Modelling Malaria Risk: an Individual Based and Spatial Explicit Approach

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Most conventional malaria models examine the dynamics of infected humans within one population. These models are mainly aimed at understanding the mechanisms that play a role in the distribution of malaria and determining points at which control measures can be applied. Currently a number of models take a different approach; examining malaria risk at a larger spatial scale these models are mainly aimed at assessing the effect of large-scale changes (most prominently climate change) on the number and location of people at risk currently and in the future. The LEMRA (Local Eco-Epidemiological Malaria Risk Assessment) model presented in this paper takes an approach somewhere halfway these two extremes; it explicitly examines the disease dynamics in the human population, in the context of a spatial setting where the local condition determine the risk for the population to be exposed to malaria. The spatial scale of analyses is such that it can include processes (like the effect of human circulation behaviour) that cannot be examined as easily in the former two approaches.

Introduction

Each year 1.5 to 2.7 million people die from malaria (WHO 1997). This is only a small proportion of the 300 to 500 million people who suffer from this disease. Malaria is constantly present in at least 91 countries, exposing approximately 40% of the world population to the risk of contracting the disease. By undermining people's health and capacity to work, malaria significantly hampers the social and economic development of the countries involved (Wang'ombe and Mwabu 1993; Gallup and Sachs 1998).

Future changes might have a significant influence on malaria risk. For example, it has been estimated that climate change might lead to an increase in malaria in especially the highlands (Lindsay and Martens 1998), but also more local changes like migration have already shown to lead to considerable (temporal) increases in for example brazil (McGreevy *et al.* 1989). To give a good assessment of future malaria risk, it is necessary to take account of the various processes that take place in an area; integrating the environmental, social and economic factors and processes that underlay malaria risk. In an Integrated Assessment approach (Rotmans 1998) we not only try to describe the cause-effect relationship of a specific problem (i.e. the relation between malaria risk and its underlying factors), but also the crosslinkages and interactions with other problems or processes. An IA approach is used in the LEMRA (Local Eco-Epidemiological Malaria Risk Assessment) model (de Vries and Martens 2000) that is presented in this paper. The LEMRA model is not being development as a predictive model, but as a tool to experiment with different possible futures and the consequences of these futures for malaria risk. This paper provides an outline of the model and the direction in which it will be evolve further.

A number of spatial explicit models for the assessment of future malaria risk have been developed (Matsuoka and Kai 1994; Martens *et al.* 1995; Martin and Lefebvre

1995; Craig *et al.* 1999; Martens and Hall 1999; Martens *et al.* 1999). These models focus mostly on the impact of climate change at either the global or regional scale. The LEMRA model focuses on a smaller spatial scale than these models, and, as consequence of the chosen scale, is able to include a number of processes that are hard to include at a larger scale (for instance the development of immunity within the population). This is illustrated in this paper by partly applying the model to an area in Kenya.

Malaria Risk

Malaria is a disease caused by a parasite that is transmitted from one human to the other by blood sucking mosquitoes. The spread of malaria is a complex process that depends on a great number of factors from a diverse set of domains. A rough classification of these factors can be made by splitting the factors in two groups: the factors that influence the *transmission risk*, i.e. the potential for the transmission of the malaria parasite, and the factors that influence the *disease risk*, i.e. the potential morbidity and mortality in the population as a consequence of this transmission of the parasite.

The *transmission risk* depends on the mosquito population and its interaction with the human population (i.e. stinging). The mosquito population size is influenced by ecological factors (temperature, rainfall and landcover), but also by social-cultural and economic factors (local knowledge of the mosquito life cycle and the means to apply this knowledge for control measures). The interaction between the human population and the mosquito population depends on ecological and biological factors (mosquito characteristics and behavioural patterns), and on social-cultural and economic factors (landuse, human behaviour or local knowledge about the malaria–mosquito link and the means to apply this knowledge for protection measures). Future development of transmission risk will therefore depend on phenomena like deforestation, climate change, changes in the educational and malaria monitoring/control system etc.

Transmission risk is mostly associated with the local conditions at a spatial position and is therefore considered homogeneous for the human population at this location, in contrast the *disease risk* affects population groups in the same area differently, therefore the heterogeousness of the population plays an important role in estimating this risk. For example the age distribution of the population can significantly alter the number of deaths, since in high endemic areas (area with a large transmission risk) infants have the highest malaria related mortality. Disease risk is mainly influenced by social-economic and social-cultural factors (local health knowledge and the (financial) capability to apply this knowledge, human migration and circulation patterns, or the wealth distribution over the population). Disease risk and its distribution over the population might change due to processes like economic growth, degradation of the health system, changes in the labour market, etc.

