 + 1.00727 x htmin4

Calculate the probability of each pixel for each category :
Category 0%: $P_0 = 1/1 + e^{s - 9.98656}$

Category 1-5%: $P_1 = 1/1 + e^{s - 10.80347} - 1/1 + e^{s - 9.98656}$

Category 6-10%: $P_2 = 1/1 + e^{s - 11.52915} - 1/1 + e^{s - 10.80347}$

Category 11-25%: $P_3 = 1/1 + e^{s - 12.42612} - 1/1 + e^{s - 11.52915}$

Category 26-50%: $P_4 = 1/1 + e^{s - 13.804767} - 1/1 + e^{s - 12.42612}$

Category 51-70%: $P_5 = 1/1 + e^{s - 14.24769} - 1/1 + e^{s - 13.804767}$

Category 71-100%: $P_6 = 1/1 + e^{s - 14.24769}$

where S = 0.0033635 x annual rainfall - 1.27823 x tmax1 + 0.7063469 x tmax2 - 0.7712254 x tmax3 + 1.664342 tmax4 -2.958864 x tmin1 + 3.678978 tmin2 -1.461983 x tmin3 + 1.00727 x tmin4.

tmax1 = maximum temperatures for December, January and February,

tmax2 = maximum temperatures for March, April and May,

tmax3 = maximum temperatures for Jun, July and August,

tmax4 = maximum temperatures September, October and November, and similarly for minimum temperatures (tmin1 to tmin4).

Annual rainfall = sum of mean monthly rainfall

check :

Po + P1 + P2 + P3 + P4 + P5 + P6 + P7 = 1

To find the maximum category per pixel :
Use Analysis > Decision support > mdchoice

- Specify each image separately
- Number of input images : 7
- Find MAX value in the set of images
- Output prefix : **maxcatsh**

1.2 For *Schistosoma mansoni* :
Raintotm = [raina] / 12

Generic Formula:
S_sm = (0.389559 x [raintotm])- (1.689384 x [tmax1]) - (2.303627 x tmin3) + (5.10582 x [tmin2])+ (1.907905 x [tmax4]) -(2.465768 x [tmin1])

1. Category 0%: $P_0 = 1/1 + e^{s - 14.15619}$
2. Category 1-5%: $P_1 = 1/1 + e^{s - 14.94952} - 1/1 + e^{s - 14.15619}$
3. Category 6-10%: $P_2 = 1/1 + e^{s - 15.60341} - 1/1 + e^{s - 14.94952}$
4. Category 11-25%: $P_3 = 1/1 + e^{s - 16.30314} - 1/1 + e^{s - 15.60341}$
5. Category 26-50%: $P_4 = 1/1 + e^{s - 17.22045} - 1/1 + e^{s - 16.30314}$
6. Category 51-70%: $P_5 = 1/1 + e^{s - 17.83996} - 1/1 + e^{s - 17.22045}$
7. Category 71-100%: $P_6 = 1/1 + e^{s - 17.83996}$

where S = 0.00389559 x mean monthly rainfall - 1.689384 x tmax1 - 2.303627 x tmin3 + 5.10582 x tmin2 + 1.907905 X tmax4 -2.465768 x tmin1.

Check :

Po + P1 + P2 + P3 + P4 + P5 + P6 + P7 = 1

To find the maximum category per pixel :
Use Analysis > Decision support > mdchoice

- Specify each image separately
- Number of input images : 7
- Find MAX value in the set of images
- Output prefix : **mxcatsm**

APPENDIX D

Temperature-suitability Maps for Schistosomiasis in South Africa

Accepted by the Annals of Tropical Medicine and Parasitology on 30th May 2003

BY I. MOODLEY, I. KLEINSCHMIDT, B. SHARP, M. CRAIG & C. APPLETON

Parasitological surveys have shown that both urinary and intestinal schistosomiasis occur widely in South Africa. Data on both diseases were incorporated into a Geographic Information System, to develop new maps based on defined temperature constraints. The disease data, obtained from a national hardcopy atlas of schistosomiasis, were used as a template to select temperature regimes that were (i) suitable and (ii) unsuitable for schistosomiasis transmission in South Africa. The temperature regimes were derived from published work relating the biology of larval schistosomes (i.e. schistosome transmission) to temperature in South Africa. It was found that temperature regimes based on minima corresponded better with the disease distribution data than regimes based on maxima as suggested in previous work as being suitable for transmission. The study also estimated the number of children living in the climate-suitable areas but was unable to predict disease prevalence rates within the context of the spatial methodology used, and the limitations of the available disease data.

Keywords: schistosomiasis, temperature, Geographic Information System, suitable, South Africa.

1. Introduction

In an assessment of the schistosomiasis situation in South Africa, Schutte, Fripp and Evans (1995) highlighted the disease as being one of the most neglected and under-estimated health hazards in parts of Northern Province (now called Limpopo Province), Mpumalanga, Eastern Cape and KwaZulu-Natal. Indeed, Waner (1999) endorsed the view of Schutte *et al.* (1995) that the prevalence of schistosomiasis in South Africa has probably increased in recent decades. They suggested that although the situation may have improved in certain parts of the country due to better living conditions, prevalences may have increased due to population growth especially in rural areas. A study done between 1987 and 1989 reported an increase in overall infection rates in the Port St. John's district, now part of the Eastern Cape province (Mqoqi, Appleton and Dye, 1996). Another district level survey conducted later in 1991 showed that migrants carrying intestinal schistosomiasis could pose a health problem in the north-eastern parts of KwaZulu-Natal (Appleton *et al.*, 1996).

