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Exploring environmental factors concerning mosquito-borne diseases in Western Europe

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1. **SUMMARY**

Worldwide mosquitoes are transmitting a wide variety of infections to humans. Not only tropical regions, but also Western Europe has a history of malaria. Nowadays malaria has disappeared from the latter region but new infections may be introduced. Therefore this research aimed to study and identify the determinants of mosquito-borne diseases in Western Europe in order to assess the risk of outbreaks in the future. Possible policy measures were assessed to prevent or mitigate outbreaks of mosquito-borne diseases.

Studying the disappearance of malaria from Western Europe was the first part of this research. This type of malaria was caused by *Plasmodium vivax* and transmitted by *Anopheles atroparvus* mosquitoes. From the 18\(^{th}\) century onwards malaria incidence started to decline slowly. Malaria was characterized by epidemics occurring every 20 to 25 years. The Netherlands was the last Western European country from where malaria disappeared. The Netherlands were declared malaria free in the 1960s. Studying literature and statistics helped to identify the most important factors concerning the presence of malaria. Especially land use changes and a decrease of mosquito contact with humans resulted in the disappearance of malaria. Nowadays many possible contributing determinants are still not in favor of *An. atroparvus* in Western Europe. Therefore it is unlikely that malaria will return the coming decades.

The second part of the research was to study literature about the Asian tiger mosquito. The Asian tiger mosquito, *Aedes albopictus*, originates from Southeast Asia, but managed to invade many countries in the world through shipments of used tires and lucky bamboo. Many studies emphasize the possible introduction and establishment of this species into Western Europe. Certain parts of Western Europe already seem to be suitable enough for this mosquito to thrive. Therefore a new threat for public health may become reality, since this mosquito can serve as a vector for over twenty viruses. Especially when the climate becomes warmer, conditions may become more suitable for this mosquito.

An epidemiologic Stella model was constructed in order to assess the behavior of mosquito-borne epidemics. An equation for the basic reproduction rate ($R_0$) was used to study the effect of different variables on malaria epidemics in Western Europe. The basic reproduction rate was used as an input for the Stella model. If certain conditions are met, the parameter $R_0$ will become larger than 1 and an epidemic can grow. The higher the value of $R_0$, the faster an epidemic will grow and the more people will become infected.

Because malaria is not likely to return in Western Europe no extra policy measures are necessary. There is however, a serious chance that *Ae. albopictus* will establish in Western Europe, so certain measures are necessary to protect public health. These measures should first direct to prevent or delay the introduction of the mosquito. If the mosquito manages to establish in Western Europe, policy measures should than be based on reducing the chance of outbreaks of certain infections.

The most important conclusions of this research are that malaria is unlikely to return to Western Europe, but the likely invasion and the epidemiologic success of *Ae. albopictus* makes certain specific policy measures necessary in order to protect public health.
2. INTRODUCTION

2.1 Mosquito-borne diseases
Every year millions of people suffer from infections transmitted by several mosquito species. Especially in tropical and subtropical regions mosquito-borne diseases are a major cause of death. Malaria is the most common mosquito-borne disease and also responsible for most fatalities. Every year more than 200 million people suffer from malaria, of which about 750,000 people decease (World Health Organization, 2010). Malaria was also present in parts of Western Europe, but since more than half a century it has disappeared.

