

**BARBARA SOLICH**



## **Increasing Malaria Risk in Eastern Africa**

**A Multi-Causal Analysis**

**KÖLNER ETHNOLOGISCHE BEITRÄGE**

Herausgegeben von Michael J. Casimir

**Heft 35**

**2010**

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im Nordwesten Namibias
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Rechtsschule
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**Options for Action in the Context of Water Scarcity and Institutional**  
**Constraints**
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## **Vorwort des Herausgebers**

Global climatic change has been analysed as a key driving force of social-ecological change in the coming decades. The increasing spread of Malaria due to warming is named as a major future problem of East Africa. In contrast to much of northern and southern Africa more humid conditions are expected for countries like Kenya, Uganda and Tanzania. Next to changing precipitation patterns and a profound snow melt on the glaciers of Mt. Kilimandjaro and Mt Kenya, warming and potentially higher rates of precipitation may bring about higher rates of Malaria infection. In fact, the empirically recorded cases of Malaria infections in the region seemingly support this argument. Infection rates have been constantly rising over the past two decades and many areas that had not been affected by Malaria for many decades, now have seasonal Malaria epidemics. It is especially the densely settled zone between 1500m and 2000m – the highly fertile Kenyan highlands – which seem to be affected most. Hence many indicators suggest a strong correlation between climatic change and the increase in Malaria.

Barbara Solich shows that underlying social-ecological processes are much more complex than that. In a multi-causal analysis she is able to show that a number of other factors may have even a greater effect on Malaria rates than climatic change. In order to present her argument systematically Solich first of all gives a short out-line of the state of research. Unfortunately most research on increasing Malaria rates in East Africa is concentrating on one explanatory variable only. Also reliable long term data is rare.

Solich presents her critique of current research foci and discusses a number of drivers that increase Malaria infections. She roughly differentiates between natural and socio-economic/political drivers – indicating a heuristic basis used in this identification. Among the natural drivers, climate change, land-use and cover changes, and drug resistance have been analysed, while demographic changes, poverty, and inadequate political responses have been identified as socio-economic/political drivers of the spread of Malaria in the region. Based on the analysis, she models the inter-connections between the factors and their influence on various stages of the malaria infectious cycle. Exemplary analysis of the Kenyan Highlands illustrates this interplay of factors and strengthens Solich's argument for further studies concerning Malaria-risk multiple causation.

Michael J. Casimir



## **Acknowledgments**

My utmost gratitude goes to my supervisor, Prof. Michael Bollig for his expertise, kindness and most of all for his willingness to help even from Namibia, where he did research.

My thanks and appreciation goes to Dr. Gabriela Litre, Dr. Cristina Inoue and Dr. Ana Peña del Vale from the International Human Dimensions Programme on Global Environmental Change (IHDP) for their scientific advice and inspiring questions.

Esra Bozkır's support and readiness to help made my work so much smoother, thank you Esra.

Above all, I thank my husband, Martin who stood beside me, encouraged me constantly and supported with technical advice. My thanks to my daughter Helena for giving me happiness and joy. Finally, I would like to thank my family for their continuous encouragement and interest in what I do.



## Table of Contents

List of Figures.....	0.....	vi
List of Abbreviations.....	0.....	vii
1. Introduction.....		9
2. State of Research .....	0.....	14
3. Regional Framework .....	0.....	16
4. Malaria and Risk of Malaria Infection in Eastern Africa .....	0.....	21
4.1. Malaria as a Vector-Borne Disease: Pathogenesis and Symptoms.....	0.....	21
4.2. Prevention and Treatment .....	00.....	25
4.3. Malaria Risk in the World and in the Countries of the East African Community: Past, Present and Future.....	0.....00	26
5. Drivers of the Increasing Malaria Infection Risk .....	0	34
5.1. Natural Drivers .....	0	36
5.1.1. Climate Change .....	0..	37
5.1.2. Land Use and Cover Changes .....	0..	43
5.1.3. Drug Resistance .....	0.	49
5.2. Social, Economic and Political Drivers .....		52
5.2.1. Inadequate Interventions .....		53
5.2.2. Demographic Changes .....		59
5.2.3. Poverty and Social Disturbances .....		62
6. Conclusion.....	00.....	68
7. Bibliography.....	0.....	70

## List of Figures

Figure 1. Physical map of Eastern Africa.....	page 18
Figure 2. Life cycle of malaria parasites.....	page 23
Figure 3. Malaria endemicity classes of Africa.....	page 25
Figure 4. Global distribution of malaria infection risk.....	page 28
Figure 5. Malaria risk in Kenya.....	page 32
Figure 6. Drivers of the increasing malaria risk.....	page 34
Figure 7. Temperature time series at the four locations in the African highlands.....	page 39
Figure 8. Development of malaria epidemic at different temperatures.....	page 40
Figure 9. Mean indoor resting density of <i>Anopheles gambiae s.l.</i> in Kabale district, Uganda, by swamp type.....	page 46
Figure 10. Spread of chloroquine resistance.....	page 50
Figure 11. Factors affecting parasite resistance.....	page 51
Figure 12. Problems and misconceptions, not addressed by public malaria preventive actions.....	page 54
Figure 13. Malaria morbidity and health care seeking behavior for malaria in Ugandan Mbarara municipality.....	page 58
Figure 14. A conceptual framework depicting the relationships between malaria and socioeconomic status.....	page 64

Cover photo by Valentina Buy

## List of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ATC	Artemisin Combined Therapy
APHRIC	African Population and Health Research Center
CC	Climate Change
DDT	DichloroDiphenylTrichloroethane
EAC	East African Community
EIR	Entomological Inoculation Rates
ENSO	El Niño Southern Oscillation
FAO	Food and Agriculture Organization
GDP	Gross Domestic Product
HBR	Human Biting Rate
HIV	Human Immunodeficiency Virus
IPCC	Intergovernmental Panel of Climate Change
IPT	Intermittent Preventive Treatment
ITN	Insecticide Treated Net
KEMRI	Kenya Medical Research Institute
MARA/ARMA	Mapping Malaria Risk in Africa/ Atlas du Risque de la Malaria en Afrique
PMO	Provincial Medical Officer of health
RBM	Roll Back Malaria partnership
RE	Risk of Epidemics
SP	Sulfadoxine-Pyremetamine
SR	Sporozoite Rate
ST	Seasonal Transmission
TP	Transmission Potential
UNDP	United Nations Development Programme
VC	Vectorial Capacity
WHO	World Health Organization
YT	Year-round Transmission



# 1. Introduction

In this study I intend to find evidence that the increasing risk of malaria infection in East Africa is a case of multiple causation. In this process various economical, political, natural and social drivers (factors), play a role. The main hypothesis I offer in this context is that the factors by themselves do not inevitably cause the phenomenon, but that they only induce the malaria risk when interacting with each other. If a particular combination of factors is in place, changes within the other factor will directly lead to changes in overall malaria infection risk. But if no supportive conditions preexist, changes within the same factor will not cause the effect of malaria risk increase.

In epidemiology multiple causation is “a believe that population patterns of health and disease can be explained by a complex web of numerous inter-connected risk and protective factors” (Krieger, 1994). In this thesis I argue that this can be transferred to malaria risk increase. Poverty, inadequate health systems, and other socio-economic factors can make people vulnerable to malaria emerging from physical or environmental (e.g. climatic) changes. On the other hand, while natural conditions stay the same, turbulences within social, political or economic factors can lead to the re-emergence of malaria and increased risk of malaria infection.

Human populations, although controlling natural conditions to some degree, are still vulnerable to changes of the environment. Humans are tightly connected to the environment they live in. They are able to regulate, in a more or less violent way, the natural setting, and are able to stimulate to some extent chosen environmental services. As people affect their natural environment, the modifications they cause may result in negative or positive feedback loops. Due to the presence of multiple bonds between humans and their environment, they are commonly being approached as one coupled social-ecological system (Anderies et al., 2004). Due to this interconnection, changes within one dimension result in modifications of the other one. Environmental changes result in populations adapting to them or regulating the modified environment in a way that it still serves their needs. The modes of those regulations, however, depend on cultural, social, economic and political characteristics of populations. Those interactions and dependencies lead to a complex coupling of social and environmental processes.

Although landscapes undergo constant changes under the influence of natural stressors, human interventions tend to have quicker and more dramatic impact on the state of landscapes. Changes in the environment that are due to human regulative and exploratory actions are called Global Environmental Changes and are seen often as threats to the natural equilibrium of ecosystems (Exener et al., 2008). Those changes include: global Climate Change, loss of

biodiversity, global ozone depletion, and the global decline in natural areas. Climate Change is the most commonly recognized factor causing malaria infection risk increase. It is true that climatic conditions play a very important role for the development of malaria parasites and its mosquito hosts. However, in this study I argue that other changes within either environmental or social, economic and political factors play a significant role in malaria infection risk as well. They all influence and alter ecological conditions in which the malaria parasite *Plasmodium sp.* and vector *Anopheles sp.* develop and reproduce.

## **The Presuppositions**

I base my hypothesis of multiple malaria risk causation on three presuppositions:

1. Malaria parasites have a complex life cycle that includes two hosts: mosquitoes of genus *Anopheles* and humans. Complexity and length of the parasite's life cycle allow various factors to affect it.

The complexity of *Plasmodium sp.* life cycle and accelerating anthropogenic pressure on the natural environment impede attempts to fully understand the factors that influence and alter this cycle. The variability of factors and feedback loops between them is enormous. These unsolved issues underlie the ongoing discussion on the causes of the growing numbers of people being exposed to malaria risk as well as the fact that many diverse theories have been developed to explain the foundations of the present malaria distribution dynamic<sup>1</sup>.

2. Development of malaria parasites and their host mosquitoes is directly correlated to the presence of vital natural resources in the environment.

Inadequate amounts of just one resource restrict biological development. Therefore, the lack of any essential natural resource, even in presence of all other factors enhancing malaria infection risk, results in a malaria-stable situation.

The relationship between the abundance of resources and the biological development of organisms has been described by the Law of the Minimum. It has been proposed by Justus von Liebig in 1840 and states that the growth of a plant (applicable also to animals, prokaryotes and protozoa) is limited by the resource that is represented in too small amounts (meaning: below a

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<sup>1</sup> The Malaria parasite life cycle is of high importance for understanding the processes that affect and alter it. Therefore this issue is going to be studied more in-depth in chapter 4, which is devoted exclusively to malaria and the risk of malaria infection in Eastern Africa.

minimum requirement) in the environment. At the beginning of the 20<sup>th</sup> century Liebig's Law has been substituted by the Law of Ecological Tolerance. It acknowledges that additionally to too small amounts of one resource, also too high ones may limit growth (and development) of the organism. Modern understanding of the Laws of Minimum and Ecological Tolerance is broader, and therefore allows more application to the malaria infection risk. Nowadays it is known that those laws may be applied also to whole populations<sup>2</sup>. Too low or too high temperatures and/or precipitation, lack of breeding sites/hosts or nutrition for host larvae and many other natural resources limit the development of both: malaria vectors and parasites. What's more, availability of resources may influence tolerance and requirement of another resource. If the amount of one necessary resource is slightly above the minimum value, it may, for example, induce an increase of the organism's minimum requirement towards another resource.

3. In some regions of East Africa an increased incidence of malaria infection has already been observed. In other areas it is consistently projected that the risk of getting ill will increase in the future.

The population at risk of malaria infection is defined as “the total population living in an area where conditions are suitable for malaria transmission, meaning the presence of the vector, adequate precipitation and temperatures suitable for parasite development” (Martens et al., 1999). “Risk of malaria infection” as used in this report corresponds to the nursing diagnosis of “risk of infection” that deals with individuals having special predisposition towards getting infected with particular infectious agents due to personal characteristics or to the fact of being exposed to a particular environment. In this case the risk of getting infected is highly dependent on the risk of being exposed to malaria. Malaria exposure is measured in person-months (Patz & Olson, 2006) and therefore dependent on the presence of conditions supporting parasite and vector development. Additionally the malaria infection risk is dependent on the Transmission Potential which is higher when more mosquito blood-meals end up with an uptake of parasite sporozoites. Thus, when more people are already infected, more healthy people are at risk of getting ill<sup>3</sup>. Despite a few malaria eradication programs, a tenfold increase of population at risk of malaria infection in the whole African Regional Office (WHO grouping) during the 20<sup>th</sup> century has been observed (Hay et al., 2004). This is accredited to a number of phenomena of which Climate Change is the one of the most represented in literature (eg. Martens et al., 1999; Rogers et al., 2002; Pascual et al., 2006).

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<sup>2</sup> This refers to the community level; however, there are many controversies as to if and to which scope they may still be correct. See Danger et al. (2008) for recent contributions to the discussion on Liebig's Law.

<sup>3</sup> This is the so called „community effect”. For more please see chapter 5.1.3.

Other determining factors include i.a. increased mobility, landscape transformations and political trends. The risk rise is the result of enhanced malaria Transmission Potential<sup>4</sup> in regions where conditions previously have not been suitable, or of a turn from seasonal towards year-round transmission.

## Methods

In this study I concentrate on exploring factors involved in the multiple causation process and do not isolate their individual quantitative inputs to the process. For fulfilling this goal I have selected scientific papers and research reports dealing with the issues of the increasing risk of infectious diseases - or specifically with malaria infection - on the global, regional and local scale. Appropriate data for the analysis has been identified through on-line search engines and obtained from World Wide Web resources as well as traditional libraries. The publications have been cross-referenced for the identification of further sources. Reports and statistics published on the official websites of World Health Organization, East African Community, Kenya Ministry of Health, and Kenya Malaria Information Service have also been reviewed.

To investigate the increasing risk of malaria infection in East Africa I propose a factor-analyzing tool I have created for this purpose. The tool consists of three main questions and two secondary questions. In Chapter 5 the different drivers are analyzed by using this tool. The tool inquires about the essential characteristics of the drivers involved and about their importance for malaria risk increase:

1. What processes underlie the driver and what are its characteristics?
2. How does each driver affect malaria distribution and the risk of malaria infection?
  - 2.1. How does it affect parasite and vector capacity?
  - 2.2. How does it affect human vulnerability?
3. What are the links to other drivers?

The analysis is supported by concrete examples and factual numbers extracted from statistics and other secondary data regarding the member-states of the East African Community.

In order to show when and how different factors may affect the process of malaria infection and lead to risk increase, I will present the complex life cycle of *Plasmodium* and its dependence on hosts presence and survival. I will also examine historic and present data as well as future projections of malaria infection risk in the region and analyze various factors that have already been

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<sup>4</sup> More about methods of malaria risk estimation can be found in chapter 4.

identified in previous studies as decisive for increasing numbers of people being at risk of getting ill now or in the near future. To demonstrate that the variables causing increase of malaria infection risk create a set of correlated issues and as such have to be analyzed together, I will examine the case of the Kenyan highlands. Lately, malaria emergence has been observed there and may be attributed to a combination of natural and socio-economic causes.

## 2. State of Research

In biological and medical sciences, systems of multiple causality are commonly analyzed with the use of statistical techniques like path analysis and multiple regression (Petraitis et al., 1996). Despite their usefulness for many types of scientific trials, they are being used when controlled experiments are conducted. This allows the identification of a *factual causation*, which can be statistically analyzed. Neither for this paper, nor in any report examined for this study, was a series of controlled experiments possible. The construction of a model successfully verified by a path analysis would be rather an explanation of the causality in a particular social-ecological system at a particular moment in time, than a general explanation of the multiple causality of the process (ibid.).

More common in malariology is the analysis of non-experimental data with the use of linear regression (Pongtavornpinyo et al., 2008). This is useful in the case of measurable changes in precipitation or temperature. However, its applicability is controversial when baseline and follow up values are not available and qualitative indicators are often confounding (Petrais et al., 1996).

Therefore in the literature I studied for this paper, most common was the analysis of how a single chosen factor influences malaria risk. And here studies of Climate Change - malaria nexus prevailed (Martens et al., 1999; Zhou et al., 2004). Studies on this issue gained popularity in the 1990s (Martens et al., 1995; Martens et al., 1999). The modeling of future impacts of Climate Change on malaria risk takes advantage of well-based Climate Change scenarios as well as modern satellite imagery and GPS systems (i.a. Omumbo et al., 1998; Rogers et al., 2002). Still, there are limitations to those high-scale predictions which are based on correlation and do not straightforwardly imply causation (Omumbo et al., 2005). Therefore, information about global distribution of populations at risk at various stages of malaria endemicity is criticized for not being accurate (Hay et al., 2004). Despite those constraints, numerous papers have already concentrated on malaria adaptive policies (Thomson, Doblas-Rheyes et al., 2006) or strategies preventing individuals from mosquito bites (Kimani & Vulule, 2006) based on the results of malaria-risk distribution studies.

Predicted increase of malaria risk has often been included in a broader context of infectious diseases emergence and malariology contributed to some comprehensive reviews on practical actions to be taken towards decreasing negative impacts of climatic changes on health of African (Patt & Winkler, 2007) or even global populations (McMichael & Campbell-Lendrum, 2003).

There has also been some, but not very extensive, research done on the influence of other than climatic factors on malaria infection risk. Studies included such issues as: land use and cover changes (i.a. Afrane et al., 2005), socio-economic status (i.a. Worall et al., 2002), drug resistance

(i.a. Olliaro, 2005), and demographic changes (i.a. Omumbo et al., 2005). Those natural and socio-economic factors that need to be taken into consideration are commonly mentioned in articles (Lindblade et al., 2000), but they are rarely elaborated longer than in a few sentences. However, Pascual et al. (2006) for example very clearly state that their studies on the influence of temperature changes on malaria can be interpreted only in the context of other factors (land use change, demographics and other), and that only an understanding of the interplay between them would result in a better understanding of malaria emergence. Still, as yet there have been not many papers taking multiple causation or at least a more-than-one-cause approach to the increase of malaria infection risk. Some attempts to analyze malaria infection risk as the phenomenon affected by a set of issues rather than by just one have been made within natural or social sciences separately (see i.a. Williams & Jones, 2004, for social scientific study). Interdisciplinary research on causes of malaria emergence has sometimes a political overtone (see Pattanayak et al., 2006, on the malaria-deforestation-poverty nexus). Nevertheless, there are some contributions to research on multiple causes of malaria risk increase worth mentioning, especially regarding the situation in the East African highlands. Lindsay and Martens claim the inter-relation of factors that govern malaria incidence in African highlands. In their review from 1998 they analyzed environmental and socio-economic factors that interact with each other and together affect biological factors that determine malaria incidence. Zhou et al. presented in 2004 an interesting model of highland malaria emergence that includes both natural and socio-economic factors leading to the recent epidemics.

### **3. Regional Framework**

The area of the East African Community presents a wide range of malaria risk categories due to its climatic and topographic characteristics (Martens et al., 1999). Together with the presence of political and economic bonds within the East African Community this region provides a rich material for an in-depth analysis of natural as well as social, economic and political causes of malaria risk increase. To understand the regional background I present in this chapter the social and ecological characteristics of the East African region in general, and of the Kenyan highlands in particular.