Heterogeneity in the occurrence and type of transmission sites makes it difficult to precisely define the areas where schistosomiasis occurs, or to establish the areas at risk of disease based solely on factors such as the presence of suitable water bodies and snail hosts. There are in fact several areas in southern Africa where snail hosts do occur but where there is no disease (Pitchford, 1976). Further, schistosomiasis is not only associated with a lack of proper water supplies, sanitation and recreational facilities such as swimming pools, but it also presents in some areas of South Africa where there is a relatively better infrastructure such as those associated with irrigation schemes and dams (Gear and Pitchford, 1979). It is important also to consider the possibility that patients may present with symptoms of schistosomiasis after travelling to endemic areas within and outside the country (Pitchford and Schutte, 1967; Appleton *et al.*, 1996). It is here that geographic information system (GIS) software has emerged as a useful tool to perform new types of data analyses and to assist in informed decision-making.

In South Africa GIS technology has been applied to studies on malaria (Craig, Snow and le Sueur, 1998) and tuberculosis (Beyers *et al.*, 1996). GIS based studies on the distribution of schistosomiasis have been carried out elsewhere, e.g. the Philippines (Cross *et al.*, 1984), the Caribbean (Cross and Bailey, 1984), Nile Delta (Malone *et al.*, 1994; Malone, 1995; Malone *et al.*, 1997) and Brazil (Bavia *et al.*, 1999). These studies mainly use climate data derived from satellite imagery to spatially define the relative suitability of habitats for the host snails, parasite development and disease transmission.

The earliest geographical description of South African schistosomiasis dates back to 1934 (Porter, 1938). Forty-two years later a detailed Atlas of Bilharzia in South Africa was published using parasitological prevalence surveys (Gear, Pitchford and van Eeden, 1980). These publications show the spatial trends of both urinary and intestinal schistosomiasis as being confined to the eastern regions of the country. Incorporation of this information into a GIS allows the database to be updated, manipulated and accessed as required.

Published studies on the abiotic factors which impact on the survival of the snail intermediate hosts and schistosomes prove useful because they reveal which conditions are likely to determine a habitat's suitability or unsuitability as a disease transmission site (Appleton, 1978). It was concluded from this review that two factors, temperature and habitat stability, were together largely responsible for determining the distribution of the host snails (*Bulinus africanus* group and *Biomphalaria pfeifferi*) and schistosomes (*Schistosoma haematobium* and *Schistosoma mansoni*) in sub-tropical South Africa.

Of these, temperature is probably the most influential and it has been well established that although the poikilothermic snails can tolerate a wide range of field water temperatures they are sensitive to low temperatures (Joubert *et al.*, 1984). Both snail fecundity and survival are also reduced at extremely high temperatures above 27°C (Appleton, 1977; Appleton and Eriksson, 1984).

The host snails are sensitive to high temperatures while the parasites are sensitive to low temperatures. De Kock and van Eeden (1986) showed that 27°C is a near- optimal temperature for growth and development of the eurythermal *B. pfeifferi* but Appleton (1977) found that these snails performed optimally over a range of moderately high temperatures from 22.8°C to 27 °C. de Kock and van Eeden (1986) also showed that *B. pfeifferi* performed better in terms of its intrinsic rate of natural increase (designated *r*) under broadly fluctuating temperature regimes than under narrow ones. Pflüger's (1980) work on *B. pfeifferi* illustrated a broad temperature range of approximately 16°C to 35°C as being suitable for *S. mansoni* cercarial production, but that temperatures of 15°C or less were unsuitable. However, the extremes of this temperature range did cause reduced cercarial production and high mortality. Pflüger (1980) also identified 14.2°C as the so- called temperature threshold or developmental null point which is the temperature at which *S. mansoni* development should cease. However, Pflüger (1980) showed that some development does occur below the null point, i.e. between 11 to 14°C. These studies suggest that *S. mansoni* and *B. pfeifferi* perform better over a plateau of moderately high and low temperatures rather than at specific temperatures as is the case for *S. haematobium* and the *B. africanus* group snails.

The optimal temperature for the stenothermal *Bulinus africanus* group snails' peak performance was shown to be 25°C (Shiff, 1964a, 1964b; Brown 1994). Pflüger, Roushdy and Emam (1984) found the theoretical development null point for *S. haematobium* to be 15.3°C. South African *S. haematobium* has a short incubation period during warm months and a long incubation period during cool months (Pitchford, 1981), implying that they are able to tolerate the warm subtropical and tropical temperatures dominating the country.

Temperature, which is dependent on altitude, is probably responsible for the fact that transmission of *S. mansoni* is year-round on the KwaZulu-Natal coastal plain (Donnelly and Appleton, 1985), but becomes seasonal as altitude increases, especially in areas such as the Mpumalanga escarpment and highveld plateau of Zimbabwe (Pitchford and Visser, 1965; Pitchford *et al.*, 1969; Shiff *et al.*, 1975). Therefore,

several permutations of the prevailing temperature regimes are used in this study to designate areas of tropical/sub-tropical South Africa that are either suitable or not for the establishment of schistosomiasis.

GIS tools offer the ability to plot both disease observations and temperature records together on a map, after which the temperature data can be manipulated and accessed as required and the responses of the parasites and their snail hosts predicted. Further applications include (1) factoring in the current evidence and observations (2) looking at localized and general trends (3) analyzing the relationship of different datasets such as temperature and rainfall, with prevalence data and further (4) modeling and scenario testing using these datasets.

This paper documents the use of GIS to develop easily accessible maps depicting where schistosomiasis occurs in South Africa using disease locality data, climate data and experimental evidence on the thermal requirements of transmission. It also provides an estimate of the numbers of children living in these areas.

2. Methods

Climate Data

Monthly mean values for daily minimum and maximum temperatures at a spatial resolution of 0.05 degrees were used to derive the maps (Hutchinson *et al.*, 1995). The grid (raster) data represented the period 1920 to 1980. Another dataset was obtained from the South African Atlas of Agrohydrology and Climatology (Schulze, 1997) for comparison purposes. This dataset was built from a one minute by one minute grid of altitudes, making up 437 000 grid points which were subjected to regression analysis and other simulation models.