The LEMRA model uses the two risk concepts described above to assess malaria risk. For simplification it uses only a subset of the described factors. The next two sections describe how the two risks are estimated. Although both risks are described the focus is on the disease risk.

Transmission Risk

Most malaria models are either directly related to the Ross-MacDonald model (Ross 1909 ; Macdonald 1957) or borrow many of their concepts from this model. Although this model is conceptually very strong and includes those factors that directly influence malaria risk (for instance mosquito deathrate, biting frequencies or

parasite development rate), it is very hard to estimate the various parameters used in this model and to relate them to underlying factors like landcover or rainfall. To enable the investigation of the effect of changes in the underlying factors, the model presented here abstracts from the detailed description used in this kind of models and makes a more direct estimation of the relation between the underlying factors and transmission risk. This estimation is described here only shortly. For a more detailed description see (de Vries and Martens 2000).

Landcover provides breeding places for the mosquito and microclimates for the mosquito to live in; it influences the human-mosquito contact by its suitability for mosquitoes and its attraction to humans for certain human activities. On bases of the local landcover an initial transmission risk is determined (ranging from 0 to 4) according to Table 1. This transmission risk is adjusted for each month on the basis of the monthly mean temperature. Temperature influences malaria risk by affecting the survival chances of the mosquito, its biting rate, and the developmental rate of the parasite inside the mosquito.

A certain minimal amount of rainfall is needed for the mosquito population to survive or grow. However, the mosquito population will diminish if too much rain falls in a short period, because the mosquito eggs and larvae will be flooded out of the potential breeding places. The optimal rainfall for the mosquito depends on the type of landcover. Currently, the model only implements a minimal threshold of monthly rainfall related to the local landcover (Table 1). If the mean monthly rainfall stays below this threshold no risk of transmission is present.

Landcover	**TR**	**Suitability Threshold (mm/month)**
Water	0	0
Forest	1	20
Cash Crops (Tea / Coffee / Sugarcane / Maize)	1	60
Grassland	2	80
Small scale agriculture	4	80
Rice	4	120

Table 1 *Values associated with the various landcovers in the area.*

In short, assuming that the human host is available in sufficient quantity for transmission to take place, landcover determines which transmission risks are possible, and temperature and rainfall control the fluctuation of this risk over time. In the next session the influence of and the effect upon the human population is taken into account by explicitly modelling the human population in order to determine the disease risk.

Disease Risk

Not everyone infected with malaria becomes badly ill or dies. Individuals show a wide range of responses on first contact with the malaria parasite; from seemingly no effect to death. These individual differences can either be genetically determined, or obtained through environmental influences. Immunity against malaria can also be the result of regular exposure to the malaria parasites. This, contact dependent, form of immunity is called acquired immunity. Due to this kind of immunity, the temporal pattern of exposure plays an essential role in the impact of an infection on the health

of the exposed human; a temporal high exposure preceded by no exposure during a substantial period results in a high probability for the human to become ill, while the same temporal high exposure might not have any effect on an individual that has been exposed for many years already. This effect makes the prediction of effects of control measures or changes in general very difficult; after all, might not lead a decrease in exposure to a decrease in immunity and subsequently in an increase in morbidity and mortality? Acquired immunity is also responsible for a not homogeneous distribution of the disease over the population. For example, in a stable endemic situation (ie year round high transmission risk), it are the children who are affected mostly by malaria, since they had the least time to build up immunity, while in unstable epidemic areas (ie. transmission risk during a limited period) the effects are visible in the whole population. Again this complicates the prediction of the effects of control measures and other changes; if transmission is limited for part of the population (for example due to bednet provision programs) how is this group affected and how does it effect the transmission probabilities for other groups in the population.

The current knowledge about the immunology of malaria is rather limited. Although research on the molecular and cellular level has increased during last few years, so far it has not brought us major insight that not already could be derived from epidemiological, clinical and experimental evidence. Since the immunity model that is introduced in this chapter is limited to a very simple mechanism for building up immunity, it is not justified to discuss in any detail the molecular and cellular working of immunity and we will restrict ourselves here to a population level analysis of our current knowledge.