#### **The East African Community**

The East African Community (EAC) is an intergovernmental organization established in 1999 by three countries of the region: Kenya, Tanzania and Uganda. In 2007 Rwanda and Burundi joined the Community. EAC's objective is to enhance the cooperation between the member states within economic, political and social dimensions (see EAC Treaty, 1999, chapter 5). Since the EAC's establishment, a custom union and a common market as well as working groups on social challenges experienced by all member states have already been introduced to a certain degree. Up to the year 2012 it is planned to establish a Monetary Union and finally a Political Federation of the East African States (see EAC Treaty, 1999, preamble).

The five member states of the EAC not only share ecological, climatic, and topographic characteristics, but also history and many cultural features. This results in multiple economic and personal bonds between the countries and justifies drawing a common hypothesis regarding the phenomena of malaria risk increase.

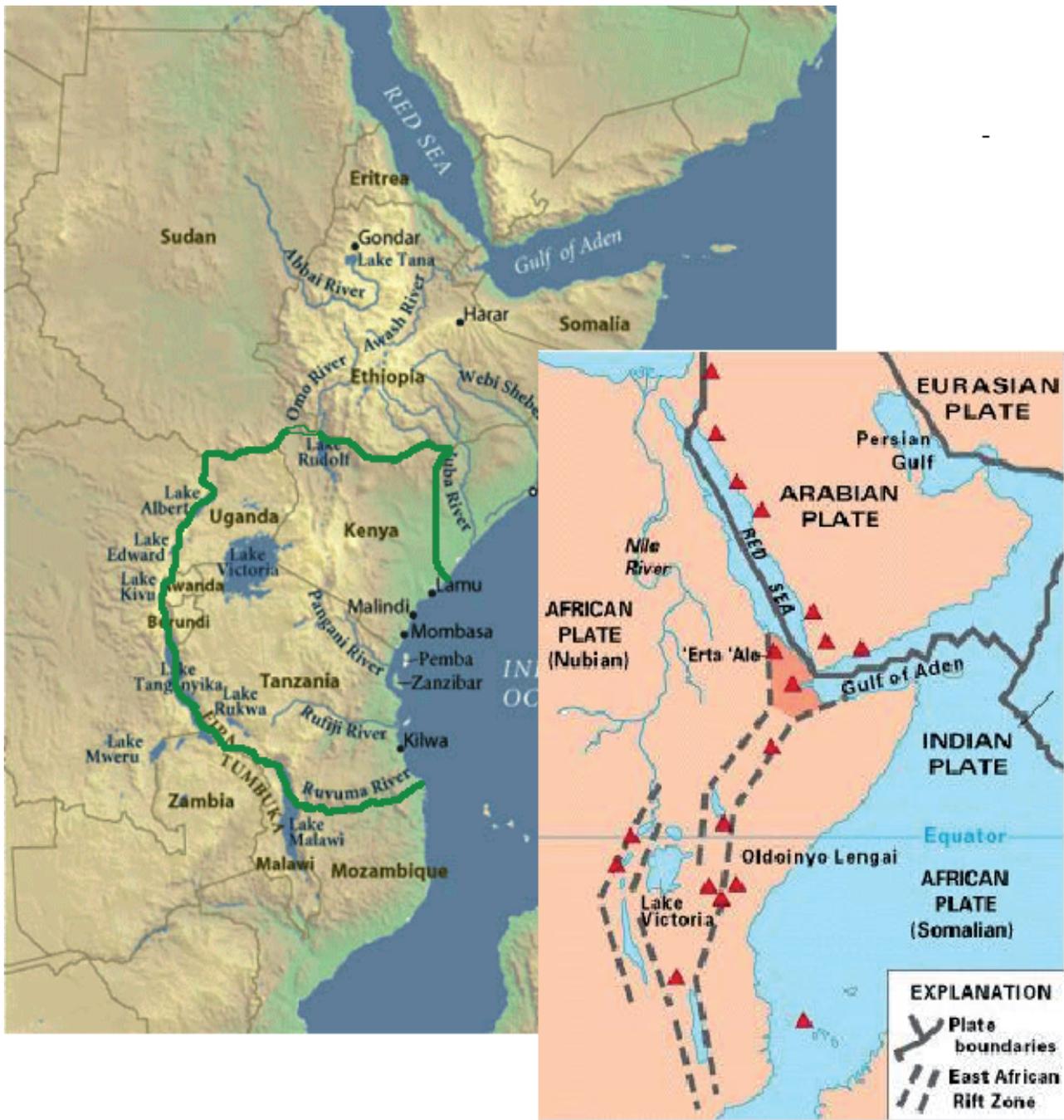
Due to the fact that Kenya, Tanzania, Uganda, Rwanda and Burundi cooperate within the East African Community, some actions have already been taken to standardize anti-malaria policy within those countries. The following steps towards the achievement of the EAC Treaty goals have been taken (see EAC Treaty, 1999, chapter 21, article 118; EAC Second Development Strategy, 2001, chapter 4.6.1):

- Enhancement of the EAC capacity to co-ordinate the implementation of health services and the exchange of experience within the community
- Harmonization of national health and drug policies
- Harmonization of pharmaceutical standards
- Undertaking of joint actions towards the prevention and control of communicable and vector-borne diseases

First outcomes of this harmonization policy include common action plans for the identification, monitoring and control of the main threatening diseases in the region established by the EAC health sub-sector organ - the East African Integrated Disease Surveillance Network (EAIDSNet).

Population density is very diverse within (Kenya, Tanzania) and between the countries of the EAC and ranges from 0-2 inhabitants per square kilometer in eastern parts of Kenya to more than 200 in Burundi, Rwanda and the Kenyan highlands. The richest country in the region is Kenya, with \$1800 US per capita placed on the 188<sup>th</sup> position in the world, whereas Burundi, the poorest of EAC with \$400 US is on the 227<sup>th</sup> position (CIA, 2008).

The East African Community member states are located astride of the Equator and are also called the Great Lakes Region as they are situated around the lakes Victoria, Tanganyika, and Nyasa - huge sweet water basins within the Rift Valley. The Rift Valley - divergent boundary between the core of the African Tectonic Plate and its Somali Subplate (see Figure 1) is edged by some of the highest mountains in Africa. The climate of the EAC countries varies strongly from hot in the lowlands to moderate in the highlands and from dry in the north-east to wet in the west. It is also affected by the displacement of a few wind convergence zones. Seasonality of rainfall differs strongly between locations from year-round near the lakes to the rainy season being as short as 1-4 months in the north of Kenya. Those topographic, hydrological and climatic characteristics determine the vegetation of the eastern EAC member states to consist of drier types than the vegetation of the countries west of the Rift Valley. North-eastern lowlands of the region are dominated by bushland and scrub, partially even having a desert character. Towards the western end of the East African Community, savanna and woodland savanna prevail. The south-west of the region is covered with woodlands and forests, just as the coast of the Indian Ocean is. The vegetation of highlands and mountains of the East African Rift Zone follows altitudinal patterns with mountain forests and afro-alpine vegetation (Davenport & Nicholson, 1993; Ge et al., 2008).



**Figure 1:** Physical map of Eastern Africa (left). Great Rift Valley (right). Green line is a border of the East African Community (EAC) that includes Burundi, Kenya, Rwanda, Tanzania and Uganda. (Modified from maps by Indian Ocean World Center, East African Community website and the on-line resources of the Astronomy Group at the Minnesota State University)

The five member states have topographic conditions that are responsible for altitudinal differences in malaria distribution. A great part of the region is made up of valleys cutting deep into highlands. The flat-bottomed valleys have moderate climate and high water accumulation potential. Thus they are characterized by the conditions suitable for malaria epidemics, whereas in high elevations malaria epidemics have lately been observed for the first time. Malaria-infection risk rose, followed by the frequency of epidemics. Also infection-caused mortality and morbidity in the highlands are observed to increase (e.g. Lindblade et al., 2000; Ndenga et al., 2006). Risk of infection, not only in the highlands, has increased in all countries of the EAC and is projected to increase even more (WHO, 2008). Up to now there have been numerous studies to the reasons of those phenomena. They provide sufficient information and data, but no agreed-upon explanation of the malaria risk increase in the region. This can be explained by the fact that parallel to the rise of malaria risk, also other processes took place. Firstly, in highly populated regions there has been a great increase in agricultural production. Cultivated areas have been obtained from previously natural ecosystems that often did not support malaria-host breeding, in contrary to agricultural lands (Ndenga et al., 2006). Secondly, anti-malarial drug resistance has spread in the eastern part of the African continent with an extraordinary speed (Greenwood et al., 2005). Thirdly, political and economic bonds within the East African Community, as well as extensive use of Kiswahili as lingua franca, have enhanced migration and exchange of knowledge between member states and individuals. Due to these dynamics within the social-ecological system of the East African Community no consensus has been reached as far as the reasons of malaria-risk increase are concerned. The variety of theories on which factor could have been decisive for malaria-risk increase provides an appropriate basis of argumentation for a multiple causation approach to this phenomenon.

## **Kenyan Highlands**

In the beginning of the fifth chapter of this paper the multi-causation of increased malaria infection risk is studied holistically on the example of the Kenyan highlands. Epidemics in the western highlands of the country at altitudes of 1500 – 2200 meters above sea level have spread dramatically at the end of the 20<sup>th</sup> and the beginning of the 21<sup>st</sup> century (Githeko & Ndengwa, 2001; Ndenga et al. 2006). Recently also malaria outbreaks in the central highlands of Kenya have been reported (Chen et al., 2006). Many environmental and social transformations take place in those regions with an increasing intensity and accompany changes in malaria transmission patterns.

Kenyan malaria situation in the highlands, which is of a major public health concern (Afrane et al., 2005), has been studied relatively in-depth. Additionally there are a few leading regional scientific institutions in Kenya that have studied vector-borne diseases in the highlands like the

Kenya Medical Research Institute (KEMRI) or the African Population and Health Research Center (APHRIC).

## 4. Malaria and Risk of Malaria Infection in Eastern Africa

According to the WHO, in 2006 half of the world's population, 3.3 billion people, was estimated to be at risk of malaria. 247 million malaria cases have been reported and 881 thousand people died of malaria (WHO, 2008). For the countries of the East African Community WHO estimated that there were more than 39 million cases of malaria in 2006 (WHO, 2008). That means that in just five countries 16% of the estimated global cases were concentrated. This depicts the importance of the malaria issue for politics and economy in the region for the well-being of its inhabitants. Furthermore, malaria is currently being observed in regions, which were considered previously as malaria free and it is re-emerging in areas where malaria control decreased its burden in the past. Malaria distribution expands, local incidence increases as well as the infection's severity, duration and resistance to treatment (Martens et al., 1999; Greenwood et al., 2005; Pattanayak et al., 2006; WHO, 2008).

In this chapter I will present the complex life cycle of malaria parasites, which includes two hosts and many stages of development. A description of malaria pathogenesis and symptoms will be followed by a short review of available preventive measures and possibilities of malaria treatment. The second part of this chapter will be devoted to changes of malaria risk over time. I will also discuss what exactly is meant by malaria risk and which aspects of malaria burden this term includes. The final section of the chapter will be the analysis of future malaria risk projections.

### 4.1. Malaria as a Vector-Borne Disease: Pathogenesis and Symptoms

Malaria is a vector-borne disease caused by a one-cell parasitic protozoon of genus *Plasmodium* and transmitted from man to man by mosquitoes of the genus *Anopheles*.

Four *Plasmodium* species account for most malaria infections in humans: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae*. In Africa *Plasmodium falciparum* prevails and is responsible for severe forms of infection. *Plasmodium vivax* and *Plasmodium ovale*, on the other hand, can produce resting forms that cause relapses after longer dormancy (Greenwood et al., 2005). *Plasmodium vivax* develops within the mosquito host at lower temperatures and therefore has the most extensive geographic range (WHO, 2008).

Seventy out of 422 species of genus *Anopheles* are vectors of malaria parasites (Martens et al., 1999). However, in Africa - and thus in the countries of the East African Community - the transmission by mosquitoes of the *Anopheles gambiae* complex accompanied by *Anopheles funestus* prevails. Especially *Anopheles gambiae* is characterized by high anthropophily and longevity. It is the most effective malaria vector in the world. In the areas of the EAC, where

density of mosquitoes is very high, average inoculation rate equals 121 infected bites per person per year (Hay et al., 2004). Globally there are regions where *Anopheles* mosquitoes are not present and thus those regions are malaria free (like large parts of Polynesia). On the other hand in Europe, where malaria has been successfully eradicated, Anophelines are still present (Martens et al., 1999). Anophelines go through four stages in their life cycle: egg, larva, pupa, and adult. It takes 5 to 14 days (dependent mainly on temperature) for the adult form to develop from an egg. Larvae of most *Anopheles* species live in clean, stagnant water bodies even so small as puddles after rain. Adult males feed on nectar and other sources of sugar and live for about a week. Adult females live 1-2 weeks<sup>5</sup> and also obtain their energy from sugar sources. However, they need blood to develop eggs, which takes 2-3 days in tropical temperatures (US Department of Health and Human Services).

The life cycle of the *Plasmodium* requires two hosts: mosquito and human. A person gets infected when a female mosquito of genus *Anopheles* takes a blood meal. Hematophagous mosquitoes require blood for their egg development. The life cycle of malaria is presented in detail in Figure 2.

The complexity of this life cycle is of great importance for changes in malaria risk. Factors can affect various stages of the cycle and therefore it is very difficult to control malaria risk. Human immunity, mosquito breeding, speed of parasite development in hosts, mosquito's susceptibility to getting infected while having a blood meal, humans' susceptibility of getting infected while the mosquito takes a meal, therapy efficiency, drug resistance, and many other factors affect the Transmission Potential and thus the risk of malaria infection.

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<sup>5</sup> They may survive even up to one month.



Malaria symptoms include: fever, shivering and muscle pains. Severe infection may lead to respiratory distress, cerebral malaria or severe malaria anemia. In endemic areas, malaria is also a major cause of perinatal mortality, low birth weight and maternal anemia (Greenwood et al., 2005). The severity of malaria infection depends on both human immunity and parasite characteristics. Generally, people exposed for a longer time to intensive malaria transmission, gain partial immunity and malaria has normally benign course at them. In contrary, people from areas of low malaria transmission do not develop partial immunity and suffer from more severe courses of the disease (Greenwood et al., 2005).

There are three types of malaria transmission (based on Martens et al., 1999; WHO, 2008):

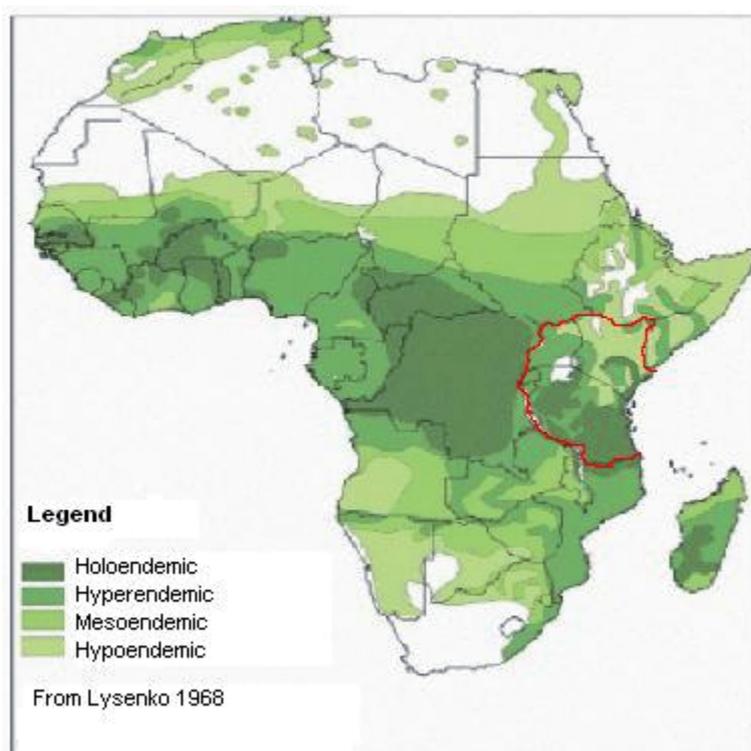
1. Year-round transmission, where climatic conditions support malaria during the whole year resulting in high yearly transmission rates (number of cases per population unit).
2. Seasonal transmission, where climatic conditions support malaria during part of the year (ranging from three to nine months) resulting in lower yearly transmission rates.
3. Epidemic transmission, where climatic conditions support malaria just on their extreme values, resulting in irregular epidemic outbreaks. Transmission rates (as well as mortality rates) are high during the epidemics, but near zero between them.

Endemicity is a term commonly used in malariology. It means the prevalence of malaria in the population that determines stability of transmission<sup>6</sup>. Endemicity is mainly being categorized into four classes (Hay et al., 2004). They are based on the Parasite Rate<sup>7</sup> in the studied population: hypoendemic  $<0.1$ ; mesoendemic 0.11-0.5; hyperendemic 0.51-0.75; holoendemic  $>0.75$ . For the three higher endemicity classes malaria transmission is generally stable. Regions of hypoendemic malaria are characterized by unstable transmission (Hay et al., 2008). Still it is possible that in areas of unstable transmission catastrophic malaria epidemics kill thousands of people (Reiter et al., 2004). Figure 3 shows malaria endemicity classes at the African continent.

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<sup>6</sup> Transmission is stable if it does not change much from year to year and is strongly insensitive to natural and man-made perturbations, including malaria-control measures. Instable transmission is highly sensitive to changes in external factors and thus to eradication programs (see Hay et al., 2004).

<sup>7</sup> The Parasite Rate is a rate of cases where asexual malaria parasites have been microscopically diagnosed in peripheral blood. Malaria epidemiological surveys are investigations on selected age-groups of a randomly sampled population in order to assess the degree of malarial endemicity in a location (see Hay et al., 2008).



**Figure 3.** Malaria endemicity classes of Africa. Red line is a border of the East African Community.

## 4.2. Prevention and Treatment

Use of mosquito bed nets is a widely recommended preventive measure against malaria, as well as is the vector control by indoor residual spraying with insecticides (eg. Greenwood, 2005; Teklehaimanot, 2007; WHO, 2008). There are two types of mosquito bed nets: non-treated and insecticide-treated nets. The latter have a great advantage over the former. They not only guard people from mosquito bites, but also kill mosquitoes when those get in contact with the net and repel vectors from resting indoors (Trklehaimanot, 2007). Nowadays a new generation of nets, long-lasting insecticidal nets<sup>8</sup>, gain popularity especially in Africa, where its supplies (sold and distributed for free) have reached 36 million in 2006 (WHO, 2008). On the African continent in average just 26% of all people at risk own a mosquito net of any kind<sup>9</sup>. Kenya is one of the few countries where population coverage is higher than 50% (ibid.).

Vector control can also be done by indoor residual spraying using insecticides. This method is used rather focally when needed. Botswana has one of the world's highest numbers of households at malaria risk that regularly use insecticides: more than 70% (WHO, 2008). DDT (dichlorodiphenyltrichloroethane) is very successful against mosquitoes, but can affect human

<sup>8</sup> Insecticide is here incorporated into the fibers, which is released over a period of 4-5 years (WHO, 2008).