Schistosomiasis prevalence data

Prevalence data for schistosomiasis were converted from paper maps obtained from the Atlas of Bilharzia in South Africa (Gear *et al.*, 1980) to digital format. The data in the Atlas are presented as categories (Table 1), without providing the sample sizes of individual surveys. During the 1960s and 1970s, the authors of the Atlas collected urine, faecal and blood samples, together with rectal biopsies, where applicable, from a representative sample of school-going children at particular localities (Gear *et al.*, 1980). Cases were defined as positive if *S. haematobium* and/or S. *mansoni* eggs were observed. Despite the fact that survey sample sizes were not available, the data were sufficient to provide "presence" and "absence" records for the two parasites which could be used for map development.

Table 1: Prevalence ranges of disease

No.	Category (%)
1	0
2	1-5
3	6-10
4	11-25
5	26-50
6	51-70
7	71-100

Deriving transmission suitability maps using temperature

Just over 20 years ago Pitchford (1981) demonstrated a close relationship between the distributions of *S. haematobium* and *S. mansoni* and various air temperature regimes in South Africa. Pitchford's work covered almost 20 years of epidemiological research within and outside the schistosomiasis- endemic areas in South Africa. His work was also the only attempt to relate temperature findings to the known distribution of urinary and intestinal schistosomiasis. It was also the most comprehensive review of its kind of schistosomiasis in South Africa. Pitchford (1981) expressed the schistosomiasis/temperature relationship in terms of suitability for transmission within South Africa and some neighbouring countries, and plotted the results on maps. Pitchford (1981) used the prevailing temperature regimes at known sites to define the thermal conditions that were suitable and unsuitable for urinary and intestinal schistosomiasis across the country. Thus, Pitchford's maps relating temperature to schistososmiasis in South Africa were forerunners of the current map products created within a GIS.

The study related the durations of specific thermal parameters in endemic areas to the intra-molluscan development of both *S. mansoni* and *S. haematobium* (Pitchford and Visser, 1969) and the seasonal occurrence of cercariae in field waters as measured using sentinel rodents (Pitchford and Visser, 1965). Suitable areas were identified from records collected over many years from observations on the seasonality of transmission as demonstrated by variation in prepatent development, schistosome infections acquired by sentinel rodents exposed to cercariae in endemic waters, and cercarial shedding patterns. Three temperature indices were used to define the thermal regimes, viz., monthly mean daily maximum (Mdx), monthly mean daily minimum (Mdn) and the monthly range (R). The outputs of Pitchford's (1981) study were maps of southern Africa south of 17° S in the west and south of 11 ° in the east, delineating areas that were suitable, unsuitable and intermediately suitable for schistosome transmission.

Temperature regimes identified by Pitchford (1981) as being suitable or unsuitable for schistosome transmission were selected from the digital climate dataset of Hutchinson *et al.* (1995), using the raster

capabilities of the Idrisi software package (Clark Labs, 1999). This involved an automated step- by- step selection of the temperature data contained in each raster cell. Suitable regimes were assigned a value of 1 and unsuitable regimes a value of 0 and the point prevalence data superimposed to test the goodness of fit. The aim was to determine which of Pitchford's (1981) identified temperature and time combination(s) would best account for the disease observations in different areas of the country. The optimal combination of all temperature regimes produced the final temperature suitability map. The goodness of fit was determined by finding the specificity and sensitivity of the disease observations to the suitability map.

Estimates of population

Two population datasets were used to estimate the population living within the climate-suitable area. The first was derived from an African population density dataset (Deichman, 1996) with predictions for 1995 and the second was South African census data for 1996 (Census South Africa, 1996). Population data for 5 to 14 year old children were superimposed on the raster images and totals were extracted. The reason for choosing estimates of only this age group is that they are more likely to be infected with schistosomiasis than other age groups (Schutte *et al.*, 1995), and hence are largely responsible for maintaining transmission in endemic areas.

3. Results

Suitability Maps using Temperature

The distribution of *S. haematobium* extends from the North-West Province, Gauteng, Limpopo Province and Mpumalanga southwards to KwaZulu-Natal and Eastern Cape (Fig. 1a). The distribution of *S. mansoni* (Fig. 1b) lies entirely within that of *S. haematobium*, mainly in Limpopo, Mpumalanga and KwaZulu-Natal provinces. For *S. haematobium* (Fig. 2a), the optimal mask was created using the following temperature cut-offs, (i) minimum temperature not more than 1°C, for one month or more, (ii) temperature range not less than 14°C during December and January (mid-transmission season) and (iii) a minimum temperature not less than 14.5°C, for four months or more. Grey denotes the areas that are identified in this study as experiencing suitable temperatures for the transmission of *S. haematobium*. Pitchford (1981) concluded that areas experiencing a minimum temperature not less than 14.5°C, for four months or more were suitable for transmission and that cooler temperature regimes were unsuitable.

The map for *S. mansoni* (Fig. 2b) was obtained using the following temperature regimes, (i) a minimum temperature not more than 3°C, for one month or more, (ii) a temperature range of 14° or more during December and January (mid-transmission season) and (iii) a minimum temperature not less than 16°C for two months or more. As with *S. haematobium*, the cooler temperature regimes were rated by Pitchford (1981) as being unsuitable for *S. mansoni* transmission while the relatively warmer regimes (16° or more) were considered suitable.

The sensitivity of the derived temperature map for *S. haematobium* was calculated to be 87.78% and the 95% confidence interval for the presence of urinary schistosomiasis was 86% to 89%. This indicates that 87.78% of the positive disease data points lay within the temperature-suitable zone. The proportion of true negatives that were correctly identified by the temperature mask was 52.57%, but this estimate was not very precise (95% confidence interval 48-57%). The derived temperature suitability map for *S. haematobium* thus had a high sensitivity (87.78%) but a relatively low specificity (52.57%).