In general it appears that three types of immunity can be distinguished (Gupta and Day 1994; Snow and Marsh 1998; Gupta *et al.* 1999): anti–infection, anti-mild disease, and anti-severe disease. Since the protection provided by anti-infection immunity is almost never complete, it is assumed that a lower parasite load in an individual does not influence the transmission probabilities and the effects of anti-infection immunity are ignored. The last two types of immunity, called clinical immunity, will be modelled. Various studies indicate that immunity against life-threatening diseases develops much faster than that against mild disease (Gupta *et al.* 1999, Snow). Currently, only the anti-mild disease immunity is implemented.

The conventional and most common approach to modelling the epidemiology of malaria within the human population is the use of mathematical models (Bailey 1982). These models take (subsets of) populations as the unit of calculation. In contrast, the population model presented here focuses on individual humans as unit of calculation. This approach is known under various names. Currently it is most often referred to as “agent based” modelling; however, in this particular case, a more appropriate designation might be “individual-based” modelling. Unlike the term “agent”, “individual” is not associated with autonomy, decision making, intentions etc., while at the same time stressing the importance for the model of individual behaviour and differences between individual entities.

The individual-based approach enables a more or less natural translation of processes into model terms: for instance, infection probability, can be described at the level of an individual and individual differences like age, bednet use etc. can be taken into account explicitly. Analyses of the model can take place at the level of the individual as well as the level of the population as a whole or of subgroups of the population (for instance age groups). These various possible levels of analyses

facilitate comparison with a larger range of research results from the field than if only population wide process descriptions are used.

The aim of the presented immunity model is to provide a simple flexible system capable of catching some important characteristics of malaria immunology. Its aim is not to be a precise representation of the complex immunology system. The immunity module can be seen as a metamodel (Rotmans *et al.* 1997), i.e. a simplified representation of the more sophisticated immunity models

The central computational units in the population model are the individually simulated humans. Here we will use the denotation HUMAN to distinguish a simulated human from its real world counterpart. In the simplest form the model entity HUMAN has the following properties:

- Gender
- Age
- Infected
  Is true when infected by the malaria parasite, is false when not infected.
- Infection time left
  The amount of time left, before the individual looses its infection.
- Ill
  Is true if HUMAN is ill (i.e. shows clinical symptoms of malaria), is false when not ill.
- Illness time left
  The amount of time left until the individual is no longer ill.
- Immune
  A number between 0 and 1 indicating the amount of immunity, i.e. 0 is no immunity and 1 is full immunity.

At birth a HUMAN is not infected and has an immunity of 0. The transmission risk to which the population is exposed, combined with the proportion of infected HUMANS in the population, form the risk for an individual HUMAN to contract malaria. Each month a HUMAN is exposed to this infection risk P_{inf} . P_{inf}, the probability of infection, is defined as

$$P_{\inf}(t+1) = \alpha * \frac{risk(t)}{MaxRisk} * \frac{POP_{\inf ected}(t)}{POP_{total}(t)},$$

where $POP_{infected}$ and POP_{total} are the number of infected individuals and the total number of individuals in the population of a cell respectively, *risk* is the transmission risk to which the population is exposed, *MaxRisk* is the highest transmission risk possible, and α incorporates other factors that influence an individual's chance of contracting the disease, for instance an individual's use of anti-malarial drugs, its use of bednets, the kind of labour it is involved in etc. Once infected a HUMAN stays infected for *infectionPeriod* time.

Everytime that a HUMAN is infected its immunity increases in accordance with the function immunityIncrease(), every time the HUMAN is not infected the immunity decreases following the function immunityDecrease(). These two functions can be altered to reflect various possible assumptions about acquired immunity. For the current analyses of the model simple linear functions are used:

If HUMAN is infected then
    immunity(t) = immunity(t-1) + 1/*ImmunityIncrease*

If HUMAN is not infected then
immunity(t) = immunity(t-1) – 1/*ImmunityDecrease*
(where 0 <= immunity <= 1)

Since immunity is updated every month, a value of 12 for *ImmunityDecrease* means that a fully immune HUMAN who is not exposed to any infection loses its immunity in 12 months. Equivalently, a non-immune HUMAN who is continuously exposed to infection becomes fully immune in *ImmunityIncrease* months (24, see Table 2). See Figure 1.