<sup>9</sup> It has to be noted that not all people who own a net actually sleep under it. Using or non-using of bed nets is associated with their costs as well as with personal behavior and believes. Additionally, some non-treated nets are in bad physical state (torn) and not all people that own an insecticide treated net regularly re-treat it with an insecticide (WHO, 2008).

health negatively. Thus, other insecticides (i.a. carbamates, pyrethoides) are being used as an alternative to DDT (see Greenwood et al., 2005).

Further preventive measures include: traditional plant products or commercial mosquito coils that, when burned at night, repel mosquitoes; repellent in form of a cream to put directly on uncovered skin; environmental management like clearing of bushes or drying of ponds (Alaii et al., 2003); and prophylaxis drugs based on chemoprophylaxis, which are, however, still used exclusively for highly vulnerable groups: travelers, pregnant women and children below 5 years of age (Greenwood et al., 2005). There is still no vaccine against malaria and despite the current efforts it will be probably not before 2015 that one is available (ibid.).

Historically malaria has been treated with chloroquine as a first-choice medicine. However, since the drug resistance to chloroquine started to grow some alternatives have been developed. The first one was sulfadoxine-pyremetamine, but recently more and more cases of resistance also against this drug have been reported (Greenwood et al., 2005). Now treatment based on artemisin (Artemisin Combined Therapy) is commonly recommended. However, coverage of the ill with any treatment is still poor. A rare exception is the United Republic of Tanzania, where all reported malaria cases have been treated with ACT<sup>10</sup> (see WHO, 2008).

### **4.3. Malaria Risk in the World and in the Countries of the East African Community: Past, Present and Future**

Population at risk of malaria infection is defined by the World Health Organization as “the total population living in areas where malaria is endemic (low and high transmission)” (WHO, 2008). This definition excludes people who live in areas where the Parasite Rate is lower than 0.1. However, in those regions the risk of epidemics remains if changes in natural and/or man-made conditions support an increase in malaria transmission (Hay et al., 2004). Thus, more appropriate seems the definition of Martens et al., who describe the population at risk of malaria infection as “the total population living in an area where conditions are suitable for malaria transmission, meaning the presence of the vector, adequate precipitation and temperatures suitable for parasite development” (Martens et al., 1999). Risk of infection is estimated with the use of various methods but none of them is universally applicable (Doolan, 2002). Direct methods include i.a. measures of passive and active surveillance<sup>11</sup>. Passive Surveillance bases on the ratio of confirmed malaria cases

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<sup>10</sup> Interestingly the number of patients that received anti-malarial drugs are higher than the estimated cases (101.5%). This can be due to no blood-test diagnosis of some cases and ACT treatment based on febrile symptoms (WHO, 2008).

<sup>11</sup> For exhaustive information on methods used in malariology please refer to: Doolan, 2002.

to some defined total (for example all hospital admissions or deaths). This method is appropriate for hypo-and meso-endemic areas, where malaria is symptomatic. Active Surveillance is used in hyper-and holo-endemic regions where parasitemia is not always accompanied by fever. In this method population is screened for parasite presence in blood. Malaria risk can be also estimated indirectly by observation of environmental factors supporting or not-supporting malaria transmission, or entomological aspects of malaria infection cycle (Doolan, 2002). Indirect estimates of malaria risk prevailed in sources studied for this paper. Most commonly the entomological measure of Transmission Potential (TP) has been used. It is expressed as:

$$TP = \frac{b * c * a^2 * p^n}{-\ln(p)}$$

where (after Martens et al., 1999):

- a* is the *human-biting rate*: mosquito bites per person per day
- b* is the *human susceptibility*: efficiency with which an infective mosquito infects a human
- c* is the *mosquito susceptibility*: chance that an uninfected mosquito acquires infection from biting an infectious person
- p* is the *daily survival probability* of the mosquito
- n* is the *incubation period* for the parasite inside the mosquito.

Each of those variables has to be calculated basing on various empirical data.

Transmission Potential bases on the concept of the Vectorial Capacity (VC) that is defined as “the number of new mosquito infections daily that arise from one infected individual in a non-immune population if all biting mosquitoes become infected” (Githeko & Ndegwa, 2001). Transmission Potential additionally takes two facts into consideration: that not every biting mosquito inevitably gets infected (variable *c*) and that some members of the population may be more vulnerable to infection than others (variable *b*)<sup>12</sup>.

According to the WHO, regions can be classified as being of low or high malaria risk. Regions are ranged as “low risk” if less than 1 case per 1000 people is reported. “High risk” means the opposite: 1 or more malaria cases per 1000 people<sup>13</sup> (WHO, 2008). Figure 4 below presents global distribution of low and high risk of malaria infection based on microscopically confirmed cases. This classification already includes results of malaria control interventions that influence the

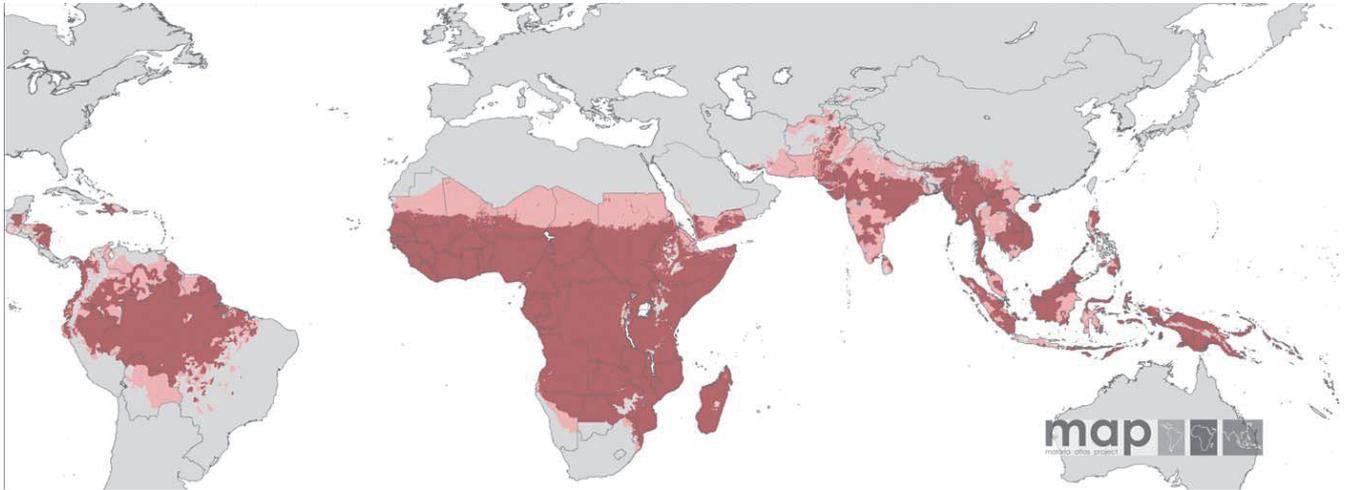
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<sup>12</sup>Martens et al. (1999) classify malaria risk besides the Transmission Potential also according to the seasonality and endemicity of infection in the area. The three categories they propose are:

- Risk of epidemics (RE)- low values of Transmission Potential (TP) for three or less consecutive months a year
- Risk of Seasonal Transmission (ST)- TP>0 for more than three, but less than seven consecutive months
- Risk of Year-round Transmission (YT)- TP>0 for seven or more consecutive months.

<sup>13</sup> Of course this categorization is afflicted with high uncertainty due to incomplete malaria reports.

number of reported cases. However, due to highly unequal access to malaria prevention, not every member of the population classified as being at high risk of malaria infection actually is at high risk and vice versa (Martens et al., 1999).



**Figure 4.** Global distribution of low and high risk of malaria infection. Dark-red are areas of high malaria risk where malaria transmission is stable; pink are areas of low malaria risk where malaria transmission is unstable; light gray are areas where there is no malaria transmission. The few areas, for which no data could be obtained, mainly found in India, are colored in dark gray. The borders of the 87 countries defined as *Plasmodium falciparum* endemic are shown. Highland areas where risk was excluded due to temperature appear in light gray. The aridity diminishes risk mainly in the larger extents of unstable (pink) areas particularly in the Sahel and southwest Asia (southern Iran and Pakistan). Note that this map presents only risk of malaria due to *Plasmodium falciparum*. (Guerra et al., 2008).

Historically the maximum malaria distribution in the world was around the year 1900 when it reached latitudes of 64° north and 32° south<sup>14</sup>. However, there is evidence that the parasite-host relationship between *Plasmodium falciparum* and humans can be dated back to the Pleistocene<sup>15</sup>. During the 20<sup>th</sup> century there has been a great decline in areas at malaria risk due to intensive prevention and control efforts. In 2002 malaria areas made up 27% of the Earth's land surface, whereas in 1900 it was 53%. However, those gains were greater in areas with low malaria endemicity, whereas they were negligible wherever endemicity was high (no reduction of holoendemic malaria area). Therefore after the first very quick reduction in areas, countries and population at risk, the decline lost its momentum (see Hay et al., 2004).

The malaria control era started after the discovery of the fact that Anophelines transmit malaria. Worldwide the efforts concentrated on the eradication of mosquitoes by destroying their

<sup>14</sup> This shows that malaria is not exclusively a tropical disease, but that its present distribution is rather an effect of extensive control measures (Hay et al., 2004).

<sup>15</sup> Those latitudes correspond with the 15° isotherm that supports also *Plasmodium vivax* transmission (Hay et al., 2004).

breeding sites. Later, when dichlorodiphenyltrichloroethane (DDT) had been discovered, it was used for killing the mosquitoes themselves. Due to its effectiveness DDT insecticide has been used alongside with chemoprophylaxis on a big scale in the global malaria eradication program that the WHO implemented between 1955 and 1969. Although successful, the program had some weak points: consolidation and maintenance were insufficient (in India malaria re-emerged), and sub-Saharan Africa has been completely excluded from the efforts (Hay et al., 2004). After the WHO eradication program was terminated, national efforts in Central and South America, China, the Middle East and latitudinal extremes of Africa brought only a slight further decline in malaria-risk areas. Population at risk, however, even increased between 1992 and 2002 (ibid.). In Africa the increase in malaria-caused mortality has been higher in east and south than in the western part of the continent (Greenwood et al., 2005). Due to various reasons malaria emergence and re-emergence<sup>16</sup> have been lately observed in a number of regions in the world (Possas, 2001).

In the late 1990s international efforts for the first time turned towards malaria control in endemic areas. Currently the Roll Back Malaria Partnership<sup>17</sup> has formulated its main targets to be achieved before the end of 2010: 80% coverage of population at risk with vector control; 100% coverage of pregnant women with Intermittent Preventive Treatment (IPT), 80% of malaria cases diagnosed and appropriately treated; reduction by half of malaria cases and deaths compared to the numbers from 2005 (RBM, 2008).

Presently WHO estimates that there are 2.1 billion people at low risk of malaria and 1.2 billion at high risk. Just 49% (647 millions) of the latter live in Africa, but as much as 91% of the people at any risk in Africa are at high risk. Additionally, 86% of the world's malaria cases happen there, which means that Africans are exposed to higher actual risk of getting ill<sup>18</sup> (WHO, 2008). At the population level high risk of infection leads to an increasing mortality risk (Omumbo et al., 2005). It thus does not surprise that more than 90% of all malaria deaths are estimated to happen in Africa, 85% among children below 5 years of age. Therefore the risk of death from malaria is much higher in Africa than in other regions of the world (ibid.).

The countries of the East African Community, as already mentioned, make up 16% of global malaria cases. The United Republic of Tanzania and Kenya are even among the five countries<sup>19</sup> in which more than half of the African malaria cases were estimated to have happened in 2006 (WHO, 2008).

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<sup>16</sup> Emerging are diseases whose pathogenic agents are unknown and unexpected or whose incidences have increased in the last two decades. Re-emerging are diseases that resurge in the region after a significant decline (from Possas, 2001).

<sup>17</sup> The RBM Partnership was launched in 1998 by WHO, UNICEF, UNDP and the World Bank, in an effort to provide a coordinated global response to the disease.

<sup>18</sup> This is due not just to high Transmission Potential, but also to poor malaria prevention and treatment.

<sup>19</sup> The others are Nigeria, Democratic Republic of Congo and Ethiopia.

However, it is important to note that malaria cases and death records are far from being accurate. Lack of infrastructure often does not allow blood tests for clinical diagnosis of every malaria case or death. Symptomatic diagnosis results in overestimation of malaria cases, with fever cases being treated as malaria “just in case”. On the other hand just one of five malaria deaths is reported and national inventories are in some countries highly incomplete. Incomplete reporting results in underestimation of malaria cases. And so does the fact that a big proportion of people suffering from malaria does not seek help in the public health sector and falls out of the records (WHO, 2008). Therefore the lower and upper estimates of malaria cases may differ dramatically: in case of 2006 analysis of malaria in Kenya the difference was fivefold (WHO, 2008). Lack of reliable data forces researchers to seek help in remote sensing. Geographic features observed by satellite or ground-based systems can be matched to the patterns observed in areas where malaria epidemiology is known (Greenwood et al., 2005).

Predictive models of the development of malaria risk in the future may be classified as either biological or statistical (Haines et al., 2006). Biological models aggregate the influence of different factors on the components of the transmission cycle. Statistical models seek for correlations between observed changes in factors and changes in malaria incidence and/or distribution. It is difficult to validate global models as they analyze systems that are never closed and they are based on incomplete, often unreliable data. Researchers are forced to use simplifications and assumptions that may decrease accuracy of results. Still, there are quite a few future malaria risk scenarios that refer to the global scale and they consistently predict an increase in both population and areas at risk of malaria infection. Hay et al. (2004) estimated that in 2010<sup>20</sup> there will be an increase in the *number* of people living in all endemicity areas. However, they believe that *proportionally* to global population at risk of malaria infection, only hyper- and holoendemic classes would experience an increase. As the past experiences show it is easier to control hypo- and mesoendemic malaria. Still, this projection takes just demographic changes (adjusting for increasing urbanization) into consideration and refers to an assumption that endemicity would not change or that, due to effective control, it would decrease by one class for the given area. Natural factors that affect malaria endemicity (climatic conditions and vector species distribution) have not been taken into consideration. Simulations of future climatic conditions have been included into projections of malaria incidence (not risk!) by Zhou et al. (2004) who studied malaria in the East African highlands. They estimated that the malaria incidence could increase even threefold if the average temperatures (both minimum and maximum) rise by 3.5°C. And, according to scenarios proposed by the Intergovernmental Panel on Climate Change (IPCC) such an increase in air temperature is possible already by the end of the 21<sup>st</sup> century (Solomon et al, (eds.), 2007). Therefore the margins

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<sup>20</sup> At the time this publication went to press, no numbers were still available.

of malaria distribution (both latitudinal and altitudinal ones) could experience an increase in malaria Transmission Potential and so in malaria infection risk.

The global distribution of malaria vectors is not known with full certainty due to the fact that reliable data is not available for large areas of the world. Probably this is the reason why most projections of future malaria distribution do not take vector distribution (neither at present nor estimated for the future) into consideration. Still this may be of basic importance as vector presence is a prerequisite for malaria transmission. One of the rare exceptions was the study by Martens et al. (1999). The authors estimated future changes of malaria risk and adjusted scenarios of climate changes for vector distribution. The result was a projection of malaria risk increase in all regions of the world with just a few exceptions. However, the magnitude of those changes depends on the climate change scenario and the vector species in the region. Additionally, the authors examined the Transmission Potential in the course of the year and estimated that it would change towards more months supporting malaria transmission.

More evidence on how malaria risk could increase in future due to changes in external factors will be presented in the next chapter, where each of the factors will be analyzed in-depth.

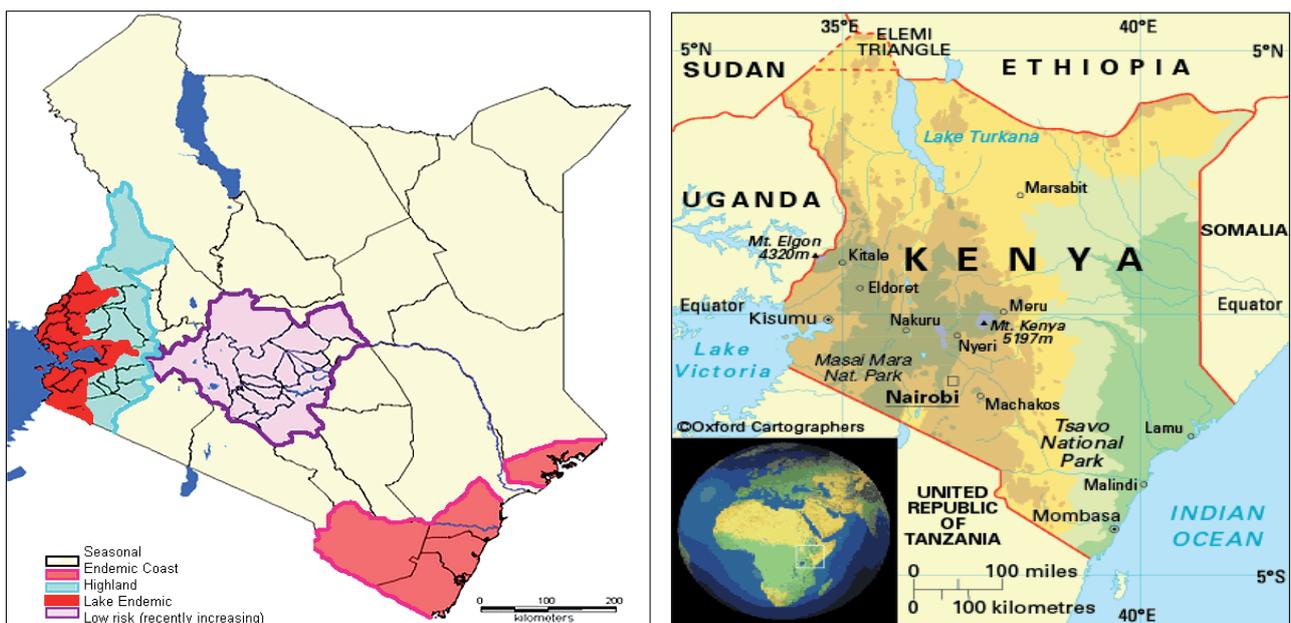
### **Example: Malaria Risk in the Kenyan Highlands**

On the Nandi Plateau north-east of Lake Victoria malaria has been introduced by the soldiers returning from Tanzania after the First World War in 1918 and 1919 (Lindsay & Martens, 1998). Additionally, in the first decade of the 20<sup>th</sup> century a railway from the coast across the highlands and down to Lake Victoria as well as roads on this route have been completed, which facilitated the gradual spread of infective mosquitoes into the highlands from the low-lying hyperendemic disease areas (Malakooti et al, 1998).

Today malaria is the most common cause of morbidity in Kenya and is responsible for 23 percent of hospital admissions (Republic of Kenya, 2009a). The greatest part of Kenya's population lives in the highlands (37 out of 68 Kenyan districts) where they are exposed to “acutely seasonal malaria transmission where frequent epidemic conditions are met” (Shretta et al., 2000). Due to the fact that malaria patterns are unstable, local inhabitants do not develop a partial immunity as in regions of endemic malaria. Thus, when an epidemic breaks out all age groups are affected and the risk of infection and death is elevated (Afrane et al., 2005). Most malaria cases in the highlands appear due to *Plasmodium falciparum* infections. Vector species however differ between the various highland regions of Kenya.