The map for *S. mansoni*, derived using different permutations of temperature, had a lower specificity than the *S. haematobium* model because only 45% of the true negative data points lay outside the unsuitable temperature zone (95% confidence interval 41-48%). The sensitivity was 93.10% with a 95% confidence interval of 91% to 95%. Thus, the optimal temperature mask for *S.mansoni* was highly sensitive (93%) but not as specific (45%) and hence did not adequately account for disease absence.

Comparison of outputs using climate data from Hutchinson et al. (1995) and Schulze (1997)

Idrisi-based cross classification of the maps obtained using the different climate data sourced from Hutchinson *et al.* (1995) and Schulze (1997) produced a 0.84 Kappa indicating a close correlation (Fig 3). Cross classification of the actual climate data produced 0.81 as the overall Kappa, also indicating a close correlation with differences observed along the border between North-west and Limpopo provinces.

Number of school-age children living in temperature-suitable zones

About 3.9 million children live in temperature-suitable zones according to the Deichman (1995) population data run against the Schulze's (1997) climate data (table 2). This increases to 4.1 million when the data of Hutchinson *et al.* (1995) are used. Feeding back the same climate datasets against the 1996 South African population census data produced higher estimates of between 4.3 and 4.4 million respectively.

Table 2: Estimated number of children living in temperature- suitable zone

Climate Data Source	**Deichman (1995) Population Data**	**Census SA (1998) Population Data**
Hutchinson *et al.* (1995)	4102334	4379079
Schulze (1997)	3903734	4258475

4. Discussion/Conclusion

The derived suitability maps confirm the eastern regions of the country as being suitable for both intestinal and urinary schistosomiasis transmission. Pitchford (1981) maintained that the distributions of both diseases were limited by lower temperatures. High temperatures (> 27°C) did not affect *S. haematobium* as much as they did *S. mansoni.* Pitchford (1981) regarded Mdn 14.5°C and Mdx 27°C for 4 months as minimal for transmission. However, once Mdx exceeded 27°C, there was a decline in *S. haematobium* cercarial shedding.

None of the maximum temperature-based regimes that Pitchford used was included in the derivation of suitability masks for this study because they did not fit well against the disease observations. Consequently the model does not include the high and fluctuating temperatures that have been shown to be important in determining host snail distributions (Appleton, 1977; Appleton and Eriksson, 1984; de Kock and van Eeden, 1986). Indeed, Malone *et al.* (1994) found a positive association between the diurnal temperature difference (ΔT) and the risk of schistosomiasis in the Nile Delta in Egypt.

Following Pitchford (1981), a maximum temperature of 27°C for four months or more should be suitable for *S. haematobium* transmission. However, the zones where this temperature regime (maximum temperature of 27°C for four months or more) occurs, extend well beyond the disease's endemic area into the western regions of Free State but were too restricted in the Eastern Cape when compared with the observed distributions of the disease there. Hence, this temperature regime was excluded from the final *S. haematobium* model. Currently the southerly limit of *S. haematobium* is believed to lie in the former Transkei (Eastern Cape).

The optimal temperature mask for *S. mansoni* covers a marginally wider area along the eastern and southern coasts than that observed for *S. haematobium*. As mentioned earlier *S. mansoni* transmission is more sensitive to fluctuations in temperature than *S. haematobium* and this limits its distribution. *B. pfeifferi* also has a patchy distribution in the relatively warm parts of South Africa but it can tolerate wider temperature fluctuations than the *B. africanus* group snails. The optimal temperature for *B. pfeifferi* lies in the range 22°C to 27°C whilst that of the *B. africanus* group snails is 25°C (Appleton 1977; de Kock and van Eeden, 1986). The model developed in this study did not take into account the preferences of *S. mansoni* and *B. pfeifferi* for high and fluctuating temperatures, which may explain its low specificity.

Even though suitable temperature patterns extend beyond the Eastern Cape into Western Cape, no disease occurs in that area. Appleton and Stiles (1976) attributed this to the natural acidity of rivers in the area, which may be expected to adversely affect the snail hosts.

The anomalies between Pitchford's (1981) observations and the conclusions of this study illustrate the difficulty in defining strict domains for the occurrence of schistosomiasis based on temperature-derived criteria alone. While *S. haematobium* could thrive at high temperatures, there are other prevailing environmental factors such as rainfall and the stability of snail habitats which may restrict transmission and consequently limit the distribution of urinary schistosomiasis. Clearly, these other environmental variables deserve consideration if the aim is to construct a robust spatial model for schistosomiasis. The results reported here are unique because they are based on Pitchford's (1981) comprehensive description of the temperature/schistosomiasis relationship in South Africa. However, these results are not directly comparable to other GIS models of schistosomiasis transmission from Egypt (Malone *et al.*, 1994;

Malone, 1995) and Brazil (Bavia *et al.*, 1999) because they used different methodologies to spatially analyze their disease and climate data and statistically determine associations among their variables.

In the absence of national research or control programmes for schistosomiasis in South Africa, it is difficult to estimate the burden of schistosomiasis in the country and the corresponding risk of infection. A broad definition of risk is "the probability of harm" and generally risk assessment determines the probability and impacts resulting from contact with certain exposures such as climate, activities and individuals who carry a disease (McMahon and Pugh, 1970). Available estimates range from 3 million (Gear and Pitchford, 1979) to 3-4 million based on incidence data among school children (Wolmarans and de Kock, 2000) and 4 million (Schutte *et al.*, 1995). The latter authors based their figure on historical data, recognizing that a lack of recent surveys precluded a more reliable estimate. Utroska *et al.* (1989) estimated that 1 575 000 children under 15 years were infected in South Africa (estimated total population at risk: 20 000 000). However, these authors noted that the risk population on which their calculation was based was subject to error due to limited information on the focal distribution of schistosomiasis, as well as census data for the country at the time.