2.2 Malaria
Malaria is an infectious disease caused by single-celled parasitic organisms called plasmodia which are transmitted by Anopheles mosquitoes. In Western Europe malaria was caused by Plasmodium vivax, a different type of plasmodium than the ones in many tropical countries. The disease in Europe was characterized by intermittent fevers, occurring every third day. Therefore it was often called tertian malaria (Maguire & Baird, 2010). In tropical countries other plasmodium species are present (e.g. Plasmodium falciparum), related to more severe types of malaria and are responsible for many fatalities (World Health Organization, 2010). The mosquito transmitting P. vivax was Anopheles atroparvus, which lived in coastal regions, especially in East England and the Dutch province of North Holland (Dobson, 1989; Swellengrebel & de Buck, 1938). Figure 2.1 shows the transmission cycle of malaria. Only female mosquitoes bite in order to obtain blood for egg development. If a female mosquito bites an infected person it can become infected itself. Under the right conditions, the mosquito can become infectious and infect other persons after biting them. When a mosquito fed enough blood it will develop eggs and lay them in a body of stagnant water. These eggs can finally develop into a new generation of mosquitoes. Many factors influence this cycle. If certain conditions become less favorable for the mosquito or parasite, the cycle can be broken and an epidemic may die out. In Western Europe this has happened and malaria has disappeared.

Rumors were spreading in the media at the end of the 1990s about the return of malaria in The Netherlands (Koren, Van Knapen, & Van Bronswijk, 1999; Takken, Kager, & Van der Kaay, 1999). The reason for this fear was the increasing chlorinity of the water and the construction of water bodies within housing districts. It is also a hot topic within scientific research due to global warming. Many studies about the possible return of malaria in Western Europe look at temperature as a driving factor for vivax malaria epidemics (Lindsay & Thomas, 2001; Lindsay, Hole, Hutchinson, Richards, & Willis, 2010; Schroeder & Schmidt, 2008). Some researchers think however that other factors are determining the risk of malaria (Zhang, Bi, & Hiller, 2008). By studying the determinants of this mosquito and disease it can be assessed if there really is a potential risk for the return of malaria in Western Europe. If it is known what factors determine the risk, policy measures can be carried out to prevent the return of malaria outbreaks.
2.3 Aedes Albopictus
The Asian tiger mosquito or Aedes albopictus is the successful invading mosquito of the last few decades. This aggressive mosquito has adapted very well to human environments and bites during daytime, which increases the chance of people getting bitten (Kawada, Takemura, Arikawa, & Takagi, 2005). Because this mosquito can serve as a vector for a wide range of viruses, a lot of (scientific) attention is given to this mosquito (Benedict, Levine, Hawley, & Lounibos, 2007; Gratz, 2004). In order to assess the risk for public health in Western Europe, more understanding of the factors concerning Ae. albopictus is needed.

2.4 Research Aim
The aim of this research was to get a better understanding in the environmental factors related to mosquito-borne disease epidemiology in Western Europe. Because both malaria (An. Atroparvus) and Ae. Albopictus are studied, differences and similarities between determinants of these mosquitoes are observed and discussed. When the risk of future outbreaks are better comprehended, possible policy measures can be discussed in order to prevent or mitigate outbreaks.

2.5 Research questions
The main research question for this research is:

Which environmental factors can predict or explain the (dis)appearance of mosquito-borne diseases in Western Europe and which policy measures can mitigate or prevent outbreaks?
The research is divided in five subquestions:

1. Which environmental factors are correlated with the epidemics and disappearance of malaria in Western Europe?
2. Which environmental factors are related to the establishment and spreading of Ae. albopictus?
3. Can the appearance and disappearance of mosquito-borne diseases be simulated with a STELLA model based on the most important environmental factors?
4. Are the main environmental factors suitable for future mosquito-borne disease epidemics in Western Europe, and can outbreak be expected in the future?
5. What are the effects of different policy measures on mosquito-borne diseases?

2.6 Methodology
In the first part of this research a literature study was performed to determine the main environmental factors related to malaria epidemics and the disappearance of malaria from Western Europe. The literature was mainly found on ISI Web of Science and in the university library. Also data has been gathered from the KNMI (temperature and precipitation) website. Possible correlations between climate factors and malaria incidence were studied with SPSS16. Data of the selected environmental factors from malaria endemic period and present times was compared to assess the risk of future outbreaks. Also a literature study was performed in order to examine the global invasion of Ae. albopictus and the possible introduction and establishment in Western Europe.