In the western highlands *Anopheles gambiae s.l.*<sup>21</sup> and with a smaller presence *Anopheles funestus* (Munga et al., 2006) prevail. The latter has been associated with some highland malaria epidemics during the 1990s (Lindsay & Martens, 1998). Central highlands usually experience malaria transmitted by *Anopheles arabiensis* (Chen et al., 2006).

Further south of Mount Kenya, malaria disappeared already in the 1930s from the highlands surrounding Nairobi. The use of insecticides in the 1960s resulted in further malaria eradication: I.a. in the highland cities of Nairobi and Kisii. In the 1980s first cases of malaria were reported again in Kisii followed by Nairobi (Alsop, 2007). The highlands surrounding Mount Kenya were historically malaria free until the mid 1990s when first cases have been reported in close proximity of the cities of Naru Moru, Nyeri and Karatina (Chen et al., 2006). The western highlands of Kenya have experienced a dramatic rise in malaria cases during the last 15 years (Ndenga et al., 2006). In Kericho District the number of severe cases rose from 16 per 1000 inhabitants in 1986 to 120 cases in 1998 (Hay et al., 2002).



**Figure 5.** Malaria risk in Kenya (left). Physical map of the country for reference (right). (Modified from on-line resources of The Division of Malaria Control in Kenya and [www.commonwealth.org](http://www.commonwealth.org)).

How the malaria situation in the Kenyan highlands is going to change in future is not clear. However, the increase in malaria risk during last 30 years was stable enough to indicate further worsening in the region. Still, computer simulations do not bring consistent results on that matter.

<sup>21</sup> *Anopheles gambiae* sensu lato – this term includes all species of the *Anopheles gambiae* complex and is used when no detailed identification of the species has been conducted or the study has been carried out before a new species has been identified and it is not clear which vector species it was. For more information about the mosquitoes of the *Anopheles gambiae* complex and their African distribution, please check Coetzee et al (2000).

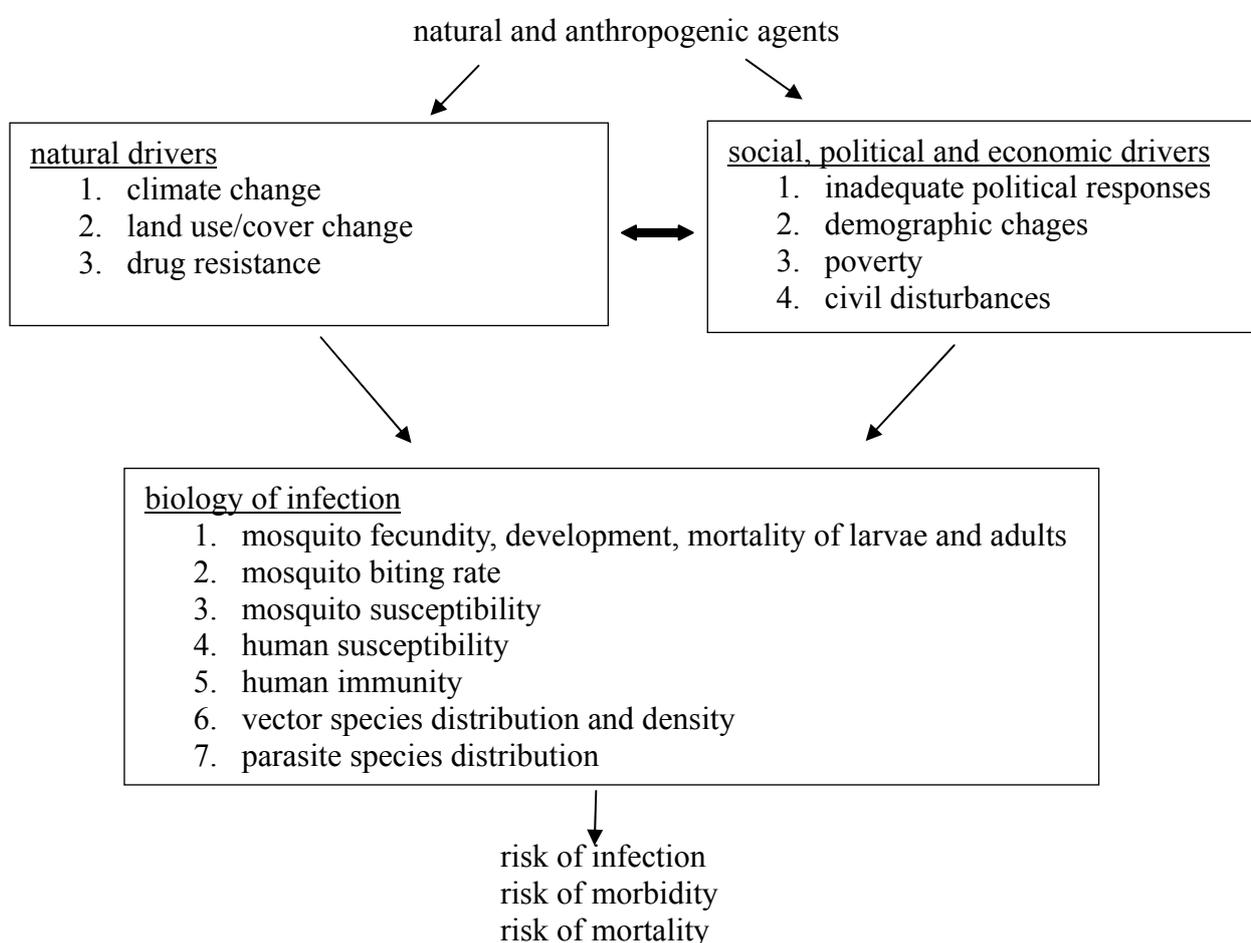
Despite the fact that most of them suggest an increase in malaria risk, they differ in the estimation of speed and in the course of change. According to the results of the simulations by Thomas et al. (2004), the malaria situation in African highlands<sup>22</sup> will not change much until the year 2020. The Kenyan highlands would experience stabilization of the malaria situation between the years 2050 and 2080. However, the model used in this study and developed by Mapping Malaria Risk in Africa/Atlas du Risque de la Malaria en Afrique (MARA/ARMA) is based only on two factors: vegetation and climatic projections. The suitability of this model for highland regions may be further questioned as it does not predict the epidemic potential but just a stable malaria transmission situation. The emergence of epidemic malaria, however, is consistently being projected as a threat to highland regions that are still malaria free according to many Climate-Change-based models (Martens et al., 1999; Zhou et al., 2006). Far-reaching climate-based models of the future malaria situation predict a much greater change in malaria exposure in the Kenyan highland region than MARA/ARMA projections. Tanser et al. (2003) modeled that, depending on which Climate Change scenario is used, the number of months suitable for *Plasmodium falciparum* malaria transmission will increase in some areas even from 0 to 7-12 months. The change in number of people exposed to malaria has been predicted to rise dramatically (simulation for whole Kenya), even by factor of five assuming a constant population (Tanser et al., 2003).

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<sup>22</sup> With an exception of a small upland area in northern South Africa.

## 5. Drivers of the Increasing Malaria Infection Risk

The risk of malaria infection, morbidity and mortality is dependent on the biology of infection which in turn is affected by many biological processes and characteristics. Natural as well as social, political and economic drivers<sup>23</sup> affect the biology of malaria infection. Increase or decrease in malaria risk is a result of changes in drivers that determine the biology of infection. Those drivers are influenced by forces of natural or anthropogenic character. The analysis of anthropogenic forces however dominates lately the discourse and they are given the greatest responsibility for recently observed changes in drivers affecting the biology of malaria infection and in turn its risk. This conceptual framework is presented in the graph below.



**Figure 6.** Drivers of the increasing malaria risk.

Multitude of factors influencing malaria risk as well as of relationships between them can be illustrated by the conceptual model of malaria risk in the Kenyan western highlands. A complex conceptual model that I propose covers to a great extent multiple causation of malaria risk increase

<sup>23</sup> Called also further interchangeably factors.

in the region. It is modified from Zhou et al. (2003) and includes a few aspects not covered in their model (Climate Change, behavioral patterns and socio-economic status). Of crucial importance for the development of current and future malaria risk in the highlands of Kenya are the topographic conditions of the region, particularly in the western part of the country, where the most severe outbreaks of malaria happened recently with an increasing frequency. Climate and vegetation support malaria transmission in the deep valleys to a far greater extent than in the hills. Thus, valleys were in the past undesirable places for settlement as opposed to the upland locations that were more densely populated. Recent rapid population increase in the East African highlands has changed those patterns and more people settled in the valleys. This has led to an increase in the malaria reservoir. As inhabitants of the valleys were exposed to a relatively high malaria transmission, they gained partial immunity and malaria had benign courses except for a small proportion of residents, mainly children. Inhabitants of the uplands did not develop partial immunity against malaria as they had little contact with *Plasmodium*. Recently, migration and traveling increased also between valleys and uphill locations. Residents of uphill villages generally have a lower economic status than the inhabitants of valleys, where climate and soils support agriculture. This enhances labor migration downhill, where the risk of infection with malaria is significantly higher. Infected workers spread the disease when visiting their families in uphill villages.

Increasing population density in the region resulted in considerable land cover changes, both in valleys and uphill locations, which supported mosquito development through increased number of breeding sites and change of micro-climatic conditions into positive for vectors. So whenever climatic conditions were supportive even for a short period of time, mosquito vectorial capacity increased rapidly. The outcome was an enhanced frequency of malaria epidemics in the uphill locations of the Kenyan highlands. Enhanced risk of morbidity and mortality due to malaria observed recently in the region originated from: inadequate public malaria control and prevention programs; poor treatment of malaria; deficiencies in individual knowledge and behavioral patterns; as well as increasing drug resistance and HIV infections in the region, which intensify the vulnerability of highland residents.

It has been reported that climatic changes in the East African highlands have been very subtle so far (Zhou et al., 2003; Pascual et al., 2006). However, Climate Change scenarios by the International Panel for Climate Change all predict a further increase in temperature around the globe and project rather consistently that a further increase in precipitation in the region will follow. Thus, it can be assumed that in future modifications of weather patterns in Kenya due to Climate Change will enhance the risk of malaria transmission in highland regions of the country.

Each of the drivers of malaria risk increase in the countries of the East African Community will be presented in details in the chapters 5.1. and 5.2. The analysis will be structured by the use of the tool described in the chapter one. Kenyan highlands will remain of a special interest and the local examples will be presented on the components of the conceptual model described above.

## 5.1. Natural Drivers

Currently changing patterns of exposure favor conditions of human and mosquito vulnerability to the malaria parasite. In addition to the enhanced intrinsic processes that promote malaria risk increase, extrinsic factors affect the biology of both pathogens and mosquito hosts towards the patterns of improved transmission. Malaria risk has been, and still is, regulated by environmental and physical factors like the natural variability of global and local climatic conditions<sup>24</sup> accompanied by corresponding changes in land cover, as well as activities of biological organisms and interactions between them resulting in evolutionary processes. Currently, however, human activities influence the natural environment and its processes so powerfully that they can be perceived as a new fly wheel of natural changes resulting in malaria risk increase. Additionally, by interfering with the natural selection, collective and individual human actions are very powerful components of the currently ongoing evolutionary process. Land use and land cover changes; Climate Change due to the anthropogenic emissions of greenhouse gases; drug resistance resulting from undifferentiated medical treatment; all those phenomena indirectly affect the biology of malaria parasites and their two hosts: mosquitoes and humans. Disturbances of the ecological equilibrium result in unexpected and rapid increase in malaria infection, morbidity and mortality risks. Possas (2001) concludes that ecosystems increasingly transformed by human activities do not provide the balance that could buffer malaria burden any more.

Factors affecting malaria and presented in this subchapter contain physical or biological characteristics that are components of the natural environment. Recent changes within those components are extraordinarily rapid and thus their impact on malaria risk increase cannot be ignored. The responsibility of humans for transformations of climate and land cover is almost consistently agreed upon by specialists (i.a. Solomon, 2007; Lambin & Geist, 2007). The human role in the evolution of drug resistance is evident with a simple fact that anti-malarial pharmaceuticals are human creation.

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<sup>24</sup> Tropospheric aerosol changes (due to e.g. volcanic eruptions), activity of the Sun, and inclination of the Earth's axis are some of the physical causes of this variability. For more information see e.g. Crowley et al. (2000).

### 5.1.1. Climate Change

*What processes underlie Climate Change and what are its characteristics?*

Climate Change is the process of changes in global and local weather patterns, mainly towards warmer and more humid conditions. According to the vast majority of scientific sources (e.g. Salinger, 2005; Solomon, 2007), this process is caused by the rising atmospheric concentration of greenhouse gases due to human activities (mainly burning of fossil fuels). Already during the second half of the 20<sup>th</sup> century the mean global temperature has risen by 0.6°C (Salinger, 2005; Solomon et al., eds., 2007). Land surface and sea surface temperatures in the tropics have both followed similar rising trends. A further increase by 3°C<sup>25</sup> is expected by the year 2100 according to the United Nations Intergovernmental Panel on Climate Change (IPCC). Lately observed changes in the world's climate are faster than in any period in the last 1000 years<sup>26</sup> (Solomon et al., eds, 2007). On the local level, Eastern Africa has experienced increasing minimum nighttime temperatures and decreasing diurnal temperature ranges (Pascual et al., 2006). An additional increase in mean global temperature by 2°C may result from the greenhouse gas releases from warmer oceans and soils (Torn & Harte, 2006).<sup>27</sup>

According to the IPCC the distribution of malaria within its current range is likely to spread and its incidence to increase (McCarthy et al., 2001). The impact of Climate Change on human health is not limited to an increase in malaria infection risk. Other adverse effects may be: elevated mortality and morbidity due to the increased frequency and intensity of heat waves, or elevated susceptibility to infective agents due to malnutrition resulting from an increase in flood and drought catastrophes. However, vector-borne diseases are much more sensitive to positive changes in temperature and precipitation than diseases caused by directly transmitted pathogens (Rogers et al., 2002). Transmission Potential may be strongly reduced due to processes that limit human susceptibility or transmission coefficients. Still, if the limitations disappear the Transmission Potential may raise rapidly. Increases in temperature and/or precipitation due to Climate Change would eliminate the main barrier of parasite development and vector breeding (Patz & Olson, 2006).

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<sup>25</sup> This is a mid-range estimate. There is some uncertainty as to future greenhouse-gas emission and to slightly different designs of models.

<sup>26</sup> The evidence comes from the analysis of air trapped in ice centuries ago.

<sup>27</sup> Warming due to the release of greenhouse gases into the atmosphere affects the earth system and leads to further releases from other than anthropogenic sources. E.g. oceans have a capacity to uptake CO<sub>2</sub> from the atmosphere. This capacity is higher in cold water. Therefore when the ocean warms it releases some amount of carbon dioxide. Additionally, warmer soils decompose quicker and also release more CO<sub>2</sub> and CH<sub>4</sub>.

Climatic changes that may affect malaria transmission include: temperature, rainfall, humidity and soil moisture (Haines et al., 2006). Most of those factors limit transmission currently or have limited it in the past. An increase in their values leads generally<sup>28</sup> to an increase in malaria transmission if other factors (e.g. land cover type, demographic and social factors) support it.

It is projected that in 2080 there will be 300 million additional people in the world at risk of *Plasmodium falciparum* malaria and 150 million of *Plasmodium vivax* malaria due to Climate Change<sup>29</sup> (Martens et al., 1999). For Africa it is suggested that population at risk would just increase by 5-7%. This is due to the fact that the increase in population at risk would be broadly countered by a decrease in the areas where the changed climate will not support malaria as it does now. This decrease of population at risk is projected mainly for western Africa, whereas the East African highlands will experience a rapid increase in malaria transmission (Tanser et al., 2003)<sup>30</sup>.

In many sites of the East African Community, a slight - but significant - increase in temperatures (mean or/and extreme) and/or rainfall has been observed (see Figure 7 for temperature trends from 1950-2000 for four highland locations). The annual variance in temperature has increased especially significantly in the highland areas and can be strongly associated with the number of malaria out-patients (patients that do not stay in hospital overnight) (Zhou et al., 2004; Pascual et al., 2006).

Extremes in rainfall are by some researchers associated with the El Niño Southern Oscillation (ENSO). This phenomenon originates from an anomalous sea-surface temperature in the Eastern Tropical Pacific Ocean and affects precipitation in the whole tropics of the world. Currently the frequency of ENSO increases, which might be associated to Climate Change (Rogers et al., 2002; Collins et al., 2005). El Niño events include extremely high (like in East Africa) or low precipitation and temperature values, that may enhance (but also decrease) malaria risk. Currently its periodicity lasts approximately four years and correlates with the times when weather conditions supported past malaria outbreaks in Kenyan highland locations (Rogers et al., 2002). However, there is no consistency in opinions to what is the influence of ENSO on local weather in East African highlands. Some surveys report even no or very little correlation between those two or a negative influence of intensive rains through washing out mosquito breeding sites (Kovats et al.,

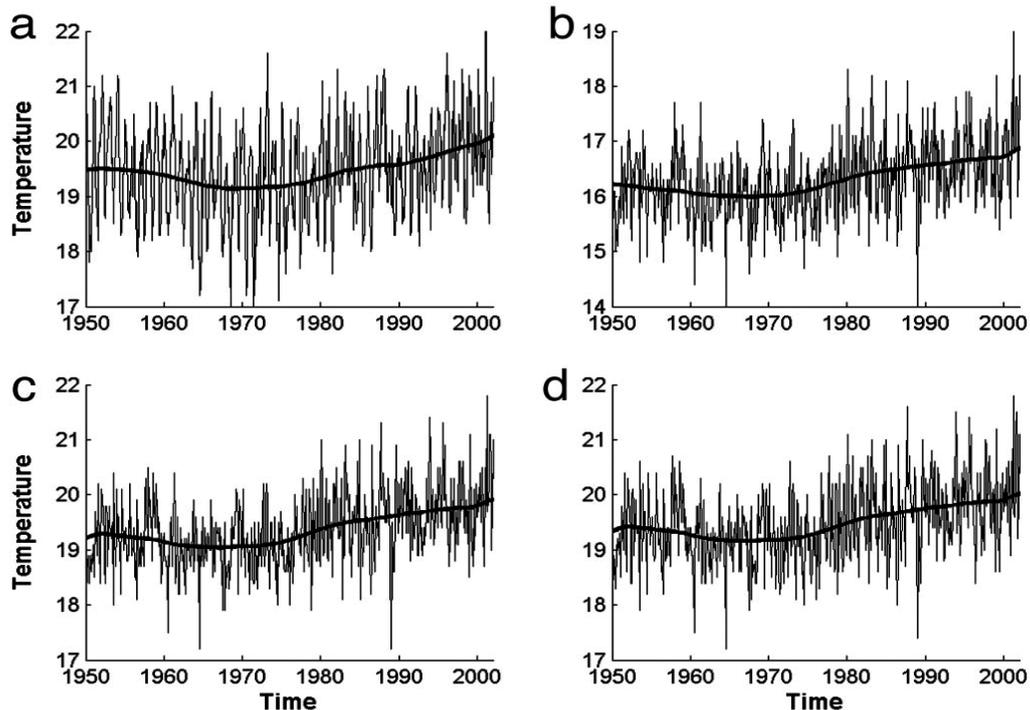
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<sup>28</sup> There is a maximum temperature level for the parasite's survival. However, those values are very high (33-39 degrees in the host) and therefore far from being exceeded even after projected air temperature increase.