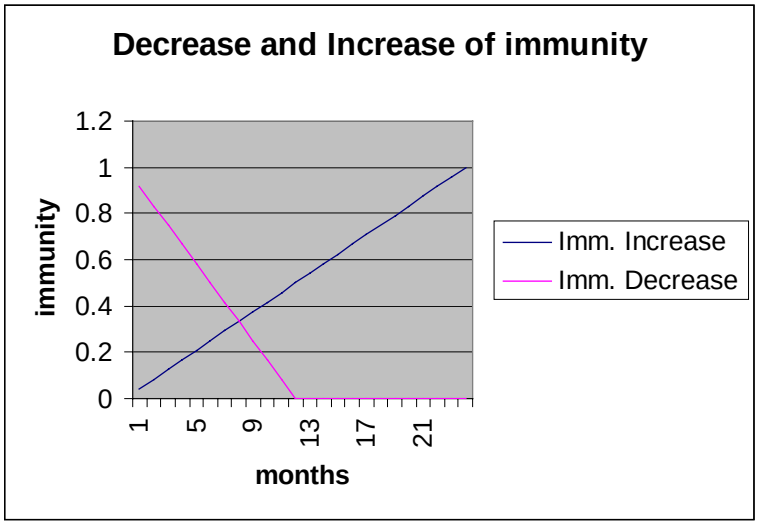


Figure 1 *The increase and decrease of immunity for an individual under the assumption of continues infection and continuous non-infection respectively.*

Finally, a changing immunity level leads to a change in morbidity and mortality. The following formula is used to determine whether at the moment of infection, a HUMAN becomes ill, and for how long it stays ill:

pill= (1 – immunity) * *MaximumDiseasePeriod*

Where *pill* is the period of illness after the initial infection, *immunity* is the immunity of the HUMAN and *MaximumDiseasePeriod* is the maximum amount of time a HUMAN can be ill. Note that it is possible for human to be infected with a malaria parasite without being ill, either because it has full immunity or because it "looses" its illness before it looses its infection.

name	value	unit	description
ImmunityIncrease	24	months	number of infections needed to gane full immunity when continuous infection takes place
ImmunityDecrease	12	months	number of non-infections needed to loose full immunity when no infections takes place
infectionPeriod	1,5	months	period needed to loose infection
MaximumDiseasePeriod	2	months	maximum length of period during which an infected person can become ill
alpha	0.8	[0..1]	modulator
Initialisation			
initialFractionInfected	0.5	[0..1]	initial fraction of the population that is infected
initialPopulationSize	500	integer	size of initial population

Table 2 *Parameter values used to produce the presented results.*

From transmission risk to disease risk

Figure 2 shows for five different transmission risks (ranging from no risk 0 to the highest risk 5) the percentage of infected humans in a population over time. Two discrepancies with the real world situation can be noticed. Firstly, the percentage of infected humans does not decrease as would be expected for a population that is exposed to a high transmission risk over a long time interval. This is a consequence of the choice for only modelling clinical immunity and excluding anti-infection immunity from the model. Secondly, it can be observed that except for the highest transmission risks, malaria infection cannot be maintained in the population. This is caused by the omission from the model of patent infections and of human population movement.

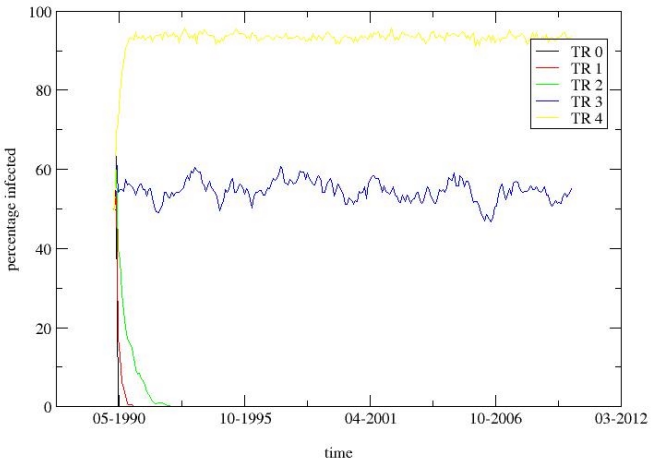


Figure 2 *Percentage infected humans in a simulated population exposed to 5 different Transmission Risks (TR).*

The effect of human population movement is illustrated further on in this paper when a spatial setting for the model is introduced and circulation of humans becomes possible. Patent infections are known to exist in areas with low seasonal endimicity, where is has been shown that the malaria parasite is still present in part of the population during the dry season when no transmission takes place (Roper *et al.* 1998). To take account of this effect an influx of infected humans is introduced. Only during the calculation of the infection probability for a human (P_{inf}) it is assumed that a minimum of *infectionInflux* (0.02) percentage of the population is infected. (Thus, after calculating P_{inf}, unless these individuals got infected, they loose their infection again). How this changes the outcome of the model is visualised in Figure 3.