A compartment model based on the determined environmental factors was developed in STELLA 6.0, a tool to model dynamic systems and is available for use at the University of Groningen. This model was mainly used to study malaria in Western Europe. The basic reproduction rate was used as an input for the model. A temperature dependent equation for malaria in Western Europe was obtained from literature. This basic reproduction rate was studied in Excel. The effects of the basic reproduction rate on malaria epidemics were studied with use of the Stella model. The policy subquestion will briefly be discussed in the general discussion.

2.7 Limitations
This research restricts itself merely to Western Europe. Although different definitions can be defined which countries are included in Western Europe, mainly the United Kingdom and the Netherlands are discussed because most literature is about these countries. This research does not focus on all mosquito-borne diseases. It only focuses on infections to which humans are susceptible. Due to the limited time-span of this research a disease from the past was studied (malaria) and a possible threat for public health in the future (Ae. albopictus). Other limitations will be discussed in the relevant chapters.
3. MALARIA IN WESTERN EUROPE

In this chapter, a literature review about malaria in Western Europe will be presented in which the most important factors concerning malaria outbreaks and the disappearance of malaria are identified. Also the results of a more extensive correlation study between the climate factors and malaria incidence will be discussed. A comparison of the malaria determinants in historic times (when malaria was still present) and present times is presented in paragraph 3.4 in order to assess the risk of malaria outbreaks in the present and future.

3.1 Introduction

Malaria has been an endemic disease for many centuries in the coastal areas of Western Europe. The main pathogen causing malaria in Western Europe was *Plasmodium vivax*, although *Plasmodium malariae* was also seen occasionally (Van Seventer, 1969). The main vector in this region was the mosquito *Anopheles maculipennis atroparvus*. This mosquito needs brackish water in order to proliferate and was therefore seen in coastal areas (Takken, Geene, Adam, Jetten, & van der Velden, 2002).

In the United Kingdom malaria was mostly seen in the eastern parts of England. In these areas the so called “agues” were very common in the coastal marshes and fens (Dobson, 1989; Nicholls, 2000). The ague caused high levels of mortality from the 15th to the 19th century. It was not until early 19th century that evidence was found that the ague was indeed malaria in most cases. The advances in diagnosing and the increasing use of quinine made it possible to distinguish between malaria fevers and other fever types (Kuhn, Campbell-Lendrum, Armstrong, & Davies, 2003). There are also indications however, that the high mortality rate of agues was caused by poor sanitation and hygiene instead of the malaria parasite (Hutchinson & Lindsay, 2006).

In The Netherlands malaria was mainly reported in the coastal regions except for the province of South Holland. In South Holland the waters were generally fresh so the breeding conditions were not suitable for *An. Atroparvus* (Swellengrebel & de Buck, 1938). There, *Anopheles maculipennis messeae* was mainly found. This mosquito is a close relative of *An. atroparvus*, but not an efficient malaria vector in nature and is only found in areas with fresh water (Sallares, 2006).

3.2 The decline of malaria incidence in Western Europe

Approximately around the second half of the 18th century, malaria incidence decreased gradually and it completely disappeared from Western Europe in the 1960s (Knottnerus, 2002; Van Seventer, 1969). There are two main reasons why malaria incidence decreased; the decline in *An. atroparvus* populations and the decline in the number of plasmodium carriers.

Although malaria has disappeared, the vector is still present, although its populations are much smaller and scarcer than in the past (Takken et al., 2002). The Netherlands was the last country in Western Europe from where malaria disappeared (Van Seventer, 1969). In figure 3.1 the variation in malaria morbidity between 1902 and 1949 is shown for Wormerveer, a village in the Dutch province of North Holland. It is one of the most complete records of malaria incidence at that time. It is an adequate representation of malaria incidence for the whole of North Holland, although in some places malaria incidence was higher or lower. In 1902, Korteweg and van Asperen started to diagnose malaria in Wormerveer (see Appendix A) based on finding the responsible plasmodium in bloodsamples (Swellengrebel & de Buck, 1938). Figure 3.1 shows that malaria incidence had an epidemic character in the first half of the 20th century, with epidemics in 1902, 1922 and 1946. It is also known that there has been an epidemic in 1880, although accurate data from that time is lacking (Swellengrebel, 1950).
Figure 3.1 Variation in malaria incidence per thousand inhabitants in Wormerveer between 1902 and 1949. (After: Swellengrebel, 1950).