<sup>29</sup> The numbers are calculated by subtracting the base-line numbers from those obtained with the HadCM3 Climate Change scenario.

<sup>30</sup> Prognoses of malaria risk depend on the micro-climatic conditions often not recorded by ground-based devices. Remotely sensed images of seasonal vegetation changes help to estimate local weather and thus dynamics of mosquito populations and the parasite incubation period (Rogers et al., 2002). However, remote sensing is quite a new tool for the malaria risk assessment. Assessing the influence of climate variability on the changes of malaria risk through time is difficult because of the high spatial climate variability and the lack of long-term data on weather and malaria cases (Zhou et al., 2004).

1999)<sup>31</sup>.



**Figure 7.** Temperature time series at the four locations in the African highlands. The bold line shows the trend obtained for each of these data with SSA<sup>32</sup> (Pascual et al., 2006).

*a*, Kericho in western Kenya; *b*, Kabale in southwestern Uganda; *c*, Gikongoro in southern Rwanda; *d*, Muhanga in northern Burundi.

*How does Climate Change affect malaria distribution and the risk of malaria infection?*

*How does Climate Change affect parasite and vector capacity?*

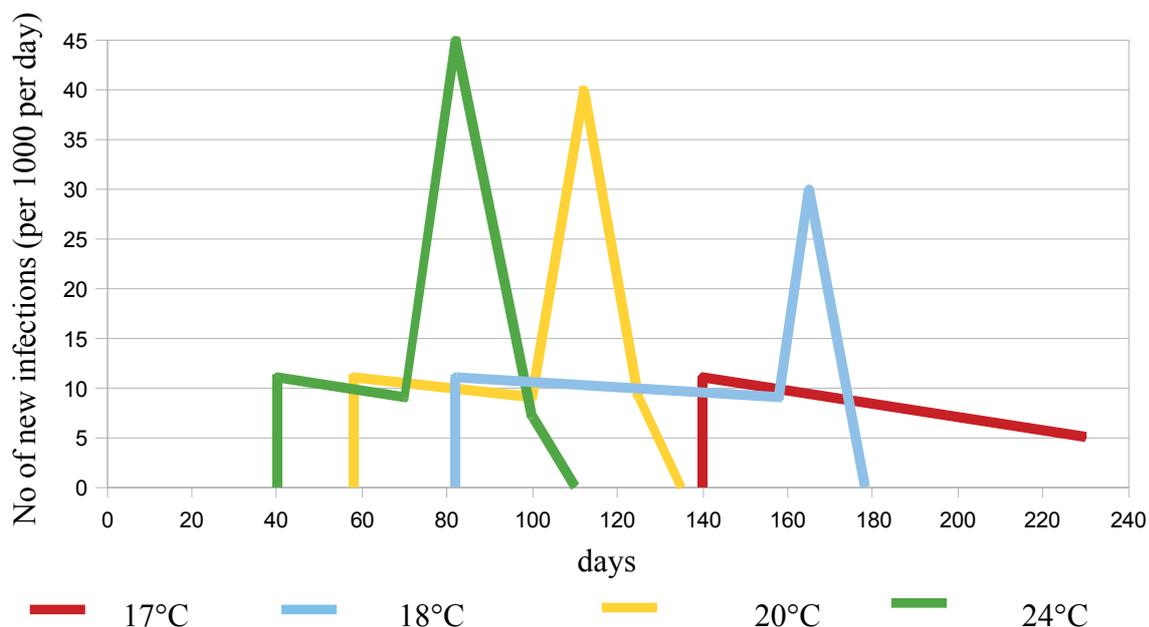
Malaria parasites spend a part of their life cycle outside of human bodies. Therefore they are particularly sensitive to weather conditions. The increase in temperature may increase the parasitic capacity in a few ways: by speeding up the parasite's development that results in the increased possibility of parasite reaching the sporozoite stadium and getting into the human vascular system before the life of the mosquito terminates; by lengthening the transmission period in areas of seasonal malaria transmission; or by changing climatic conditions towards being supportive of the development of *Plasmodium* in areas previously characterized by an unsuitable climate.

The minimum temperature for transmission of *Plasmodium falciparum* lies between 16-19°C, for *Plasmodium vivax* it is 14.5-15°C. *Anopheles* vectors however maintain biological

<sup>31</sup> For more information about the impact of ENSO on climate of East Africa see Plisnier et al. (2000).

<sup>32</sup> Singular spectrum analysis: a type of time series analysis (for more information on SSA and its use in malariology, see Pascual et al (2006).

activity even at 8-10°C (Patz & Olson, 2006). In many regions malaria has a seasonal or year-to-year pattern which is explained by the climatic conditions and Climate Change can lengthen the local transmission period or precipitate epidemic outbreaks (Figure 8). Tanser et al. (2003) project that the number of person-months of exposure (number of persons exposed divided by number of months with malaria in the region) could increase by the range of 16-28%. Small changes in transmission seasons might lead to much greater changes in transmission rates as they tend to increase non-linearly in relation to time (Haines et al., 2006). Pascual et al. (2006) found out that even an increase of temperature by half a degree centigrade may lead to a 30-100% increase in mosquito abundance, which they call the ‘biological amplification of temperature effects’. This is unique for areas of low vector densities like the highlands (Minakawa et al., 2002). A small increase in mosquito abundance influences here very strongly the risk of infection. In endemic areas the abundance of mosquitoes is already so high that the risk of infection is also very high and reaches the plateau where it is influenced essentially by factors other than vector density (Pascual et al., 2006). Pascual et al. suggest that the local expression of the global Climate Change plays a significant, if not decisive role in the increasing risk of malaria infection. Climate Change expressed by global warming could thus drive the geographical spread of malaria and increase its incidence in regions of unstable transmission where temperature was previously the limiting factor but is increasing slightly due to Climate Change.



**Figure 8.** Development of malaria epidemic at different temperatures. The incubation time inside the mosquito is 111 days at 17°C, 56 days at 18°C, 28 days at 20°C and 14 days at 24°C. The parasite incubation time in humans is assumed to be 15 days. (Modified from Lindsay & Martens, 1998).

Climate Change is also likely to affect the biodiversity (Haines et al., 2006). Ecological niches

abandoned by species sensitive to extreme weather events, temperature increase and/or changes in precipitation can be potentially colonized by malaria vector species. This would result in their population increase and potential presence in areas, where they used to be absent due to interspecific competition. However, introduction of a species into a new habitat occurs often unpredictably. There are many factors other than climatic that influence this process like geographic barriers and further biological interactions (Martens et al., 1999).

Furthermore, as the larvae development and pupation as well as the adult survivorship rates of vector mosquitoes are limited by temperatures<sup>33</sup> (Martens et al., 1999; Munga et al., 2006), a slight increase may result in biological responses at least one magnitude higher. This might have a great impact on malaria transmission especially in regions with low temperature values where it used to be the limiting factor for the development of vectors, for example in the East African highlands. Population dynamics of mosquitoes may change dramatically there (Pascual et al., 2006). Higher temperatures accelerate in addition the frequency of blood feeding by adult mosquito females on humans as faster blood digestion shortens the gonotrophic (egg production/laying) cycle (Afrane et al., 2005). Of course temperatures above maximum values may decrease the survivorship of mosquitoes, but even in such cases, as reported for example by Lindblade et al (2000), overall Entomological Inoculation Rates<sup>34</sup> (EIR) would be greater due to the larger proportion of mosquitoes positive for sporozoites (as parasites develop faster).

Also enhanced rainfall may affect vectors' demography by influencing the number of mosquito larvae habitats. In Eastern Africa it is projected (with a high consistency between various models) that rainfall will increase by around 20% by the end of the 21<sup>st</sup> century (Solomon et al (eds), 2007). Zhou et al. (2004) project for the East African highlands that an increase in rainfall by 22% would lead to an increase in malaria out-patients by up to more than 100% (depending on the particular location)<sup>35</sup>. This would be mainly due to the enhanced mosquito longevity (as relative humidity rises<sup>36</sup>) and to the increase in the number of still-water ponds suitable for mosquito breeding.

Temperature and rainfall can have synergistic effects on malaria transmission. When they both increase, malaria transmission could raise even fourfold in the East African highland regions

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<sup>33</sup> With the optimum being between 20 and 30°C. The minimum required temperature for mosquito development is 16°C below which aquatic stages of tropical Anophelines fail to grow.

<sup>34</sup> EIR is the product of Human Biting Rate (HBR, number of mosquito bites per night per person) and Sporozoite Rate (SR, proportion of mosquitoes hosting the sporozoite form of *Plasmodium sp.*).

<sup>35</sup> Monthly value of 80mm rainfall for at least four consecutive months is assumed to be essential for a stable seasonal malaria transmission (Martens et al., 1999; Lindblade et al., 2005). However, a monthly precipitation above 300mm may result in floods that flush mosquito larvae and thus reduce malaria transmission. It is still not clear if man-biting rates are also affected by rainfall (Githeko & Ndegwa, 2001).

<sup>36</sup> Higher mosquito longevity potentially increases the parasite's lifespan. Still the exact relationship between those parameters and their interaction with temperature are not clear.

(Zhou et al., 2004). Mean temperature and rainfall records may not be the most suitable data for analyzing malaria risk. In areas where climate variability is very strong, short-term fluctuations may correlate better with malaria outbreaks. Despite this problem most analyses examine the mean climatic values (ibid.).

#### *How does Climate Change affect human vulnerability to infection?*

Generally, in some regions of the world Climate Change may have a negative impact on human vulnerability to any kind of infection by enhancing the risk of malnutrition. Deficiencies in nutrients weaken human immune system and account for a total disease burden of estimated 15% (McMichael et al., 2003)<sup>37</sup>. Climate Change will modify local weather patterns as well as increase the prevalence of extreme weather events like droughts and floods. It has been modeled that this will negatively affect the availability of food in East African countries and by far overcome the positive impact of an increased CO<sub>2</sub> concentration on crop yields. Crop yields are projected to decrease by as much as 10% (Parry et al., 2005).

Additionally, Climate Change will affect transmission not only of malaria, but also of other infectious, food- and water-borne diseases many of which are threatening East African population. Changes in temperature and precipitation will affect the distribution, breeding and development of vectors (mosquitoes, ticks etc.) and infectious agents (bacteria, viruses and parasites) (McMichael et al., 2003). These diseases interact with each other and with malarial infections, so that the severity of one is increased by the presence of another (Mendis et al., 2001). Thus the presence of other infections increases the risk of morbidity and mortality among malaria patients.

#### *What are the links of Climate Change to other drivers?*

Climate Change and its impact on malaria risk have mainly been studied in isolation from other factors. However, it is and will be experienced against a background of other global changes like demographic changes or land use changes. Haines et al. (2006) claim that these other changes may interact with the Climate Change and magnify its health effects.

Climate Change may increase the frequency of floods, droughts and extreme weather events, leading to population displacements. The situation of environmental refugees does not often differ from the experience of war and civil conflict refugees. The enhanced vulnerability of the latter to malaria infections will be described in detail in the next chapter.

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<sup>37</sup> Currently, approximately 800 million people are undernourished with close to half of them living in Africa (Patz et al., 2005). The IPCC projects that Climate Change will increase the number of hungry and malnourished people in the twenty-first century by 80 to 90 million (IPCC 2001).

Poverty is currently another factor that supports increasing malaria transmission in the countries of the East African Community. If this situation will not change in the future, poverty may undermine the countries' ability to deal with climate-induced malaria. Additionally, Climate Change threatens the economic development of the poorest countries. Resources will be required for adapting to the adverse effects of Climate Change that are likely to affect the least developed countries to the greatest extent (Haines et al., 2006).

Climate Change as one of the causes of malaria risk increase is tightly connected to inadequate political responses. Decision makers concentrate on malaria prevention and treatment, but are rarely paying much attention to the physical factors underlying the increase in malaria incidence. Environmental management is still, despite its potential effectiveness, not a favored anti-malarial method (Pattanayak et al., 2006).

Micro-climatic conditions are strongly influenced by patterns of land use change. As many areas of malaria transmission undergo abrupt vegetation cover changes, there is a great synergy between Climate Change and land use change in their influence on malaria risk.

Climate plays definitely a very important role in the distribution of malaria, just as it does in the distribution of any infectious disease, particularly a vector-borne one. Still, one needs to keep in mind that there are enough examples showing that climatic conditions are not the only factors affecting malaria risk. Already in 1937, L.W. Hacket wrote:

Certainly climate lays down the broad lines of malaria distribution [...]. Nevertheless, although this is a very simple and plausible explanation [...] even the early malariologists felt that there was something unsatisfactory about it [...]. In Germany it is the northern coast which is still malarious, the south is free [...]. There is [...] no climatic reason why [malaria] should have abandoned south Germany or the French Riviera.

(Hacket L.W., 1937).

### **5.1.2. Land Use and Land Cover Changes**

*What processes underlie land use/cover changes and what are its characteristics?*

Land cover is defined by the “attributes of the land surface and immediate subsurface, including biota, soil topography, surface- and ground-water and human (mainly built up) structures” (Lambin & Geist, 2006). Land cover may be changed by the transformation of the cover type e.g. deforestation, urbanization or expansion of agricultural land. It may also be modified, when the structure of the cover type changes but not its category (e.g. tree species composition changes

within the forest) . Both land cover changes and modifications lead to changes of the land surface attributes as listed above.

Land use is defined as “the purposes for which humans exploit the land cover” (ibid.). As a result, the biophysical attributes of the land are manipulated. Land cover changes and land use changes are being distinguished to account for interactions between socio-economic (land use) and biophysical (land cover) processes. However, they are usually studied together as they are tightly connected. Land use/cover changes influence climate, soil quality, biodiversity, human health, and socio-economic conditions (Lambin & Geist, 2006).

Deforestation<sup>38</sup> is the most significant manifestation of land cover change. The last decade of the 20<sup>th</sup> century was characterized by an extensive deforestation all around the globe. It has been estimated by different authors at the range of 9.4 million hectares per year (FAO, 2001) or even 16 million hectares annually (Pattanayak et al., 2006) and did not slow down in the beginning of the new millennium (ibid.).

Deforestation and other land cover changes have accompanied increases in malaria infection rates in Asia, Africa and Latin America, which prompted many scientists to study the relationship between them (see Lindblade et al., 2000; Rogers et al., 2002; Munga et al., 2006).

Generally land use/cover changes are rooted in multiple causes that may be clustered into biophysical, economic and technological, demographic, institutional and cultural causes that altogether constitute structural conditions in human-environment relations (Lambin & Geist, 2006). All factors are interlinked and may have synergistic effects. However, which different factors play a decisive role may be identified on a case-to-case basis only.

In Africa land use might have been in “quasi-equilibrium” for thousands of years before the 20<sup>th</sup> century (Kimble, 1962). Shifting cultivation accompanied hunting, gathering and herding, may have allowed vegetation to recover for long periods. Despite the little existing data from that period, population, and thus the crop demand, in many African regions is thought to have declined a bit during the 19<sup>th</sup> century (ibid.). Land use/cover changes gained momentum after the 1930s when local population increased rapidly and colonial powers demanded a high export of crops (Lambin & Geist, 2006). The population increase may be associated to improved health care and to turning from a “traditional” towards a “western” (settled, urban etc.) lifestyle. Increased crop demand in the colonies may be associated with the economic crisis of the 1930s and improved transportation routes within the African continent. Population growth and export demand have not decreased till present times (Lambin & Geist, 2006). The Food and Agricultural Organization (FAO) estimates

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<sup>38</sup> The Food and Agriculture Organization defines deforestation as “occurring when tree canopy cover falls below 10% in natural forests or when a forest is transformed to other land uses even if tree canopy cover remains higher than 10% - e.g., shifting cultivation” (FAO, 2001).

that cropland in sub-Saharan Africa has increased by 37% in 40 years (from 119 million ha in 1961 to 163 million in 2000). Worldwide the last 30 years have been characterized by a turn from the expansion of agriculture towards its intensification. This trend however is not as visible in Africa as in other continents. Here in many regions land clearance for agricultural purposes (as well as for urbanization) has remained intensive (Lambin & Geist, 2006).

*How do land use/cover changes affect malaria distribution and the risk of malaria infection?*

*How do land use/cover changes affect parasite and vector capacity?*

Vector-borne diseases are particularly sensitive to land use/cover changes as their distribution depends on the presence of vectors and thus on the presence of their habitats. The term “mal aria”, coming from Italian, means “bad air” as people used to associate malaria with the mosquito typical habitats like swamps or marshes (Lambin & Geist, 2006). Land use/cover changes that are said to increase vectorial capacity include: wood extraction and forest removal, agricultural intensification, infrastructure extension, urbanization and human population dynamics (ibid.). In which way those modifications may affect vectorial capacity is described below.

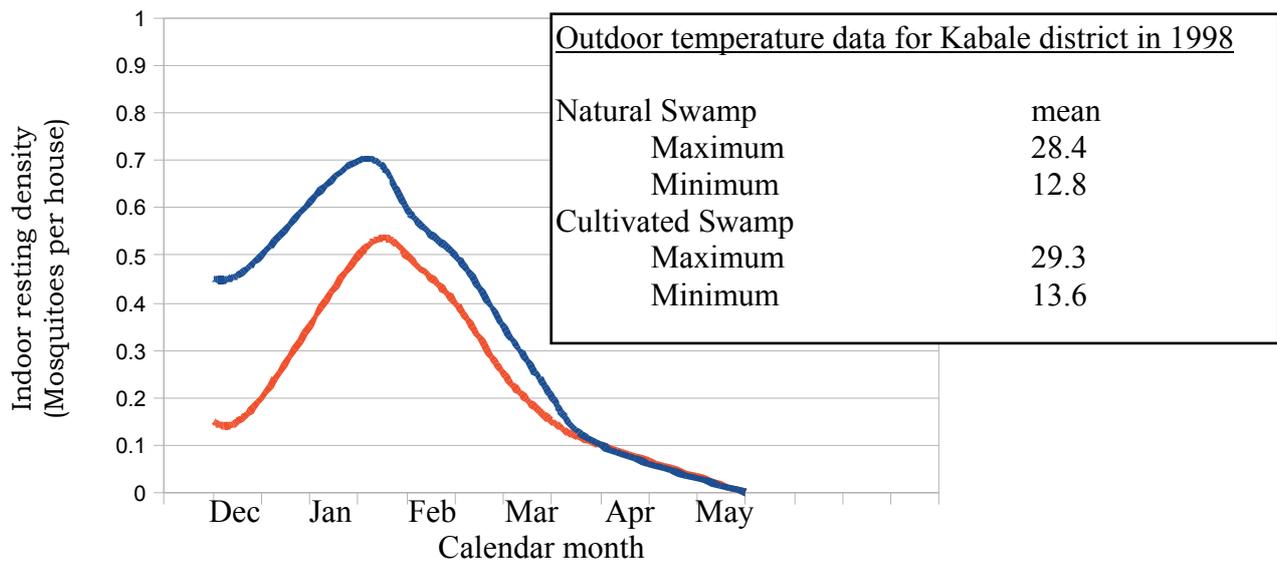
The changing of landscapes may affect local micro-climates stronger and quicker than the global Climate Change. This influence includes changes in evapotranspiration, temperature and surface run-off (Patz & Olson, 2006). Temperature is directly affected by alteration of radiation budget and energy balance. Changes in vegetation due to the conversion of forest and grassland into cropland can result in a decrease of mean surface temperature by 0.9°C in temperate latitudes but can increase the surface temperature by 0.8°C in tropics and subtropics<sup>39</sup> (Afrane et al., 2005). Temperature increase appears locally where deforestation takes place. The effects of this increase however spread after a short period and affect even remote regions, as Zhou et al. (2001) examined.