The present study's calculations using two different population models shows that between 3.9 and 4.4 million school-age children live in areas where temperature conditions are suitable for schistosomiasis transmission. Although these calculations were derived from different climate datasets, the results show some congruency. There are 9316804 children between 5 and 14 years living in the country (Census South Africa, 1996), and approximately 42% –45% of these children are at risk of schistosome infections. The lack of adequate information on the way in which the prevalence categories used by Gear *et al.* (1980) were calculated, restricts further analysis of the disease dataset using the current spatial methods. It is thus not possible to predict prevalence rates using this model. Different raster GIS analyses will allow the prediction of prevalence rates but this will be discussed in a separate communication.

5. References

Appleton, C.C. (1977). The influence of above-optimal constant temperatures South African *Biomphalaria pfeifferi* (Mollusca: Planorbidae). *Transactions of the Royal Society of Tropical Medicine and Hygiene,* **71**, 140- 143.

Appleton, C.C. (1978). Review of literature on abiotic factors influencing the distribution and life cycles of bilharzia intermediate host snails. *Malacological Review*, **11**, 1-25.

Appleton. C.C., & Stiles.G. (1979). Geology and geomorphology in relation to the distribution of snail intermediate hosts in South Africa. *Annals of Tropical Medicine and Parasitology,* **70**, 190-197.

Appleton, C.C. & Eriksson, I.M. (1984). The influence of fluctuating above-optimal temperature regimes on the fecundity of *Biomphalaria pfeifferi* (Mollusca: Planorbidae). *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **78**, 49- 54.

Appleton, C.C., Nxgongo, S.M., Braack, L.E.O. & le Sueur, D. (1996). *Schistosoma mansoni* in migrants entering South Africa from Mozambique- a threat to public health in north-eastern KwaZulu-Natal? *South African Medical Journal,* **86**, 350- 353.

Bavia, M.E., Hale, L.F., Malone, J.B., Braud, D.H. & Shane, S.M., (1999). Geographic information systems and the environmental risk of schistosomiasis in Bahia, Brazil. *American Journal of Tropical Medicine and Hgyiene*, **60**, 566- 572.

Beyers, N., Gie, R.P., Zietsman, H.L., Kunneke, M., Hauman, J., Tatley, M., & Donald, P.R. (1996). The use of a geographical information system (GIS) to evaluate the distribution of tuberculosis in a high-incidence community. *South African Medical Journal*, **86**, 40-44.

Brown, D.S. (1994). *Freshwater Snails of Africa and their Medical Importance*, 2nd Edn. London:Taylor and Francis.

Census South Africa. Digital Database. (1996). Pretoria: Statistics South Africa:

Clark Labs. (1999) Idrisi for Windows version 2.008. Worcester, Massachusetts: The Idrisi Project, Clark University.

Craig, M.H., Snow, R.W., & le Sueur, D. (1998). A climate-based distribution model of malaria transmission in Africa. *Parasitology Today*, **15**, 105-111.

Cross, E.R., Perrine, R., Sheffield, C., & Pazzaglia, G., (1984). Predicting areas endemic for schistosomiasis using weather variables and a Landsat database. *Military Medicine*, **49**, 542-544.

Cross, E.R. & Bailey, R.C. (1984). Prediction of areas endemic for schistosomiasis through use of discriminant analysis of environmental data. *Military* Medicine, **149**, 28-30.

de Kock, K.N. & van Eeden, J.A. (1986). Effect of programmed circadian temperature fluctuations on population dynamics of *Biomphalaria pfeifferi* (Krauss). *South African Journal of Zoology*, **21**, 28-32.

Deichman, U. (1996). *Africa Population Database*. Internet, http://grid2.cr.usgs.gov/globalpop/africa/

Donnelly, F.A & Appleton, C.C. (1985). Observations on the field transmission dynamics of *Schistosoma mansoni* and *S. mattheei* in southern Natal, South Africa. *Parasitology*, **91**, 281-290.

Gear, J.H.S. & Pitchford, R.J. (1979). *Bilharzia in South Africa*. Pretoria: Department of Health.

Gear, J.H.S., Pitchford, R.J. & van Eeden, J.A. (1980). *Atlas of Bilharzia in South Africa*. Johannesburg. Joint Publication by the South African Institute for Medical Research, South African Medical Research Council & Department of Health.

Hutchinson, M.F.H.A., Nix, H.A., McMahon, J.P & Ord, K.D. (1995). Africa - A topographic and climatic database, CD-ROM, 1st Edn. Canberra, Australia: Centre for Resource and Environmental Studies, Australian National University.

Joubert, P.H., Pretorius, S.J., de Kock, K.N & van Eeden, J.A. (1984) The effect of constant low temperatures on the survival of *Bulinus africanus* (Krauss), *Bulinus globosus* (Morelet) and *Biomphalaria pfeifferi* (Krauss). *South African Journal of Zoology*, **19**, 314-316.

Malone, J.B., Huh, O.K., Fehler, D.P., Wilson, P.A., Wilensky, D.E., Holmes, R.A. & Elmagdoub, A.I. (1994). Temperature data from satellite imagery and the distribution of schistosomiasis in Egypt. *American Journal of Tropical Medicine and Hygiene*, **50**, 714-722.

Malone, J.B. (1995). The geographic understanding of snail borne disease in endemic areas using satellite surveillance. *Memorias do Instituto Oswaldo Cruz*, **90**, 205-209.

Malone, J.B., Adbel-Rahman, M.S., El Bahy, M.M., Huh, O.K., Shafik, M & Bavia, M. (1997). Geographic information systems and the distribution of *Schistosoma mansoni* in the Nile Delta. *Parasitology Today*, **13**, 112-119.

McMahon, B. & Pugh, T.F. (1970). *Epidemiology. Principles and Methods*. Boston: Little, Brown & Co.

Mqoqi, N.P.; Appleton, C.C. and Dye, A.H. (1996). Prevalence and intensity of *Schistosoma haematobium* in the Port St Johns District. *South African Medical Journal*, **86**, 76- 80.