3.3 Environmental factors related to malaria epidemics and the disappearance of malaria
It seems that the malaria epidemics in Wormerveer occurred with intervals of 20 to 25 years between each epidemic. Also in other towns and villages in North Holland the epidemic periodicity of malaria has been observed, although only since 1920 rather exact figures from other villages and towns are known (Swellengrebel, 1950). One could expect that the onset of an epidemic coincided with an increase in the number of *An. atroparvus* mosquitoes. Swellengrebel (1950) however, did not find hard evidence for the relation between malaria incidence and the number of trapped *Anopheles* mosquitoes. It is also remarkable that malaria epidemics in nearby villages did not always synchronize. In Uitgeest for example, a village only ten kilometers from Wormerveer, there has been a large epidemic in 1935. During the Wormerveer epidemic in 1946, malaria incidence in Uitgeest was very low (Swellengrebel, 1950). Figure 3.2 shows malaria incidence in other villages and towns in North Holland, including Uitgeest. Figure 3.3 shows the location of the different places on the map of North Holland. These figures show that the onset and size of epidemics differ, even between nearby villages.

Figure 3.1 Variation in malaria incidence per thousand inhabitants in Alkmaar, Grootebroek, Uitgeest and Wervershoof between 1927 and 1949. (After: Swellengrebel, 1950).
Not only over the years an epidemic character is observed, but also within a year. Figure 3.4 shows the malaria incidence in Wormerveer for both 1902 and 1922; both years at which a malaria epidemic peaked. In North Holland in the 20th century malaria commonly peaked within a year between May and July. Occasionally, a second peak in autumn was observed, although such a second peak in a year was uncommon in the 20th century (Swellengrebel & de Buck, 1938). Most people became infected with *P. vivax* during the autumn months when *An. atroparvus* mosquitoes were entering stables and houses. Because this strain of *P. vivax* was characterized by incubation periods in humans of 7 to 9 months, malaria incidence peaked in late spring or early summer of the following year (Swellengrebel & de Buck, 1938; Van Seventer, 1969).

In the following sections the factors or determinants related to malaria epidemics and the disappearance of malaria will be discussed. These factors are: temperature, precipitation, water chlorinity, land use and the availability of blood meals. Finally, also a few other factors related to malaria epidemics and the disappearance of malaria will be mentioned.
Temperature

Climate factors are not considered to be related to the disappearance of malaria in Western Europe, since there has not been an observed change temperature and precipitation trend while malaria incidence was slowly decreasing (Kuhn et al., 2003). But some authors assume that variations in weather over the years did lead to changes in malaria epidemics (Knottnerus, 2002). Temperature is of great influence on mosquito and parasite development and survival rate (cf. figure 3.5), since mosquitoes are cold-blooded animals. Higher temperatures in the summer, during the reproductive period of An. atroparvus, often result in higher population densities (Chin & Welsby, 2004). Nevertheless, reports in England of malaria-like symptoms were just as common during the Little Ice Age as in the warmer period before (Reiter, 2000). Therefore it is unlikely that temperature was an important factor in the decline of malaria cases, but it may have been a factor related to the epidemic character of malaria.

Figure 3.4 Monthly variation of malaria incidence in Wormerveer in 1902 and 1922 (After: Swellengrebel & de Buck, 1938).