Deforestation leads to an increase in mean daily temperature<sup>40</sup> not only outdoors but also indoors, where mosquitoes rest, as Lindblade et al. (2000) observed in Uganda (see Figure 9 below). There the number of *Anopheles gambiae* in the huts was increasing along with the minimum temperature. Matola et al. (1987; quoted by Afrane et al., 2005) also suggested that increases in local malaria transmission in the Usambara Mountains of Tanzania might be associated with the deforestation in the region. Lindblade et al. (2000) found out that temperatures have been higher where cultivated fields replaced natural wetlands. Parallel to the increase of the minimum temperature the number of *Anopheles gambiae* increased.

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<sup>39</sup> This difference in responses is due to differences in latent heat flux and energy balance between both regions.

<sup>40</sup> Mosquitoes, as all arthropods, are cold-blooded and thus their body temperature depends on the air temperature. Higher body temperature increases metabolism and so the digestion of blood and gonotrophic cycles.



**Figure 9.** Mean indoor resting density of *Anopheles gambiae s.l.* in Kabale district, Uganda, by swamp type, December 1997 – May 1998. Blue line: cultivated swamp. Red line: natural swamp. (Modified from Lindblade et al., 2000)

Deforestation and cultivation affect, moreover, the biodiversity of local ecosystems. The high complexity of processes within the ecosystem makes it difficult to predict with high certainty what those changes will look like. The impact of those changes on malaria is also species- and site-specific. Nevertheless, observations from East Africa seem to support the thesis of a positive influence of land-use changes on malaria transmission in this area (Patz & Olson, 2006). Here a tight tree-cover used to prevent *Anopheles gambiae* from breeding in high numbers, as the immature larvae do not survive the lack of direct sunlight. This situation has dramatically changed in regions that underwent an extensive deforestation (Ndenga et al., 2006). Additionally, the pH of soil and water ponds in the forest is acidic due to large amounts of organic matter that litter the ground. Clear-land ponds are filled with water of more neutral pH that favors the development of the *Anopheline larvae* (Pattanayak et al., 2006). Furthermore, deforestation may increase not only the survival of the larvae, but also shorten their larva-to-adult development time (Afrane et al., 2005).

Minakawa et al. (2005) found out that in the western highlands of Kenya larvae of *Anopheles gambiae* occurred more frequently in temporary pools in cultivated areas than in natural forests and swamps. From more than 2000 mosquitoes captured in the western highland by Munga et al. (2006) during one year (July 2002 – July 2003), all *Anopheles gambiae* mosquitoes were recovered from traps in the farmlands. No representative of this most effective malaria vector species has been caught in the swamps or forests. The water temperature, however, was according

to Munga et al. within the optimum range for the development of *Anopheles gambiae* larvae not only in the farmland water reservoirs, but also in those of swamps and forests. As an explanation, the authors point here to the complex ecological interactions of reservoir ecosystems. Aquatic habitats of forests and swamps are bigger than those of farmlands and thus remain in place long enough for predators to establish and prey on mosquito larvae. Additionally, in the studied highland sites farmers enhanced the suitability of habitats for the larval development by clearing vegetation around the drainage ditches (the most common reservoirs in the farmlands) and thus increasing the sunlight exposition of the larvae. Munga et al. conclude that there are two decisive factors for malaria vectors development in the Kenyan highlands. Firstly, land cover type of larval habitats<sup>41</sup>, and, secondly, decrease of intra-specific competition due to high food availability. Generally, larvae take longer to develop if there is a high density of larvae in the reservoir as food is a further factor limiting the development of larvae. In the western Kenyan highlands, however, the major crop is maize and the *Anopheles* larvae feed on maize pollen. The authors suggest that maize cultivation enhances *Anopheles gambiae* productivity by improving nutrient conditions of aquatic habitats<sup>42</sup>.

Also in the Ugandan south-western Kabale District cultivated swamps support malaria risk more than the natural swamps do (Lindblade et al., 2000). As has already been mentioned, highland areas of EAC are often composed of steep ridges and narrow valleys with originally papyrus-swamp covered bottoms. Dense papyrus cover together with a thin layer of papyrus-produced oils on the water surface restricted the breeding of mosquitoes (Lindsay & Martens, 1998). After the 1940s the British administration promoted the drainage of swamps and crop cultivation to feed the increasing population of the region. Nowadays, just 15% of the swamps that existed in the 1950s remain. For the purpose of agriculture, ridges with ditches have been constructed between the fields. Ditches filled with water provide optimal conditions for mosquito breeding. Lindblade et al. (2000) found consistently higher mosquito densities during the wet season in cultivated swamps than in natural ones. Human populations living next to the cultivated swamps received seven times more infectious bites than the populations living near the natural swamps.

Changes in land-cover may make the environment unsuitable for some mosquito species which may be replaced by another vector. As observed in Kenya by Ndenga et al. (2006) during ten years (1996-2006) the number of swamps in Kombewa (western highlands) increased strongly. The environment changed from supporting effective malaria vector *Anopheles gambiae* to supporting the development of the less effective vector *Anopheles funestus* larvae. This example shows that such a replacement of species is possible and thus theoretically may also happen in the other

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<sup>41</sup> This also affects the water temperature.

<sup>42</sup> For an Ethiopian case study on the influence of maize cultivation on malaria vector productivity see Ye-Ebiyo et al., (2000; 2003).

direction, in which the “better” vector takes over the habitat.

Livestock farming requires use of animal-watering cans in areas where natural sources of sweet water are limited. Mosquitoes can breed in those cans where they have no natural breeding sites<sup>43</sup>. This can lead to a vector abundance expansion as in the case of the Dadaab refuge camp in northern Kenya (Kimani et al, 2006).

Finally, cultivated areas are often irrigated, which changes the local environment and may provide appropriate conditions for the mosquito larvae development<sup>44</sup> (Martens et al., 1999; Keiser et al., 2005). This has been reported to be the case in Burundi, Rwanda, Uganda and Kenya (Keiser et al., 2005). Particularly irrigated rice fields support vector breeding<sup>45</sup>.

### *How do land use/cover changes affect human vulnerability to infection?*

Populations that enter new ecosystems are generally not immune to diseases characteristic to those habitats but not present in the ones in which they have resided previously. This increases their vulnerability to infection with malaria or other infectious agents extremely. If that happens, the immune response to malaria weakens and the risk of severe malaria and its fatal course increases. Similarly, modifications of the natural environment due to land use/cover changes may result in new species of parasites or vectors entering abandoned or new niches. In the face of no immunity, populations are particularly vulnerable to new diseases (Sutherst, 2004).

Intensive land use and non-management<sup>46</sup> of land may result in soil degradation<sup>47</sup>. In Kenya, for example, agriculture is concentrated in only 20% of the country as the remaining 80% are drylands. Despite substantial efforts from the government of Kenya and international organizations, those agricultural areas are threatened with irreversible degradation (Bai & Dent, 2006).

Land degradation results in the loss of green biomass and therefore in a decrease in land productivity, both in areas where the degradation occurs (e.g. through erosion) and where the sediments are deposited (Eswaran et al, 2001). Groundwater flow patterns may become affected and furthermore influence crop yields negatively. Food insecurity may lead both to malnutrition and impoverishment of agriculture-dependent households (Lambin & Geist, 2006). Both of those factors increase the vulnerability of individuals to infections, for example to malaria. Undernourished

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<sup>43</sup> Furthermore, it is theoretically possible that the introduction of livestock may spread the abundance of partly zoophilic malaria vectors (Pattanayak et al, 2006).

<sup>44</sup> Whether the new bodies of standing water support mosquito breeding depends of course on other physical conditions: pH of water, sunlight or shade, surrounding vegetation, water turbidity etc. (Keiser et al., 2006).

<sup>45</sup> As do mining excavations and the construction of dams that lead to the creation of reservoirs.

<sup>46</sup> Defined as “exploitation of land without compensating investment in soil and water conservation” (Bai & Dent, 2006).

<sup>47</sup> Mainly defined as a general loss in soil quality. For a basic introduction to the topic of land degradation see “Land Degradation:an Overview” by Eswaran et al. (2001). For the assessment of land degradation in Kenya, see: “Global Assessment of land degradation and improvement. A pilot study from Kenya” by Bai & Dent (2006).

people, as already mentioned, have a weakened immune response to pathogens and a low income influences expenses on prevention and treatment negatively.

*What are the links of land use/cover changes to other drivers?*

As already mentioned, land use and cover changes lead to changes in the micro-climatic conditions that may enhance or decrease the influence of Climate Change on malaria risk. Land cover changes are furthermore strongly related to Climate Change as a physical phenomenon. According to the studies of Zhou et al. (2001), land cover changes impact the large-scale circulation similarly to the increase in CO<sub>2</sub> from 280 to 430 ppmv<sup>48</sup>.

Deforestation is often accompanied by migration that may lead to the spread of malaria if newcomers are carriers of *Plasmodium*. On the other hand people from malaria-free areas have no acquired immunity and therefore are more susceptible to malaria infection and its severe outcomes.

Inadequate control over the modes of land use, results in extensive changes in land cover, especially deforestation, that may provide appropriate mosquito habitats or change micro-climatic conditions as described above.

### **5.1.3. Drug Resistance**

*What processes underlie drug resistance and what are its characteristics?*

Drug resistance is defined as "the ability of a parasite strain to survive and/or multiply despite the administration and absorption of a drug given in recommended (or higher) doses"<sup>49</sup> (Olliaro, 2005). *Plasmodium falciparum* drug resistance has been identified as the greatest challenge for national drug policies in the East African Community (Shretta et al., 2000; WHO, 2008).

Strains that are resistant to a certain drug are characterized by gene mutations due to which they are insensitive to the deadly mechanisms the drugs work by. Drug resistance is caused by spontaneously occurring single or multiple genetic mutations (Greenwood et al., 2005; Pascual et al., 2006). Mutations of the same gene may accumulate, conferring at first increasing tolerance<sup>50</sup> against the drug and finally total resistance (as in the case of antifolates). It may also happen that single multigenic, independent mutations need to be expressed for the drug resistance to develop (as

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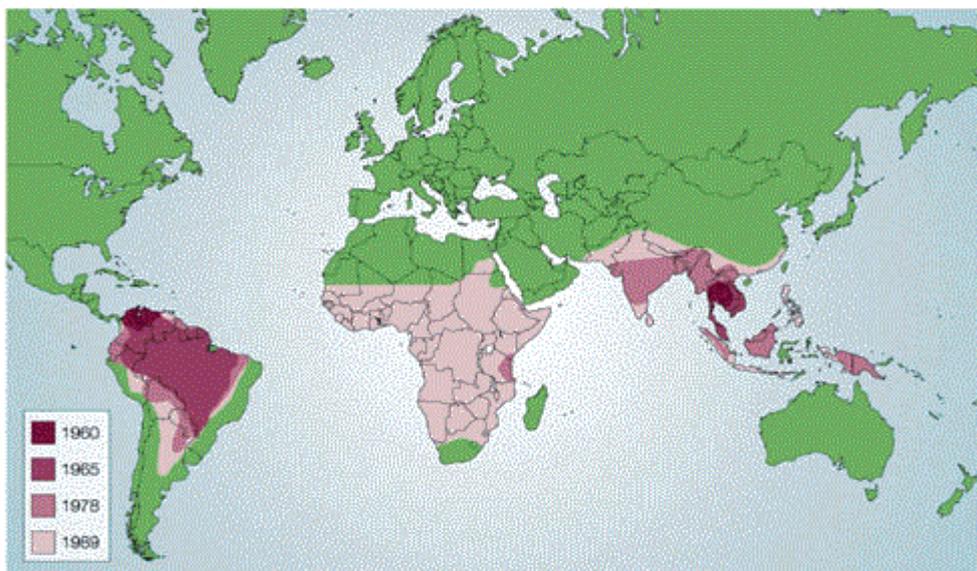
<sup>48</sup> Parts per million by volume. A concentration of 280 ppmv of CO<sub>2</sub> means that for every 1,000,000 molecules in the air, 280 of the molecules are CO<sub>2</sub>

<sup>49</sup> For information about the molecular basis of drug resistance, see Olliaro (2001).

<sup>50</sup> Tolerance may be defined as "a shift in the concentration effect (dose-response) relationship toward higher concentrations to inhibit parasite growth" (Olliaro, 2005). It means that standard doses of a medication may be ineffective, but higher doses are still able to kill parasites.

in the case of chloroquine) (Olliaro, 2005). Modern Artemisin Combined Therapies (ACTs), taking advantage of a combination of several anti-malarial drugs, seem to better prevent the development of drug resistance. Until now no cases of drug resistance have been reported, nor could any such case be induced in laboratory<sup>51</sup> (Mutabingwa, 2005). Chloroquine, primary the most common anti-malarial drug, and recently also Sulfadoxine-Pyrimethamine (an antifolate) have been reported to be so ineffective, that the turn towards ACTs has been recommended in 2001 by the WHO (WHO, 2001; for the SP resistance case in Tanzania see Mutabingwa et al., 2005). However, monotherapies and Sulfadoxine-Pyrimethamine (alone or combined with Amodiaquine) are still popular especially due to their low cost and high availability.

Resistance to chloroquine has arisen slowly from the first use in 1930s, but is now widespread (see Figure 10) due to gene flow. In 1978/79 first East African cases of drug resistance to chloroquine have been reported in Kenya and Tanzania, more than forty years after the introduction of this drug in the region (Shretta et al., 2001). Chloroquine resistance has been suggested to be the most important single factor responsible for the increase in malaria mortality risk in the region<sup>52</sup> (Olliaro, 2005). Since the 1980s drug resistance keeps rising (WHO, 1996; WHO, 2001; Schretta, 2001).



**Figure 10.** Spread of chloroquine resistance (Hartl, 2004).

<sup>51</sup> Clinical cases of tolerance in Asia have, however, been reported by media (BBC World).

<sup>52</sup> Highlands, with their lower - than in the lowlands - transmission of malaria, are especially prone to chloroquine resistance. The frequency of alleles resistant against this drug decreases directly with the increasing transmission because of the loss of resistant genotypes due to sexual recombination. In areas of low transmission the probability of self-fertilization and further transmission of the resistant genotype is higher (Olliaro, 2005).

The increase in drug resistance may be driven by malaria-control strategies that base exclusively on anti-malarial drugs<sup>53</sup>. Such strategies affect the natural selection just as physical and ecological factors do, promoting surveillance of one genotype above the other (Possas, 2001; Ndenga et al., 2006). It has been suggested that this was the reason for malaria resurgence in the Usambara mountains of Tanzania and Kericho in western Kenya (Hay et al., 2002). Hay et al. claim that an increasing number of resistant infections in western Kenyan highlands is responsible for the recent failure of malaria control programs that, although initially successful since the 1940s, failed to prevent recent outbreaks of malaria in the region. Figure 11 summarizes the factors affecting parasite resistance.

Pharmacological	Operational	Host-parasite
<ul style="list-style-type: none"> <li>• residence time</li> <li>• parasite killing rate</li> <li>• mechanism of action &amp; resistance</li> </ul>	<ul style="list-style-type: none"> <li>• policies, regulations</li> <li>• prescribing, selling</li> <li>• compliance</li> </ul>	<ul style="list-style-type: none"> <li>• transmission intensity</li> <li>• drug pressure</li> <li>• immunity</li> </ul>

**Figure 11.** A variety of factors contribute to, and have an impact on, the development of resistance in the malarial parasite, including pharmacological, host-parasite, and operational factors. Pharmacological factors include the drug's characteristics. Host-parasite factors include epidemiology and transmission intensity (in areas of low transmission resistance, once established, tends to spread more rapidly) and operational aspects (inadequate drug treatment policies, irrational prescribing and drug use, uncontrolled drug market, counterfeit products, and noncompliance) (Olliaro, 2005).

*How does drug resistance affect malaria distribution and the risk of malaria infection?*

*How does drug resistance affect parasite and vector capacity?*

Drug resistant parasites have a selective advantage<sup>54</sup> over those that do not have the gene mutations and therefore they increase in numbers and in geographical distribution (Greenwood et al., 2005; Pascual et al., 2006). Interestingly, if chloroquine and SP are not used, drug resistant parasites are not as well transmitted as wild-type parasites (Greenwood et al., 2005).

Extensive use of one type of drugs, as a therapeutic or preventive measure, supports the spread of *Plasmodium* strains that do not die after treatment with this first-choice drug. Even if the disease has been finally combated with another pharmaceutical, the period of time when gametocytes were present in blood had been prolonged (Ndenga et al., 2006).

<sup>53</sup> More about how interventions may contribute to drug resistance and thus to the increase in malaria risk, is presented in chapter 5.2.1.

<sup>54</sup> Chloroquine and SP have both long halve-lives. In the environment cleared from other strains, the resistant parasites may continue breeding before the drugs stop working.

*How does drug resistance affect human vulnerability to infection?*

Drug resistance leads to the reduction of cure rates. Lay people that do not have the knowledge of drug resistance mechanisms, may lose their trust in public health care and turn to traditional medicine and self-treatment instead, which are far less effective than modern medicine in healing malaria (Nuwaha, 2002).

*What are the links of drug resistance to other drivers?*

As already mentioned, inadequate responses contribute very strongly to the development of drug and insecticide resistance (i.a. Olliaro, 2005). Read more in chapter 5.2.1.

Poverty forces many to use cheap pharmaceuticals to which a high proportion of parasites express resistance. This supports the further development and spread of drug resistance.

Land cover changes can support the spread of resistant strains and the increase in their abundance (through the colonization of the abandoned ecological niches).

Temperature increase resulting from Climate Change may increase the intensity of malaria transmission. The evolution of drug resistance is faster in the conditions of high transmission when encoded by a single gene as described above. Thus Climate Change may increase drug resistance (Pascual et al., 2006).