Pflüger, W. (1980). Experimental epidemiology of schistosomiasis. I. The prepatent period and cercarial production of *Schistosoma mansoni* in *Biomphalaria* snails at various constant temperatures. *Zeitschrift für Parasitenkunde.* **63**, 159-169.

Pflüger, W., Roushdy, M. & El-Emam, M. (1984). The prepatent period and cercarial production of *Schistosoma haematobium* in *Bulinus truncatus* (Egyptian field strains) at different constant temperatures. *Zeitschrift für Parasitenkunde*, **70**, 95-103.

Pitchford, R.J. & Visser, P.S. (1965). Some further observations on schistosome transmission in the eastern Transvaal. *Bulletin of the World Health Organization*, **32**, 83-104.

Pitchford, R.J. & Schutte, C.H.J. (1967). Schistosomiasis in non-endemic areas in relation to migration. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **61**, 217-220.

Pitchford, R.J. & Visser, P.S. (1969). The use of behaviour patterns of larval schistosomes in assessing the bilharzia potential of non-endemic areas. *South African Medical Journal*, **43**, 983-995.

Pitchford, R.J., Meyling, A.H., Meyling, J. & du Toit, J.F. (1969). Cercarial shedding patterns of various schistosome species under outdoor conditions in the Transvaal. *Annals of Tropical Medicine and Parasitology*, **63**, 359-371.

Pitchford, R.J. (1976). Absence of schistosomes in potentially endemic areas in Africa. In: *Medicine in a Tropical Environment. Proceedings of an International Symposium*. South Africa, ed. Gear, J.H.S. pp. 667-677. Cape Town: A.A. Balkema.

Pitchford, R.J. (1981). Temperature and schistosome distribution in South Africa. *South African Journal of Science*, **77**, 252-261.

Porter, A. (1938). The larval Trematoda found in certain South African Mollusca, with special reference to schistosomiasis (bilharziasis). *Publications of the South African Institute for Medical Research*, **62**, 1-492.

Schulze, R. E. (1997). *South African atlas of agrohydrology and -climatology.* Report TT82/96. Pretoria: Water Research Commission.

Schutte, C.H.J., Fripp, P.J. & Evans, A.C. (1995). An assessment of the schistosomiasis situation in the Republic of South Africa. *Southern African Journal of Epidemiology and Infection,* **10**, 37-43.

Shiff, C.J. (1964a). Studies on *Bulinus* (*Physopsis*) g*lobosus* in Rhodesia. I- The influence of temperature on the intrinsic rate of natural increase. *Annals of Tropical Medicine and Parasitology*, **58**, 94-105.

Shiff, C.J.(1964b). Studies on *Bulinus (Physopsis) globosus* in Rhodesia. III- Bionomics of a natural population in a temporary habitat. *Annals of Tropical Medicine and Parasitology*, **58**, 240-255.

Shiff, C.J., Evans, A., Yiannakis, C., & Eardley, M. (1975). Seasonal influence on the production of *Schistosoma haematobium* and *S. mansoni* cercariae in Rhodesia. *International Journal of Parasitology*, **5**, 119-123.

Utroska, J.A., Chen, M.G., Dixon, H., Yoon, S., Helling-Borda ,M., Hogerzeil, H.V. & Mott K.E. (1989). An estimate of global needs for praziquantel within schistosomiasis control programmes. WHO/SCHISTO/89.102.

Waner, S. (1999). Health risks of travelers in South Africa. *Journal of Travel Medicine*, **6**, 199-203.

Wolmarans, C.T. & de Kock, K.N. (2000). Skistosomose, 'n onderskatte en verwaarloosde probleem, selfs in die endemiese gebiede van die Republiek van Suid Afrika. (Schistosomiasis, an underestimated and neglected problem, even in the endemic areas of the Republic of South Africa). *Suid-Afrikaanse Tydskrif vir Natuurwetenskap en Tegnologie*, **19**, 31- 36.