Figure 3.5 Panel A: The latent period of P. vivax in a mosquito related to temperature. Panel B: The survival probability of Anopheles mosquitoes related to environmental temperature (Adjusted from: Martens, 1997).
Historical data is compared in order to observe the influence of temperature on malaria epidemics in Western Europe. Temperature data for the province of North Holland from the period 1906 to 1949 (KNMI, 2010b) is compared with malaria incidence data from Wormerveer (figure 3.1). SPSS 16 was used to study possible correlations between temperature and malaria incidence (cf. appendix B). The average annual temperature and average temperature in the summer months (June-August) were compared with annual malaria incidence. It was expected that higher temperatures, especially in the summer months, resulted in higher malaria incidence. No correlation was found though.

The next approach was to compare annual temperature data with malaria incidence in the following year. This may be due to the fact that *P. vivax* has a long incubation period in humans. Therefore one could expect that infected people show malaria symptoms no earlier than spring of the following year. No evidence was found however for the hypothesis that temperature influences malaria incidence in the following year since no correlation was found between temperature and malaria incidence data for the following year.

Another approach was to look at temperature variation and not just at average temperatures. Recent insights show that daily temperature fluctuations, compared to constant mean temperatures, can speed up or slow down mosquito development processes (Paaijmans, Read, & Thomas, 2009; Paaijmans et al., 2010). First average temperature variation (\(T_{\text{max}}-T_{\text{min}}\)) in a year in North Holland was compared with malaria incidence in Wormerveer (both in the same year as in the following year). A significant correlation (at the 0.01 level) was found between average temperature variation and malaria incidence in the following year (\(R=0.40\), cf. figure 3.6 panel A). When the same method is used only for an epidemic period (1913 to 1928) an even stronger correlation is found (\(R=0.63\), cf. figure 3.6 panel B).

As a correlation is found between temperature variation and malaria incidence in the following year, a biological explanation needs to be found. Paaijmans suggests that temperature variation is more important than average temperature (Paaijmans et al., 2010). With lower average temperature, the temperature may still come within a certain limit suitable for mosquito and parasite development during a period of a day.

To study the influence of temperature variation, another approach was carried out. This time the amount of days in a year were counted when the maximum temperature was at or above a certain level. First the amount of days in a year were counted when the maximum temperature exceeded 15°C. The 15°C level was chosen, since it is the minimum incubation temperature of *P. vivax* in a mosquito (Patz & Olson, 2006). After this was done for the period 1906 to 1949, this data was compared with malaria incidence in the following year. No correlation was found however. Also other temperature limits were carefully selected. For a given year, the days were counted when the maximum temperature was higher than 22 °C, since the survival probability for *Anopheles* mosquitoes is at a maximum (cf. figure 3.5, panel B). The same was done with days when maximum temperature

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**Figure 3.6 Relation between average temperature variation and malaria incidence in Wormerveer in the following year in the period 1906 to 1949 (Panel A) and in the period 1913 to 1928 (Panel B). Every data point resembles a single year.**
exceeded 25°C, the temperature from which the epidemic potential of *P. vivax* is at least half of the maximum epidemic potential (Martens, Niessen, Rotmans, Jetten, & Mcmichael, 1995). In both cases however, no correlations were found between days in a year exceeding a certain temperature level and malaria incidence.

Nevertheless, a correlation was found between temperature variation ($T_{\text{max}} - T_{\text{min}}$) and malaria incidence. This may be due to the fact that in years when the temperature variation is large, the amount of precipitation will probably be lower. Therefore the possible correlation between temperature variation and precipitation was studied. In the next section about precipitation also the relation between precipitation and malaria incidence will be presented. After comparing temperature variation and precipitation data, indeed a strong negative correlation ($R=-0.54$, significance level=0.01) was found. (cf. figure 3.7). The next paragraph will discuss the relation between precipitation and malaria incidence, studied in SPSS16.

![Temperature variation versus precipitation from 1906 until 1949](image)

**Figure 3.7** Relation between the average temperature variation during a year with total annual precipitation between 1906 and 1949. The circled data points relate to an epidemic peak (1922 and 1946).