## **5.2. Social, Economic and Political Drivers**

Rapid social and economic changes observed in the 20<sup>th</sup> century entailed a critical disturbance of the delicate balance characterizing complex ecological systems of infectious diseases. The exchange of information and goods leads to a worldwide transfer of customs, lifestyle, pharmaceuticals and nutritional habits. This process commonly referred to as “globalization” has influenced the spread and course of infectious diseases. Boundaries between global and local, urban and rural have been blurred as traveling and migration became simpler, quicker and cheaper (Possas, 2001). Sociologists, anthropologists, economists and political scientists address with this approach the current epidemiological malaria situation. They stress the importance of poverty, demographic changes and improper political decisions as underlying the complex emergence and re-emergence of malaria around the Globe, including East Africa. As M. Wilson (2001) wrote: “human social systems, economic activities, interactions with the environment, and lifestyles represent some of the key domains of interaction that affect infection and disease risk” (cited in Pattanayak et al. 2006). This point of view implies proposed strategies to

combat malaria.

This chapter will concentrate on the influence that political, demographic and economic circumstances have on malaria risk and how they may contribute to its increase. In this respect I identified three central causes: (1) inadequate political responses, (2) demographic changes and (3) poverty/civil disturbances.

### **5.2.1. Inadequate Political Responses**

*What processes underlie inadequate political responses and what are its characteristics?*

If malaria infection risk increases or does not decrease despite all efforts (see Chapter 4.3), governments respond with various new measures and strategies. Synergistic and aversive impacts of factors as well as unintended side-effects of actions make the interventions positively influence malaria risk in the East African region. Inappropriate measures include among others: decision-making not responsive to scientific evidence (like in the case of Kenya presented below); investment in half-way measures (like the provision of insecticide treated bed-nets to selected individuals and not to communities) (Teklehaimanot et al., 2007); overestimation of the role of awareness-raising campaigns among the poor, who even being aware of their importance, cannot afford to buy mosquito nets or anti-malarial drugs (Worrall et al., 2003). On the other hand little attention is paid to raising awareness of cost-free preventive behavior<sup>55</sup> (Nuwaha, 2002). The lack of a consistent malaria diagnosis system leads to false curative responses (Worrall et al, 2002; WHO, 2006; 2008). Last but not least believes, customs and local social structures are not always appropriately addressed (see Figure 12 for personal concerns about the use of mosquito nets). They all are often obstacles for implementation of anti-malarial programs.

The process of decision-making has already gained some interest among scientists. They have tried to support officials with models and standard procedures on how to root decisions in scientific proofs<sup>56</sup>. Unfortunately, those models have not yet managed to cover the complexity of policy- and decision-making. Multiple groups of interest, lack of financial resources for purchasing pharmaceuticals, and fear of unknown risk: they all together build up a complex matrix of correlated concerns that obstruct substantial and efficient interventions (Shretta et al., 2000).

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<sup>55</sup> Malaria transmission in the Kenyan highlands is still low and thus it has been suggested that even simple disease control measures, if implemented in time, could successfully interrupt an increase. Indoor insecticide spraying and the use of bednets have both succeeded in experiments run in highland sites to decrease entomological inoculation rates by more than 90 percent (Ndenga et al., 2006).

<sup>56</sup> For the cost-effectiveness analysis of actions, please see Goodmann et al. (1999).

**Problems associated with nets and general concerns about the insecticide- treated bed net project**

Problems with insecticide	Problems with the nets
<p>Nets smell badly when new and retreated                      Chemical causes flu-like symptoms: (runny nose), and skin rashes                      Chemical may make nets unfit for babies                      Chemical may be a secret fertility and/or birth control device</p>	<p>Some nets too small                      Nets too hot on warm nights                      Not everyone was given nets                      Nets wear and tear easily on papyrus reed sleeping mats of children                      Rats like to eat the netting                      Daily hanging and removal of nets in living rooms and kitchens is tiresome                      Some people did not get twine for hanging</p>
Concerns about ITN trial	Local practices affecting compliance
<p>Suspicion over blood sampling surveys                      Concern that free distribution of nets was a trap to later get money from people                      Concern that researchers would repossess nets and reuse for research in control areas                      Security worries during night compliance monitoring</p>	<p>Mixing nets during treatment is taboo                      Night vigils at funerals prevent net use                      Influx of people into homes during funerals disrupt sleeping arrangements, and prompts locking away of nets to prevent theft</p>

**Figure 12.** Four categories of problems and misconceptions, not addressed by public malaria preventive actions, have been identified during a trial in Asembo, western Kenya ( Alaii et al., 2003).

Furthermore, the lack of internationally agreed terms is a common problem that leads to confusion and to the non-sustainability of control. An example may be the absence of an acknowledged definition of “malaria epidemic”. This leads to a situation where officials wait long before announcing epidemics hoping for financial savings. And a late implementation of emergency measures hinders their effectiveness and puts more people at risk of infection (Githeko, 2001).

It might be noticed that inadequate interventions tend to be embedded in other false responses, creating a vicious circle of wrong decisions, attitudes and strategies. This was the case of anti-malarial drug policy in Kenya. At the end of the 1980s there were strong voices for turning from chloroquine towards a combination of sulphadoxine and pyrimethamine (SP) as a first-choice drug for treating malaria. Growing evidence of increasing treatment failure had been reported while chloroquine resistant malaria parasites kept spreading. Still, there were strong voices claiming that the cheapest and most accessible drug (chloroquine) would be the most successful one and therefore its distribution should be supported by the state. This affected the decision-making process of Kenyan Government. The Kenyan Ministry of Health established a technical committee to revise national guidelines for the treatment of uncomplicated malaria. At the same time the WHO expressed skepticism towards Malawi’s decision to switch from chloroquine to SP treatment.

Because of that additional dissenting voice, doubts rose among the members of the technical committee. Finally, it took six years (from 1991 to 1997) for officials to make the decision and to revise the guidelines (Shretta et al., 2000).

How important the shift towards more effective anti-malarial drugs is, exemplifies the case of the Republic of South Africa, where the widespread use of Artemisin Combined Therapies (ACT) led to a strong decrease in malaria transmission (Mutabingwa, 2005). Still, despite ACT's effectiveness, it is in most countries not used as first-choice drug, as there is an issue of raw material shortage. Artemisia plantations are not able to deliver the amounts needed to cover the growing needs. High prices and drug inaccessibility diminish the potential of ACTs to decrease the malaria burden (Greenwood et al., 2005).

The fact that the development of vaccines and new, more effective drugs is not financially attractive for pharmaceutical companies complicates the decision-making processes further, as the lobby of anti-malarial-drug producers is known to be very influential (Greenwood et al., 2005).

The process of the Kenyan shift in malaria treatment recommendation may be further used to exemplify how of inadequate response to malaria that may positively influence malaria risk, on the stage of the implementation of regulations into practice. The majority of African countries, including the members of the East African Community, are young, low-income democracies where the process of implementation is frequently an issue. Kenyan guidelines have recommended Sulfadoxine-Pyrimethamine treatment to be used wherever “malaria is chloroquine resistant” (Shretta et al., 2000). That has left very much space for individual decisions among local practitioners who have not been provided with any research evidence on the distribution of chloroquine resistant malaria<sup>57</sup>. Shretta et al. (2000) have analyzed decisions of the Kenyan Provincial Medical Officers of Health (PMOs) after the policy change in 1997. They found out that PMOs repeatedly kept using chloroquine as a first-choice anti-malarial pharmaceutical.

Those difficulties may be partly due to the slow and unclear decisions of international organizations involved in anti-malarial programs. WHO and the Roll Back Malaria Partnership (RBM) were not efficient in giving appropriate technical advice to national governments. In the past this resulted in funding some anti-malarial drug programmes basing on ineffective chloroquine drugs (Mutabingwa, 2005). Additionally, the flow of money from The Global Fund - a financial engine behind the international support for ACTs - remained slow. This might be one of the reasons why in 2007, when 40 African countries had already adopted the ACT policy, just nine countries were implementing it (WHO, 2008).

Getting policy into practice is very difficult also due to the huge informal drug sale that is

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<sup>57</sup> Actually, even if they have been provided with such information, it would still not be reliable as the sensitivity to chloroquine kept changing dynamically (Shretta et al., 2000).

not addressed nor controlled by officials. Shops offer anti-malarial drugs of not always high quality (due to inappropriate storage, exceeded expiry date etc.) and without the control of trained health officers (Shretta et al., 2000). Purchasing of anti-malarial drugs from the unofficial pharmaceutical market often leads to the misuse of pharmaceuticals as every fever is treated with anti-malarial drugs “just in case” due to lacking access to advanced diagnostics. People tend to use the easiest, quickest and cheapest way of obtaining drugs (see Figure 14). The issue of informal drug sale represents a wide range of problems emerging from a supply-based approach of officials, who do not include the local socio-economic environment into their responsive strategies (Pattanyak et al., 2006).

*How do inadequate political responses affect malaria distribution and the risk of malaria infection?*

Generally, inaccurate responses may play a role in the increase of malaria risk. The responses very rarely address the *causes and processes* that underlie the malaria burden (namely environmental or socio-economic factors). They rather deal with *numbers and cases* concentrating on prevention and treatment.

*How do inadequate political responses affect parasite and vector capacity?*

Extensive overuse of one type of insecticide against malaria vectors - like in the case of DDT a few decades ago - leads to the elimination of mosquito strains that are sensitive to this particular active agent. Other strains and populations, resistant to this insecticide, spread and grow in numbers and are colonizing areas where insecticide-sensitive mosquitoes used to live. Furthermore, the widespread use of insecticides against mosquitoes results in a side-effect elimination of other arthropods. Their, then empty, niches are available for malaria vectors that were meant to be killed out. Therefore the insecticide-resistant mosquitoes (that often also have different transmission patterns or are hosts to drug-resistant malaria parasites) can colonize not only ecological niches emptied from insecticide-sensitive mosquitoes. They can also take over the niches emptied from other, non-vector arthropods and therefore breed and spread on rates beyond expectation (Possas, 2001).

Similarly, the extensive use of one anti-malarial drug as a first-choice treatment, leads inevitably to a selection of *Plasmodium* mutants that are resistant to this drug. Wrong diagnoses are common in East Africa due to the lack of appropriate technical equipment (mainly microscopes) or qualified medical staff to do blood tests for the detection of parasite infected/damaged erythrocytes. Treatment of other diseases that give similar symptoms to malaria infection (fever, weakness, shivering etc.) with anti-malarial drugs enhances parasitic resistance. It has been estimated that just

40% of the febrile cases in Africa may be attributed to malaria (Worall et al., 2002). However, the WHO still recommends treatment of patients reporting fever with anti-malarial drugs, wherever malaria is highly endemic (WHO, 2006).

The slow and ineffective implementation of new, effective therapies leads likewise to drug resistance. This happened in the case of Sulfadoxine-Pyrimethamine treatment (Mutabingwa, 2005). Its anti-malarial potential has not been fully exploited due to the slow turn towards SP as a first-choice drug. Therefore parasites had enough time to develop into SP-resistant forms<sup>58</sup>.

### *How do inadequate political responses affect human vulnerability to infection?*

The narrow understanding of “vulnerability” leads to the development of wrong supportive strategies among the donor agencies. It is true that children below five years of age (before they gain a partial immunity against malaria infection) as well as pregnant women (also of lowered immunity and also a favored target for feeding mosquitoes) lead in the statistical records of malaria cases (Teklehaimanot et al., 2007). Therefore, the actions of donors are focused on those groups. They are most likely to be addressed with free distribution of insecticide treated bed-nets or anti-malarial drugs. This approach excludes non-pregnant adults and older children, who are indeed less vulnerable, but still vulnerable to mosquito bites and can act as malaria reservoirs. As a result some individuals are protected from malaria infection but transmission within the community is not terminated (Teklehaimanot et al., 2007). Furthermore, the transmission might be enhanced between communities as the most mobile, professionally active individuals become the target for mosquitoes.

Similarly, the up-hill highland populations of the East African Community are seen to be particularly prone to malaria infection due to their low immunity (Lindsay & Martens, 1998). Therefore, disease control efforts in the Tanzanian Pare district have concentrated on the insecticide treatment of houses up-hill, where people are most vulnerable to malaria infection. However, it has been reported not to bring the expected effects as long as actions were not taken also within the valley communities, where the mosquito breeding sites were actually located (ibid).

Wrong diagnoses, as described above, result not just in drug resistance, but also in a range of side effects weakening patients and enhancing their vulnerability to the severe course of malaria. They also require high unnecessary expenditures from the public health system that could rather be spent on accurate treatment or preventive actions (Pattanayak et al., 2006). False diagnoses together with decreasing cure rates and low availability of public health care facilities (see Figure 13), result

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<sup>58</sup> For more information about how drug resistance develops, and how it depends on medicine’s effect on parasites, please see chapter 5.1.3.

also in common skepticism towards the public health systems and in a turn to traditional medicine and self treatment among the local people. This trend has been observed by Nuwaha (2002) in Uganda, where more than 70% of the malaria patients did not seek help from public health institutions. Unfortunately, the lack of professional treatment increases individual's risk of malaria-caused severe morbidity and death. Cooperations with communities and educational programs are often underestimated and were proposed by Nuwaha as an effective strategy to enhance trust towards public health care.

Variable	n	%
Households with at least one person who had malaria in previous 2 weeks (n= 643)	334	52
Number of persons who suffered from malaria in previous 2 weeks (n= 3309)	460	14
Place/type of treatment (n= 460)		
Government health unit	135	29
Private clinic	212	46
Drug store	105	23
Self-treatment	64	14
Traditional medicine/herbs	54	12
Others*	20	4
No treatment as yet	6	1
Drug for treatment (n= 460)	286	62
Chloroquine	215	47
Fansidar/Metakelfin	114	25
Quinine	7	2
Amodiaquine	5	1
Artemether	32	7
No antimalarial	54	12
Traditional herbs	6	1
No treatment as yet	59	13
Do not know drug I got	200	44
Blood examined (yes)	286	45
Have you or any member of your family ever used traditional medicine for malaria (yes) n=643		

\*Includes drug vendors, shops taking of leftover drugs

**Figure 13.** Malaria morbidity and health care seeking behavior for malaria in Ugandan Mbarara municipality (Nuwaha, 2002).

*What are the links of inadequate political responses to other drivers?*

Failed responses to the emergence and re-emergence of malaria are directly linked to drug resistance and poverty in different causal relationships. Unsuccessful interventions based on unilateral pharmaceutical treatment strategies, underlie the appearance and expansion of drug resistant forms of the malaria parasite as has already been described. On the other hand the failure

of official responses is often rooted in poverty. Drugs, even if recommended, will not be purchased if their price on the free market is too high for those that get ill (Mutabingwa, 2005). The same can be said regarding mosquito nets or insecticides (Teklehaimanot et al., 2007).

### **5.2.2. Demographic Changes**

*What processes underlie demographic changes and what are its characteristics?*

During the 20<sup>th</sup> century the population at risk of malaria infection grew from 0.06 to 0.65 billion people in the African region (WHO, 2008). More than 80% of those people live in areas of hyperendemic and holoendemic malaria (Hay et al., 2004). This growth is strongly attributed to the global population increase from one to six billion, whereas the geographic distribution of malaria changed just slightly (ibid.). The East African Community is characterized by an average yearly population growth of 3% per year and has experienced an increase in population from 105.8 to 118.6 million people within the four years 2002-2006. The population density increased during this period in all countries of the EAC from an average of 163.8 to 182.6 persons per square kilometer (EAC Social statistics, 2006). Those trends are projected to remain during the 21<sup>st</sup> century.

Intensified travel and migration additionally enhance malaria transmission and emergence. Besides local migrants forced by economic conditions or insecurity, there are several millions of non-immune people that travel for business or pleasure to malaria areas every year<sup>59</sup>(Greenwood, 2005).

It is difficult to associate the trend of migration from rural to urban areas undoubtedly with an increase of malaria risk or with its decrease. On one hand migrants often occupy areas characterized by low sanitation and unpaved roads where small puddles often fill with water. This provides good breeding opportunities for vectors (Lindsay & Martens, 1998; Kimani et al., 2006). In growing informal suburbs, the high population density goes along with widespread malnutrition and little financial means for buying bed-nets, insecticides and drugs (Teklehaimanot et al., 2007). This all provides good conditions for malaria transmission.

On the other hand, Omumbo et al. (2005) analyzed 333 surveys on malaria parasite prevalence between urban and rural populations and found out that within urban communities the

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<sup>59</sup> In Europe and North America there are suitable climatic conditions for malaria transmission and vectors are present there. There is an increasing number of non-immune travelers who get infected in malaria areas and travel back home. It has been estimated by WHO that between 1985 and 1989 there have been 16,000 malaria cases imported to Europe. In the USA every year about 1000 cases have been reported (Martens et al., 1999). If this trend continues, the re-emergence of malaria in those regions is possible in future, although the high efficiency of health-care systems in the region may prevent it.

numbers were lower by 10-18%. The authors argue that urban inhabitants are more likely to have the financial means or better access to preventive and curative measures.

This might be true for an average citizen, but not always for poor newcomers crowded in peripheral areas with a low provision of facilities. They influence natural ecosystems and integrate them into urban areas. Possas (2001) claims that this selective pressure on pathogenic organisms increases their plasticity by changing their recombination and production patterns. Although she does not specifically mention malaria, such processes are theoretically possible wherever urban settlers exert pressure on environments supporting development of mosquitoes and malaria parasites.

*How do demographic changes affect malaria distribution and the risk of malaria infection?*

*How do demographic changes affect parasite and vector capacity?*

The growing population of Eastern Africa exerts an increasing pressure on the natural environment. Areas of natural vegetation are being transformed into agricultural or urban lands. The disturbance of the ecosystem balance results in an unpredictable spread of malaria vectors or changes in the micro-climatic conditions that further support malaria transmission<sup>60</sup> (Lindblade et al., 2002; Munga et al., 2007).

As the population of the African continent continues to increase, people colonize previously sparsely populated areas. The increase of population density enhances transmission rates of malaria resulting in a higher overall risk of getting infected. Furthermore, the newcomers from malaria endemic areas spread parasites in regions where the incidence of malaria was previously low. This might even precipitate epidemics within indigenous populations of lower immunity (Lindsay & Martens, 1998).

Next to one-way migration, also an increase in seasonal or even daily migration can be observed. When homelands cannot feed the local population, people tend to look for jobs in the neighboring regions. Especially in rural areas more attractive job markets are associated with the locations where climatic and hydrological conditions support agriculture. Those conditions, however, also provide a good environment for the breeding and development of mosquitoes and malaria parasites. Those who work there spread malaria when they visit their families back home. Indeed it has been observed in the 1980s and 1990s in Rwanda and Burundi that men traveling to work in endemic areas were at enhanced risk of malaria infection (Lindsay & Martens, 1998).

Intensified human mobility increases the risk of passively transporting highly anthropophilic

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<sup>60</sup> More about the influence of land use/cover changes has been presented in chapter 5.1.2.

mosquito species responsible for high malaria transmission rates into regions where they have not been reported before. *Anopheles gambiae s.l.* has probably colonized the East African highlands by being brought there from the lowlands by cars, trucks or trains (Lindsay & Martens, 1998). In regions where mosquitoes find appropriate breeding habitats (see section below) and the microclimate supports larval development, malaria may become indigenous when parasites are introduced. Chen et al. (2006) suggest that this might have been the case in the Mount Kenya highland region.