Figure 1A

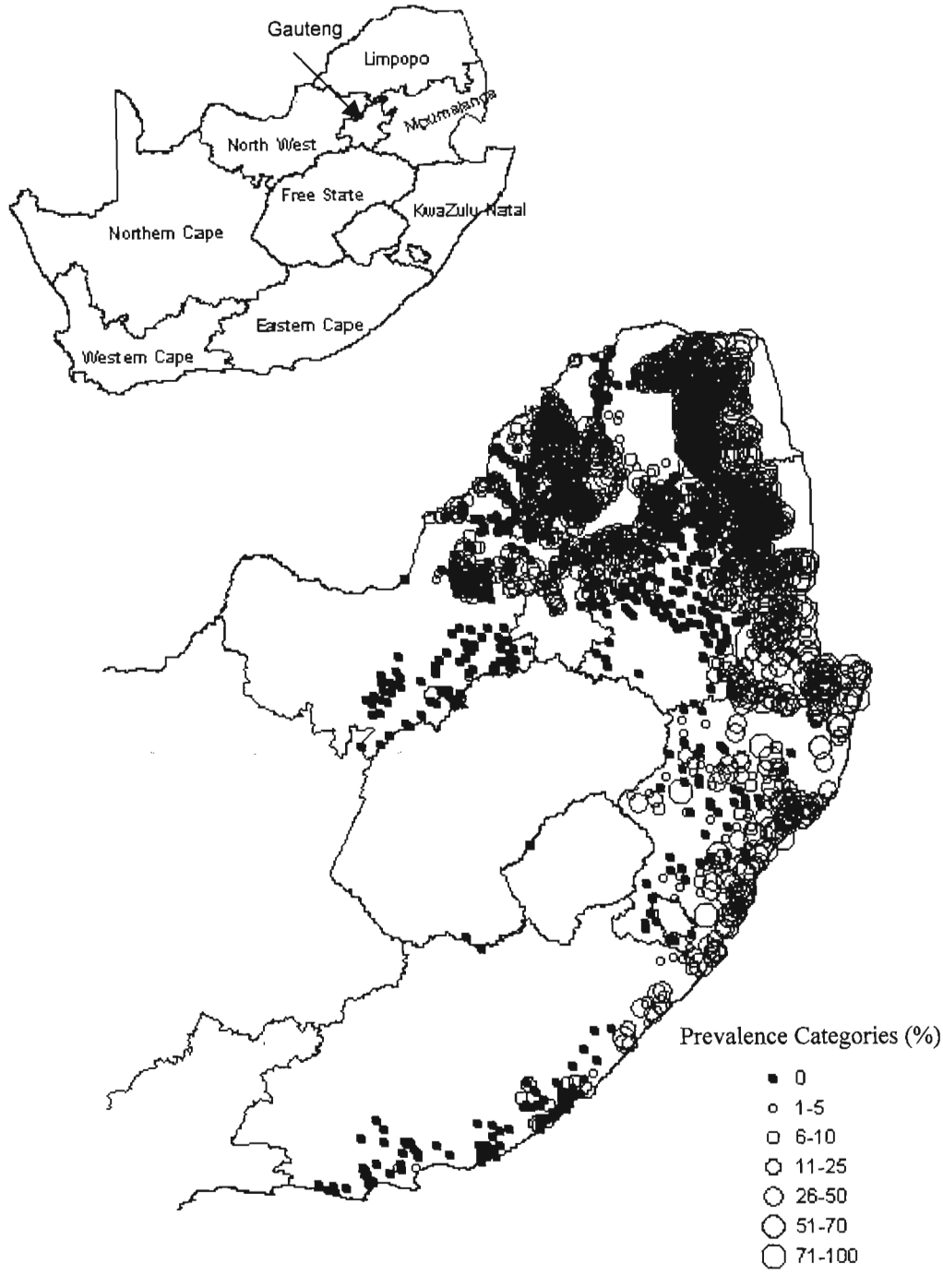

Fig. 1a The inset shows the boundaries of South Africa's nine provinces. Distribution of *S. haematobium* digitised from Atlas of Bilharzia (Gear *et al.*, 1980). The data are available as points, with each data point representing a disease prevalence category. The distribution of *S. haematobium* is broader than that of S.mansoni, with high prevalence (71-100%) extending from the Limpopo province and Mpumalanga down to KwaZulu-Natal on the East Coast.

Figure 1B

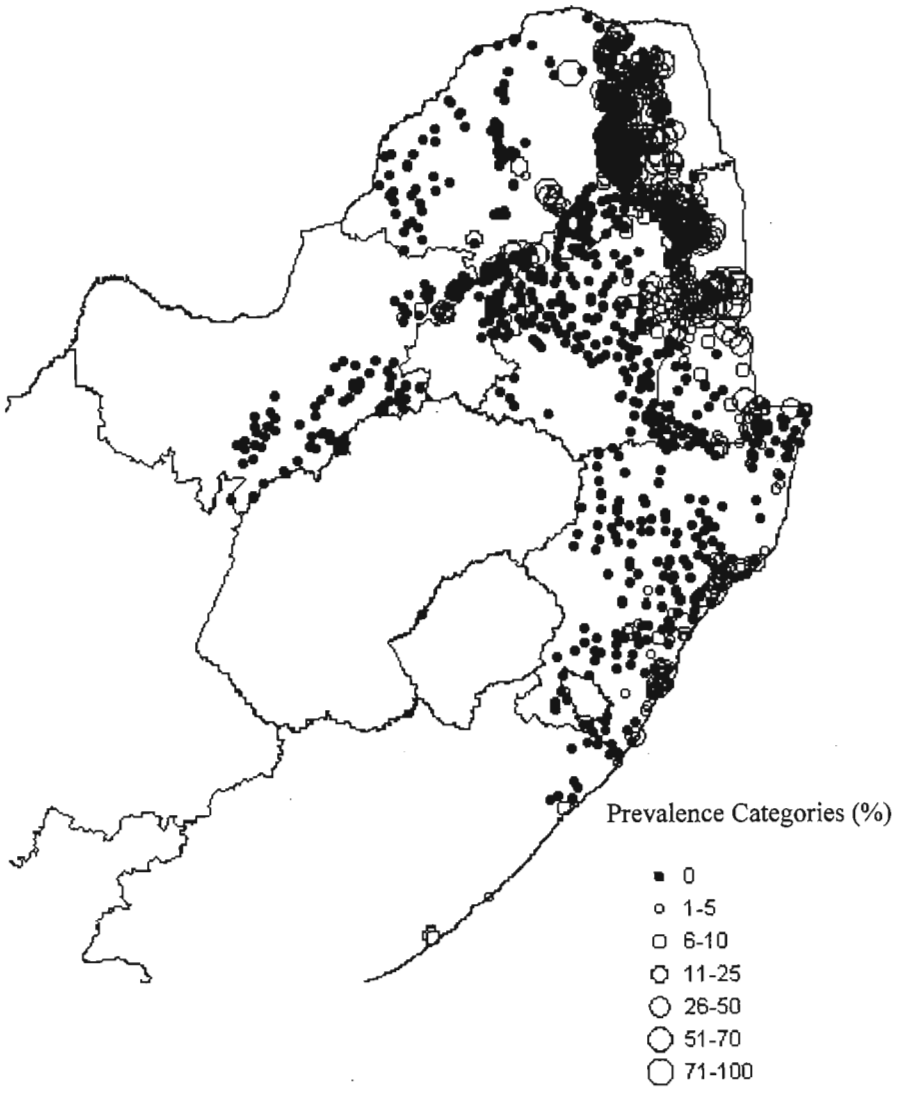

Fig. 1b Distribution of *S. mansoni* digitised from Atlas of Bilharzia (Gear *et a.l*, 1980). The prevalence of *S. mansoni* infections is contained within that of *S. haematobium*. The highest prevalence (71-100%) occurs mainly in the Limpopo province and Mpumalanga.