No change can be observed for the highest transmission risk while the lowest transmission risk the infection does not disappear from the population anymore.

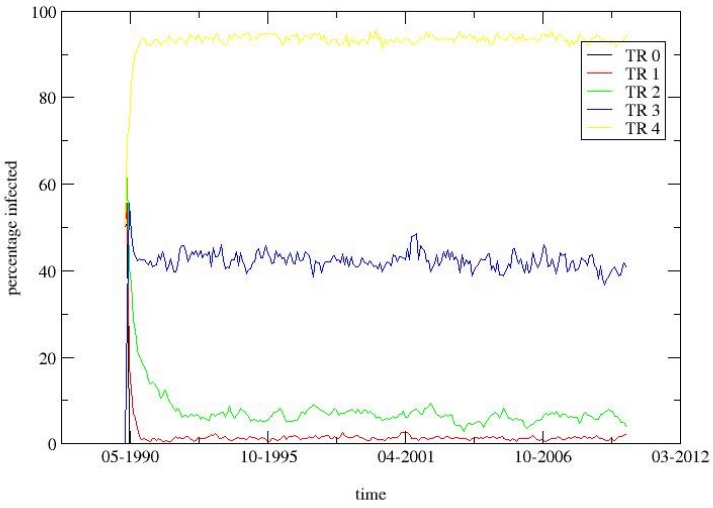


Figure 3 *Percentage infected humans in a simulated population exposed to 5 different Transmission Risks with an* infectionInflux *of 0.02.*

Figure 4 shows the percentage of humans that becomes ill when the population is exposed to the various transmission risks. For the lower transmission risks this corresponds closely to the percentage of infected humans, since individuals are not long enough exposed to build up immunity. For the highest transmission risk, however, the percentage of ill humans drops dramatically after an initial period during which immunity is build up by the individuals. Although this pattern shows a close qualitative correspondence to the real world situation, considerably tuning of the model will be needed to make a more quantitative correspondence (for example the drop in ill humans for the highest risk class is much to large). However the produced pattern can already be used to investigate some of the consequences that various transmission risks can have for the distribution of malaria disease over the population.

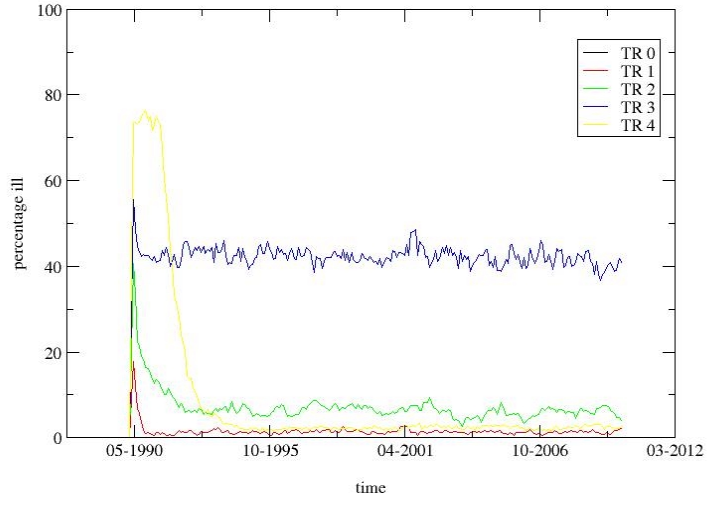
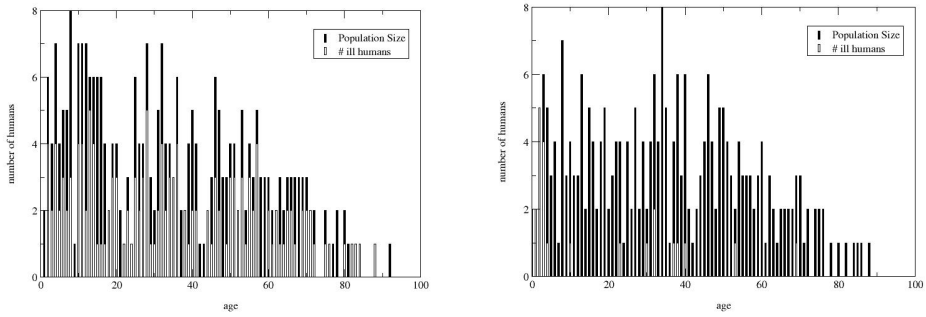