#### *How do demographic changes affect human vulnerability to infection?*

It has been empirically proved that malaria vectors do not fly distances greater than 2.5 kilometers from the place of pupation (Omumbo et al., 2005). Thus, a higher population density contributes to an increase in malaria transmission by the increasing number of people that an infected mosquito may bite within its area.

Migration implies various difficulties for the public health systems. First of all migrants are rarely treated by the same doctors during the whole time of infection. As there are scarcely any common computerized systems of personalized data collections, treatment of migrants might be incomplete or insufficient. Furthermore, people that travel before the treatment has been completed carry the parasites with them to other locations (Pattanayak et al., 2006).

Among the migrants in the highland regions of the EAC frequent malaria relapses or recrudescence have been reported. This may be associated with lower temperatures or pressure as well as with stress due to traveling (Lindsay & Martens, 1998).

#### *What are the links of demographic changes to other drivers?*

Migration may be partially caused by bad economic conditions and therefore the demographic movement is strongly connected to poverty. Social pressure of responsibility for the survival of their own family obliges people, particularly men, to seek employment even in distant locations.

Civil disturbances force people to move as well. As described in the next sub-chapter, refugees staying in temporary camps are often at elevated risk of malaria infection due to low sanitary conditions.

The increasing population density results in a higher pressure on the natural environment as related to deforestation, vegetation clearance, building of irrigation systems, and housing. Those changes support in many cases the development and breeding of mosquitoes (Zhou et al., 2004). Land cover changes or housing may furthermore change microclimatic conditions towards

supporting the development of parasitic protozoa and their mosquito hosts (ibid.).

Additionally, traveling and migration enhance the spread of insecticide resistant mosquito strains and drug resistant malaria parasites.

### **5.2.3. Poverty and Civil Disturbances**

*What processes underlie the poverty and civil disturbances and what are their characteristics?*

Poverty does not refer just to low financial means for the provision of goods. In the context of human rights, poverty can rather be seen as a human condition characterized by an ongoing deficit of resources, capabilities, choices, security and power that can be allocated for the adequate standard of living and other civil, cultural, economic, political and social activities (UNDP, 2003).

It is almost impossible to state which indicator most properly demonstrates socio-economic stratification<sup>61</sup>. It might differ from region to region, from community to community, and from individual to individual. The natural environment people live in, as well as social, economic and political conditions, determine what “poverty” can mean and how it can be measured in a particular case. This is probably one of the reasons why surveys on the linkage between malaria and poverty use a very diverse range of methods and indicators.

Still, it can be concluded that malaria risk is affected by various aspects of poverty: deprivation of resources for anti-malarial prevention and drugs; deprivation of choice of effective treatment or of a job in a malaria-safe location; and deprivation of access to public health facilities, just to mention a few. On the global level the correlation between low income and malaria burden is visible. 57.9% of all malaria deaths happen in the poorest fifth of the world’s population (Worrall et al., 2003). On the microeconomic level the survey results have not given such a consistent picture as on the macroeconomic level (ibid.), which might be due to different ways of measuring the socio-economic status. However, multiple studies from the East African region exemplify how strongly poverty may influence malaria risk of communities or individuals.

Example of Kenya shows how crucial for reducing malaria risk is not only the individual wealth but also the one of the country. Despite the fact that Kenya is a regional leader in the field of economy, the country has lately been going through economic and political difficulties. Initial gains after the independence (1960s-1980s) were followed by a decrease in the real economic growth, which reached -0.3 percent in the year 2000 (Republic of Kenya, 2009b). This resulted in a general

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<sup>61</sup> The United Nations Development Programme proposes that the proportion of people living for less than 1US\$ per day would be the most appropriate global poverty index. Among the countries of the East African Community Kenya has the lowest proportion of people living for less than 1US\$ per day (22.8%), whereas in Rwanda and Burundi those numbers are above 50%. Still, all countries of the EAC fall under the “low income countries” category of the UNDP (UNDP, 2007).

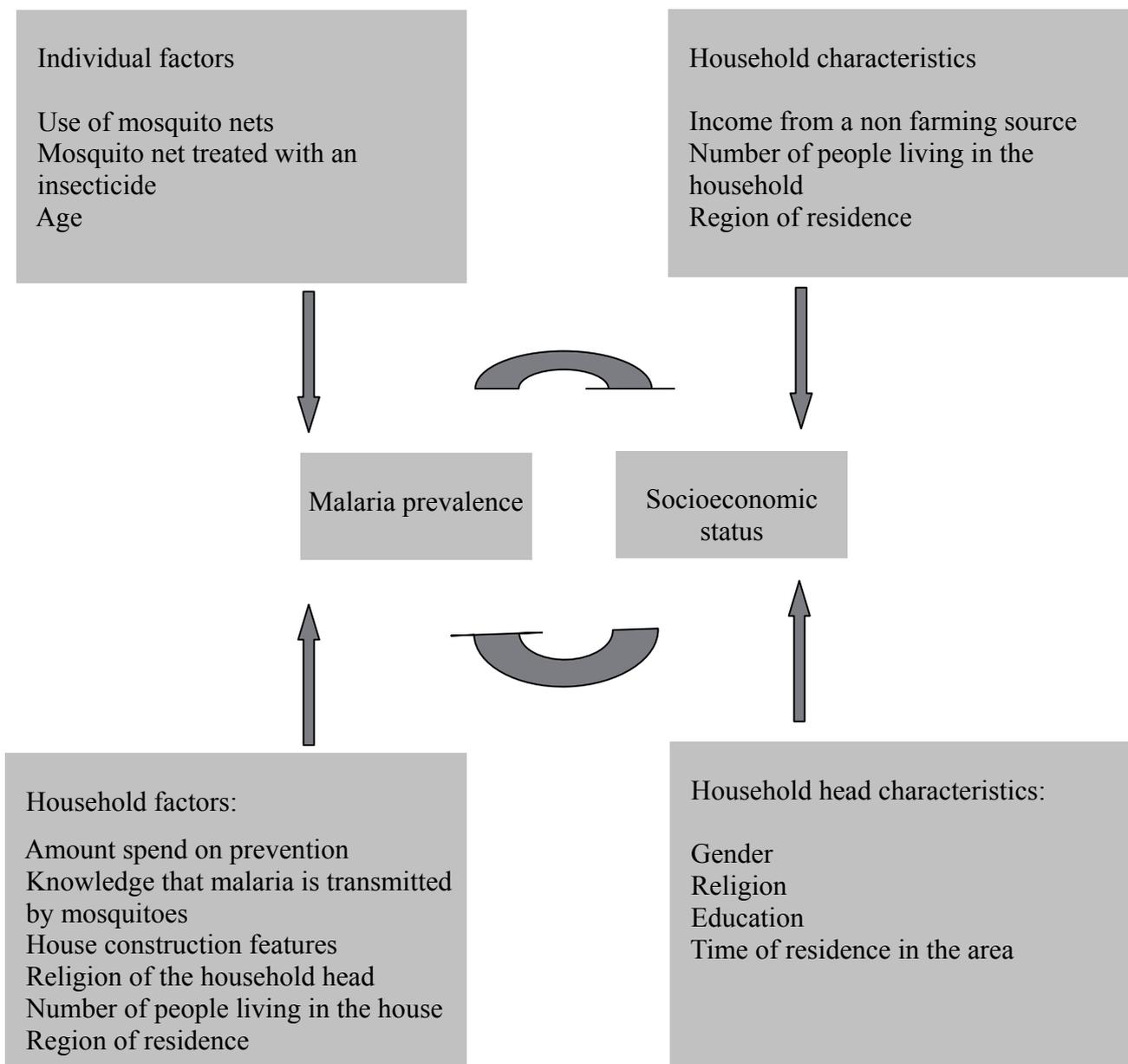
worsening of public health care and the increase of poverty among Kenyan citizens as the Human Development Report 2007/2008 (UNDP, 2007) reported. It correlates with the resurgence of infectious diseases like tuberculosis, HIV/AIDS and malaria. Health indicators worsened from 1998 to 2006 particularly in the highland provinces: Central Province, Nairobi<sup>62</sup> and Western Province (UNDP, 2007). The World Health Organization (WHO) Commission on Macro Economics and Health (WHO, 2001) agreed that basic health care can be provided if public expenditures of US 34\$ per capita are made. Kenya's total health expenditures in the budget year 2005/2006 were US 27\$ per capita and thus fell short of the WHO recommendation (Republic of Kenya, 2009b). This results in little expenditures on malaria prevention and control in the Kenya.

On the other hand, malaria may be a barrier to property accumulation and can be accounted for a decrease in the number of working days. In some regions of Cote d'Ivoire, where malaria is seasonal, farmers were found to get often ill during the harvest time which resulted in lower yields and income (Somi et al., 2007). It has been estimated that malaria reduces the annual GNP growth per capita by 0.25-1.30% in tropical countries (Sachs & Melaney, 2002). Malaria also affects Africa's human resources through the increasing children's absence at school and the neurological damages resulting from severe forms of illness (Worrall et al, 2002; Greenwood et al, 2005).

This dual causation relationship (see Figure 14) between malaria and poverty leads to a situation where household members are caught in a reinforcing cycle. They are not able to pay for preventive measures and in turn they get ill which reduces their ability to earn money they could spend for malaria prevention.

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<sup>62</sup> The Nairobi Province however, as it consists exclusively of urban areas, is not representative for Kenyan highlands in general.



**Figure 14.** A conceptual framework depicting the relationships between malaria and socioeconomic status. Outcome of the study conducted in the Kilombero, Ulanga, and Rufiji Districts, southeastern Tanzania in 2004 (Somi et al., 2007).

Civil disturbances decrease both individual and state's wealth whereby the expenditures on malaria prevention and control decrease as well (Greenwood et al., 2005). Refugees are forced out of their homes and find a shelter in refugee camps that are characterized by provisional housing, overcrowding, poor sanitation and medical care (Kimani et al., 2006). Additionally, international aid organizations have difficulties in approaching the needs with malaria control programs in instable countries.

*How do the poverty and civil disturbances affect malaria distribution and the risk of malaria infection?*

*How do the poverty and civil disturbances affect parasite and vector capacity?*

Cheap anti-malarials are generally those to which parasites' drug resistance has spread more than to the modern drugs. Artemisinin Combined Therapies, currently the most effective type of treatment, are up to ten times more expensive than monotherapies (Greenwood et al., 2005). People with a lower socio-economic status more often use those cheaper, but less effective drugs (Worrall et al., 2003). Thus, poverty prolongs treatment and supports the spread of drug resistance.

Poor sanitary practices in refugee camps may provide more mosquito breeding sites and thus increase the risk of malaria infection among refugees. The refugees in Daadab in Kenyan Garissa district used water from communal taps located outdoors in a few locations in the camp. Water spilled from the taps formed pools where mosquitoes bred in great numbers (Kimani et al., 2006).

*How do the poverty and civil disturbances affect human vulnerability to infection?*

There is no consistency among survey results whether poverty increases malaria incidence, but it seems to be clear that it increases the risk of severe consequences of infection. A correlation between malaria incidence and socio-economic status may be confounded by environmental factors, that are not always known or whose influence on malaria has not been studied in a given region. Morbidity and mortality, on the other hand, have much more to do with low access to prevention and treatment. The poor seek help first from traditional medicine, which is less effective but cheaper, as exemplified by studies from Kenya (Nyamongo, 2002).

Poor people tend more often to live in houses that are small, overcrowded and have a few or no windows at all (Worrall et al., 2003). This causes people to spend more time outdoors, also during the time of the highest vector activity: at dawn and sunset.

The use of mosquito nets, especially those treated with an insecticide, provides not only protection for the individuals that sleep under it, but also contributes to the so called "community effect", where the protection is extended to unprotected members of the community (Teklehaimanot et al., 2007). Mosquito-nets, when appropriately used, decrease malaria transmission and reduce the risk of being bitten by an infected mosquito. Thus, the lack of a net, as well as its irregular use or treatment, increases malaria infection risk for the whole community.

The low socio-economic status results in less money being spent on malaria prevention and on the treatment of malaria infection (Worrall et al., 2003). As little as 8% of the poorest members

of the Tanzanian community studied by de Savigny et al. (2002) reported a preventive usage of mosquito nets (in Worrall et al., 2003). Also in Uganda the fact of living in a permanent house, which is in turn an indicator of a relatively high socio-economic status, correlated strongly with the use of mosquito nets (Nuwaha, 2001). Insecticides used for the net treatment are cheaper than the net itself and therefore there was not such a great inequality in net treatment between poor and rich. However, there may still be observed a positive relationship between income and net treatment (for a Tanzanian case see: Worrall et al., 2003).

Ownership of an untreated net does not yet mean that the net is in a physical condition good enough to provide proper protection to people sleeping under it. Unfortunately, there are not many surveys on nets' condition. A survey in Gambia, where children's bed nets have been examined, showed that the poorest households had just 50% of the nets in a good physical condition (Worrall et al., 2003).

Hanson and Jones (2002) found out that Tanzanian farmers had difficulties in obtaining credits for mosquito nets, but got them easily when they needed to cover malaria treatment costs. Therefore, they had to wait for cash income during harvest time to buy a net (quoted in Worrall et al, 2003).

Sleeping facilities offered to refugees in camps often additionally limit the use of bed nets. Kimani et al. (2006) studied bed-nets' use in a refugee camp in Daadab. They found out that the temporary houses the refugees slept in were too small and overcrowded, making it not always possible to hang a net. Moreover, in this semi-arid region nights are hot and small houses without windows were for many unbearable to sleep in. Those who chose sleeping outside the house had therefore no protection against mosquito bites and were at higher risk of malaria infection than those who slept indoors. The authors of the study claim that this situation is common not only for refugee camps but also for other poor communities.

War and civil unrest may lead to re-emergence of malaria. 29% of the global population (80.5% of people at malaria infection risk) lives in areas where malaria transmission was once low or non-existent, but has been re-established on significant levels. Civil disturbances lead to the rapid movement of people (refugees), their settlement in overcrowded temporary camps, and the collapse of public health care and malaria long-term control strategies (Bloland & Williams, 2003).

As already mentioned before, one of the groups most vulnerable to both mosquito bites and severe malaria are pregnant women. Therefore adequate malaria prevention and treatment are very important. The Intermittent Preventive Therapy in pregnancy (IPT) protects against low birth weights of children and malarial anemia (Greenwood et al., 2005). Unfortunately, the cost of antenatal care is often too high for future mothers to bear (Worrall et al., 2003).

Another particularly vulnerable group, namely children under five years of age, also suffers

from poverty of the households they live in. In Tanzania, for example, within this group mortality following acute fever (which may be attributed mainly to malaria) was 39% higher among the poorest than the richest (Kimani et al., 2006).

*What are the links of poverty and civil disturbances to other drivers?*

Regions with a high proportion of poor households need an extensive public support towards malaria control. The same is true for refugee camps. Regions with civil disturbances are dependent rather on international interventions. Therefore the poverty-malaria nexus is strongly sensitive to inadequate responses.

Poverty is a common driver of migration, and the decrease in income may be a result of environmental changes, like the increase in frequency of extreme weather events.

Poor people tend to use cheaper drugs and to buy them on the informal market, which leads to an increased risk of drug resistance.

## 6. Conclusion

In this study I have demonstrated that there is no clear single path of malaria causation. Various natural as well as political, economic and social factors influence malaria risk. Climatic conditions affect the development of parasites and vectors; land cover decides on the region's suitability for vector breeding; socio-economic status as well as public engagement decide on access to malaria prevention and control. Therefore the result of this analysis supports the hypothesis of multiple causation of malaria risk increase observed recently in the countries of the East African Community. Changes within the above mentioned factors, together with intensified demographic movements and spreading drug resistance, have affected the biology of malaria transmission and became drivers of the increasing risk of malaria infection, morbidity and mortality.

I have explained that the complexity of the malaria parasites' life cycle severely complicates an understanding of all factors affecting malaria infection patterns. Hosts of *Plasmodium*, humans and mosquitoes (in their two forms: larvae and adult), live in different habitats and are characterized by their own biology. Various factors affect those and in turn the transmission of malaria. Human individual and societal behavior- and decision making-patterns are furthermore coupled with the ecological system they live in, as described by the concept of the social-ecological system. Due to interactions between the elements of this system, changes within the one component affect the other ones, often unexpectedly for humans not aware of all the bonds that are part of the system.

How crucial multiple drivers and their interactions can be for the development of the malaria situation has been explained in chapter 5 with the case study of malaria risk increase in the Kenyan Highlands. The population pattern of malaria risk can be explained by a complex web of numerous interconnected factors: land use changes, population density, topography, access to health care facilities and many more, identified or still waiting to be discovered. As the changes accumulate, they exert pressure on the environment that results in modified patterns of malaria infection. As a result the incidence of epidemics in Kenya has increased and malaria transmission is projected to develop into a year-round stable type before the turn of the 22<sup>nd</sup> century.

It is evident that the undesired increase in the risk of infectious diseases in East Africa and many other parts of the world is connected directly and indirectly to anthropogenic forces exerted on the natural environment through, among others, greenhouse gas emissions and urbanization.

My results raise questions about the actions that can be taken to prevent a further increase of malaria risk in East Africa and above all in its highland regions. High elevated locations have in the past been praised for their malaria-free, desirable living conditions. Nowadays, the fragile non-immune uphill communities are threatened with unpredictable malaria outbreaks. The situation is complicated further by dramatically increasing and spreading resistance to anti-malarial drugs, as

exemplified by the latest dramatic increase in parasitic tolerance to the, until very recently most recommended and effective, Artemisin therapies reported by a clinical study being carried out in Cambodia by the US Armed Forces Research Institute of Medical Science (AFRIMS) (BBC World, 2009). While it is evident that drug tolerance and resistance are going to increase, it is also clear that the development of new drugs and especially vaccines is not a financially attractive field for pharmaceutical companies (Greenwood et al., 2005).

The income lost by malaria-endemic countries due to malaria, malaria-related illnesses and death is estimated to be in average 1% of the Gross Domestic Product (GDP)<sup>63</sup>. However, those estimates do not include the more complex negative impact that malaria has on social, scientific, cultural and economic capacities of communities suffering from malaria. In Kenya the recent dramatic increase in malaria risk affects in particular the western highland region that is characterized by fertile soils and climate that supports agriculture, as well as by a very high population density. Further intensification of malaria transmission in the region may affect Kenyan economy and the existence of numerous individuals in a very negative way.

The complexity of the malaria risk situation in East Africa presented in this thesis has implications on considerations regarding the effectiveness of the present *modus operandi* in the field of malaria prevention and control. Unilateral actions that do not consider the local web of interacting risk drivers may need to be replaced by strategies based on multiple causation models. However, such strategies can be successful only if the correspondent models are in place. Research into the malaria causation loops represents an important input to international and national policy. Additional recommendation for further investigations include: modeling the impacts of changes within the drivers of malaria infection; and above all development of agreed-upon methodologies of measuring malaria risk and its multiple causes. Within the scope of this thesis it was not possible to identify sources that quantify the fractions of malaria risk attributable to each cause. Such knowledge is however required for policy actions to be accurate in future.

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<sup>63</sup> This is calculated by adding the value of lost working days based on estimated wages and the value of future lifetime earnings that a person could have earned without the premature death due to malaria (Sachs & Malaney, 2002).

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