Figure 2a

Fig. 2a Temperature mask for *S. haematobium* using Pitchford's (1981) temperature regimes. The image effectively explained the distribution of urinary schistosomiasis using a combination of minimum temperature of 1^0C or less for one month or more, temperature range of 14^0C or more during December and January (mid-season of transmission) and a minimum temperature of 14.5^0C or more for four months or more. Grey denotes those areas where these temperature regimes apply and hence provide suitable conditions for transmission of *S. haematobium*.

Figure 2b

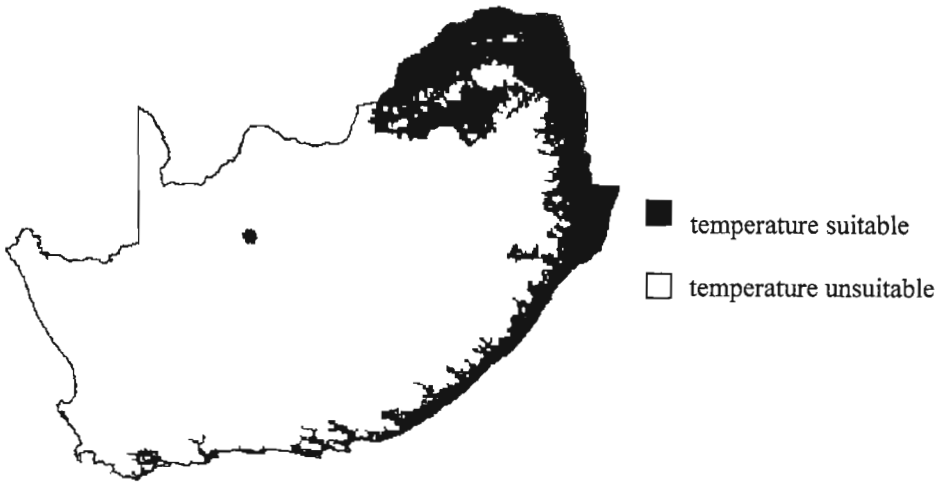

Fig. 2b Temperature mask for *S. mansoni* using Pitchford's (1981) temperature regimes. The image is a combination of a minimum temperature of 3^0C or less for one month or more, temperature range of 14^0C or more during December and January (mid-season of transmission) and minimum temperature of 16^0C or more for two months or more. These temperature regimes occur where *S. mansoni* presents. Grey denotes those areas where the temperature regimes are suitable for *S. mansoni* transmission to occur.

Figure 3

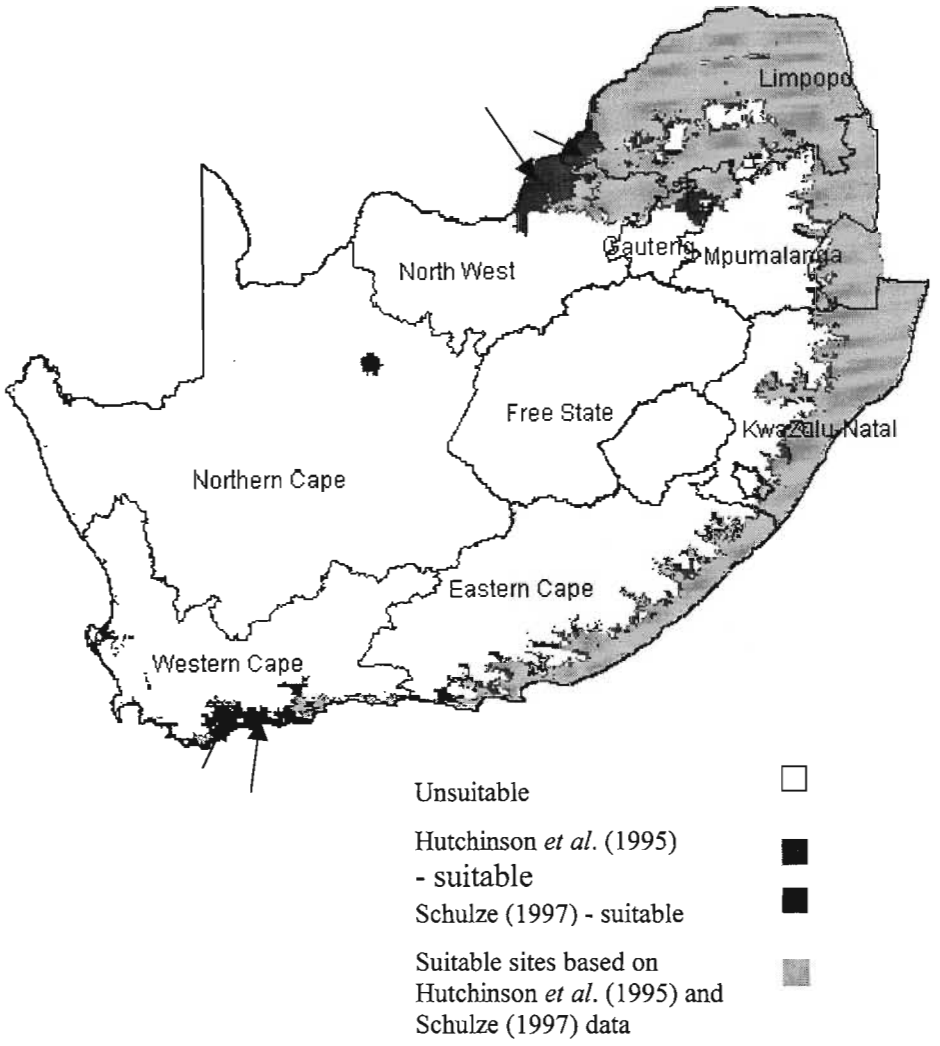

Fig. 3 Resulting map after running the *S.haematobium* temperature suitability model on two different climate datasets viz. Hutchinson (1995) and Schulze (1997). The arrows indicate where differences occur.