Figure 4 *Percentage of ill humans in a simulated population exposed to 5 different Transmission Risks with an* infectionInflux *of 0.02*

Figure 5 shows the fraction of HUMANS that are ill by age class for the two highest risk regimes. Clearly there is a large difference between the two regimes with respect to the ages that are affected.



a *b*

Figure 5 *Number of humans per age and number of those people that are infected by malaria. (a) Above average transmission risk (risk=3); (b) High transmission*

In reality transmission risk is often not continuous but fluctuating over time, either seasonal or with irregular intervals of a few years. Figure 6 shows three typical patterns of transmission risk and Figure 7 the resulting percentages of ill humans.

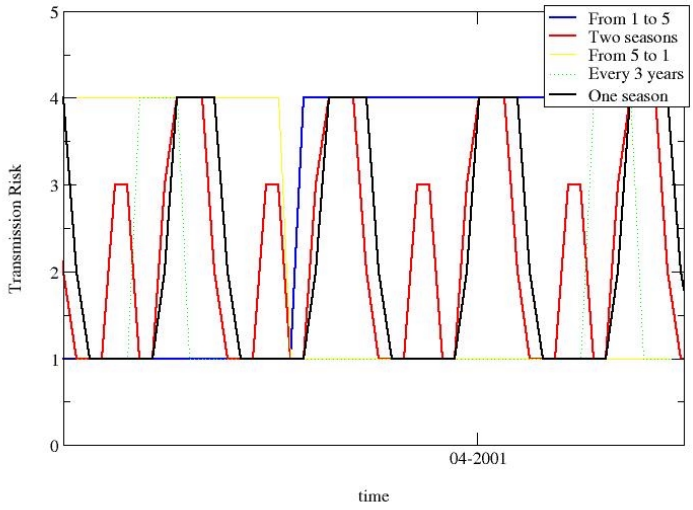


Figure 6 *Five typical temporal patterns of transmission risk.*

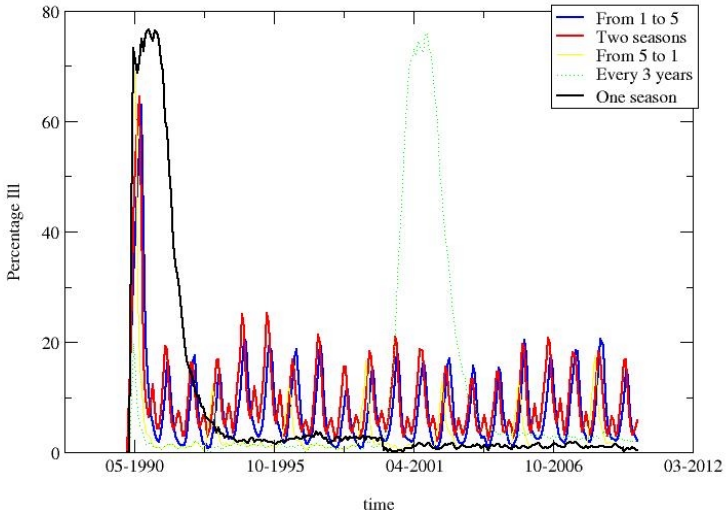


Figure 7 *The percentage of ill humans in populations exposed to the transmission risk patterns described in Figure 6.*

Spatial explicit simulation

Up till now the presented model did not take space into account. However, the dynamics of malaria can be subject to substantial local variation, resulting from various local differences. For example differences in the characteristics of mosquitoes, the environmental situation or the housing conditions of people. By imposing a grid on the area of research and applying the model for each separate gridcell, the model is made spatial explicit.

The size of a gridcell is 1x1 km, small enough to reflect local differences, and large enough to make abstraction from the complicated field situation possible. Given the size of the gridcell we cannot consider the malaria situation in one cell independent of the malaria situation in neighbouring cells, especially if we consider the fact that the flight range of a mosquito is somewhere between the 2 and 5 km (Thomas and Lindsay 2000). Therefore an additional step is put between the determination of the transmission risk and the calculation of the disease risk. A distant decay function bassed on the mosquito flight range is used to determine the weighted mean of the cell's risk and the risk in its neighbouring cells. This weighted mean is subsequently used to calculate the infection probability (P_{inf}) like described before. Note that this implies that the correction for neighbour influence only concerns mosquito behaviour and not human migration, which is modelled separately.

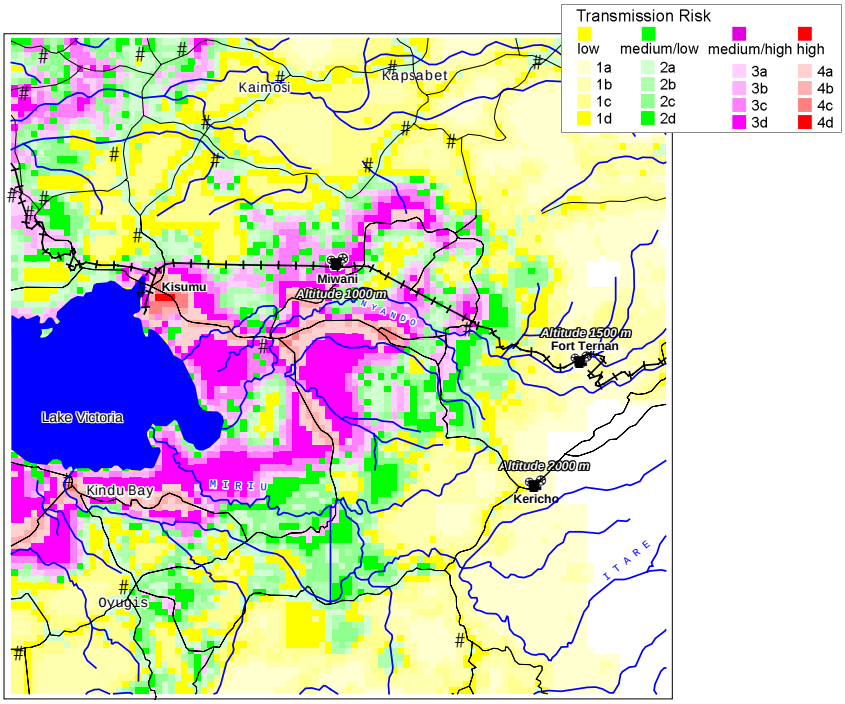


Figure 8 *The transmission risk for one specific month calculated by the LEMRA model for an area near Kisumu, Kenya.*

Figure 8 shows the spatial distribution of transmission risk calculated for an area in Kenya (near Kisumu). The shown area exists of lowland surrounded by mountains. Notice that the highest transmission risk is in the centre of the area, ie the lowlands, while in the highlands no or only a low risk is present. This is mainly explained by the temperature differences caused by the altitude difference.

Comparison of this spatial explicit outcome of the model with what is known from the area shows two points. Firstly, the figure shows a static picture of the situation in one specific month, while most available field results present number of infected and ill humans that were exposed to a dynamic changing transmission risk. This illustrates the importance of the disease model for validation and interpretation of the model results. Secondly, many places are misclassified, for example Kericho (in the South-East) is classified as a low risk area, while it is known that epidemics take place in this area every few years. One possible explanation of this misclassification is that human circulation patterns are not taken into account. Humans travelling from the valley to the highlands and visa versa might substantially influence the malaria dynamics in the area. In the next section a model of human circulation in an artificial world is shown that, if further improved, might explain some of the discrepancies mentioned.

The Effects of Circulation

People who move can spread malaria in two ways. In the first case the mover harbours the malaria parasite and transmits the disease through its movements to areas of low or sporadic transmission. In the second case, the movers originate from these areas of low and sporadic transmission and expose themselves to the disease through their movements to areas of high transmission. These people may have a low level of immunity or they may not be immune at-all, increasing their chances of acquiring the disease.

Circulation is a temporary movement from home and has been defined as “a great variety of movements, usually short-term cyclical in character, but all having in common the lack of any declared intention of a permanent or long-standing change of

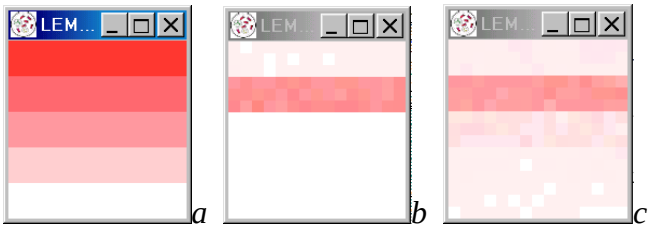
residence" (Zelinsky 1971). Circulation has three dimensions: duration, frequency and seasonality (Bell and Ward 2000), in the ideal model individuals would vary over all these three dimensions. In the current analyses circulation is restricted to daily movement without seasonality, for instance normal daily commuting.

Each gridcell contains a population of 1000 HUMANS. The effect of circulation on the malaria situation in an area is examined by assigning some of the HUMANS an additional location. In addition to the cell associated with its population, the HUMAN is assigned a location representing, for instance, the work place of the HUMAN. This second location is selected randomly from the gridspace. If we assume that the probability of infection is independent of the date and the time of the day, we can use the following algorithm to determine the infection chance for a HUMAN that is located at two positions:

$$P_x = \frac{timeSpend_x^1 * P_{\text{inf}}^1 + timeSpend_x^2 * P_{\text{inf}}^2}{totalTime}$$

where P_x is the chance of infection for HUMAN x, $timeSpend_x^i$ the time during which HUMAN x was at position i, and P_{inf}^i is the infection chance at position i. In the experiments shown $timeSpend_x^1 = timeSpend_x^2$, that is HUMAN x spends as much time at home (position 1) as at work (position 2). This approach is limited in the sense that it does not fully exploit the possibilities of the individual-based approach, like moving individual from one place to the other, however, it is sufficient for showing the importance of circulation.

In an artificial world of 15x15 cells, two different trends of circulation are compared: (1) no circulation takes place; the populations in each cell are isolated from each other, and (2) circulation does take place by 10% percentage of each population. The population model is applied for each of the cells in the 15x15 grid. The grid is divided in 5 regions of different transmission risks (Figure 9*a*). Figure 9*b* and *c* show the outcome of the experiment.



a *b* *c*

Figure 9 *The model applied in an artificial grid world of 15x15 cells. (a) The transmission risk; no risk in the south to the highest risk in the north. Percentage of ill people in the populations after 20 years of simulation: (b) without circulation, (c) with circulation.*

After 20 years without circulation, malaria has disappeared from the low risk areas, and a relatively small number of HUMANS become ill in the high-risk area (Figure 9*b*). In the case where circulation took place during 20 years the situation is quite different (Figure 9*c*): the number of malaria cases in both the low and high-risk areas is much larger. In the low risk areas this is due to humans importing malaria infections into the area. In the high-risk areas the increase in malaria incidence is the consequence of non-immune humans entering the area and acquiring the disease.

Conclusion

A spatial explicit malaria model has been introduced in which it is possible to relate various factors to transmission risk and disease risk. As is the case with many

other malaria models it is difficult to find proper parameter values, and considerably fine-tuning is needed to make the model more realistic. Nevertheless the model shows a reasonable qualitative correspondence to real world situation, various processes, that are less easy implemented using other model paradigms, for instance the circulation behaviour, can be simulated, and the effects of various changes in the underlying factors can be investigated. The next step in the development of the model is testing the model's applicability by further tailoring the model for the area in Kenya.

Martens (1998) distinguishes eco-epidemiology from conventional epidemiology. Among the differences he indicates are the use of ecological aspects to estimate future health risks (1), a focus on global and regional risk instead of local risk (2), and a long time horizon (3). The malaria risk assessment described here can be placed in this tradition.

(1) The transmission risk takes into account ecological factors as well as social-economic factors. The health impact for the population determined in the disease risk estimates includes some additional factors. Although the presented model cannot provide the precision and completeness that some of the conventional models can offer in their field of application, the integration of the various factors in the LEMRA model provides a more complete overall picture, and has the potential for a direct link with real world data and problems.

(2) Making the model spatial explicit transforms the local model into a regional one. Regional patterns become clear, for instance the analyses in Kisumu area shows the distribution of risk over the region and makes if possible to asses the risk in the region as a whole. Furthermore, the example of circulation shows how processes that take place at a larger spatial scale can be taken into account in such a spatial explicit setting.

(3) For a long-term assessment of malaria risk the model should be extended with some of the causal processes that influence the factors underlying malaria risk. Currently, scenarios are being developed to describe changes in some of these factors. Applying the model to the area in Kenya should make clear where our current gaps in knowledge are, what additional field data is needed, and whether the current model presents the proper balance the between simplicity and complexity, and between completeness and understandability.

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