**Precipitation**

Precipitation can also influence malaria incidence. A certain amount of precipitation each year is needed to maintain sufficient breeding sites. On the other hand, precipitation may also influence breeding sites negatively since it may flush away eggs and larvae. But perhaps precipitation may also influence water chlorinity and therefore suitable breeding habitats for *An. atroparvus*. A negative correlation was found between annual precipitation and water chlorinity in the next year (Van Seventer, 1969). If the chlorinity of the water decreases, conditions for mosquito development may decrease.

To study the influence of precipitation on malaria incidence, precipitation (KNMI, 2010a) and malaria incidence were compared in the same way as the correlation between temperature and malaria incidence was studied. This time a negative correlation ($R=-0.43$) was found between annual
precipitation and malaria incidence in the following year (cf. figure 3.8, panel A). The negative correlation may be explained by the theory that fewer precipitation in a year results in higher chloride concentration of breeding sites, which may increase the *An. atroparvus* population followed by a higher malaria incidence. However, historic data did not show a clear relation between the number of *An. atroparvus* mosquitoes and malaria epidemics (Swellengrebel, 1950).

Although precipitation does not seem to be related to *Anopheles* density, a correlation has been found with malaria incidence. It appears that precipitation does not regulate the onset and intervals of malaria epidemics, but it may increase the number of malaria infected people during an epidemic. The year prior to the malaria peak in 1922 was extremely dry. The year 1933 was also very dry in North Holland, and it was followed by a malaria peak in Uitgeest in 1935. Also when precipitation data during is compared with malaria incidence during an epidemic period, a strong negative correlation ($R=-0.66$) is found (cf. figure 3.8, panel B), suggesting that precipitation may influence the progress of an epidemic.

![Figure 3.8](image)

**Figure 3.8** Relation between annual precipitation and malaria incidence in the following year in Wormerveer in the period 1906 to 1949 (panel A) and in the period 1913 to 1928 (panel B).

**Water chlorinity**

As discussed earlier, the presence of *An. atroparvus* is largely dependent on the chloride concentration of the water. In Western Europe *An. atroparvus* is found in areas with brackish water, while *An. messeae*, the close relative of *An. atroparvus*, is mainly found in areas with fresh water (Van der Kaaden, 2003). Classification of fresh, brackish and salt water can be done differently. Takken et al. (2002) use the following definitions: water is defined ‘fresh’ when the Cl$^-$ content is less than 300 mg/L. Water is called ‘brackish’ when it has Cl$^-$ contents ranging from 300–17,000 mg/L. Water with Cl$^-$ concentrations over 17,000 mg/L are considered salty. Figure 3.9 shows the relation between water chlorinity and the presence of *Anopheles* larvae. In water with a Cl$^-$ content of 8,000 mg/L *An. atroparvus* larvae were still found in large numbers (Swellengrebel & de Buck, 1938). In the Dutch province of South Holland the water was mainly fresh and malaria incidence was low, while in the province of North Holland the chloride concentration was much higher. The hypothesis that a decline in water chlorinity is related to the disappearance of malaria seems invalid, since water chlorinity did not show a decreasing trend up until 1960 (Van Seventer, 1969).
Figure 3.9 Relation of An. atroparvus and An. messeae larva with chloride concentration in the Northeast Polder in 1943 (After: Zwarteveen, 1948).

Landuse

The suitable habitat for An. atroparvus is a water-rich area. Therefore malaria epidemics often occurred in regions with fens and marshes. It is no coincidence that the word “malaria” comes from the Italian “mala arià” which means “bad air”, as it was thought that the disease was caused by the smelly damps coming from the marshes (Dobson, 1989). It is widely thought that the decrease of wetlands in Western Europe helped to reduce the number of breeding sites for An. atroparvus and thus malaria incidence (Bayliss, 1985; Dobson, 1989; Kuhn et al., 2003; Van Seventer, 1969). It is important however to understand that suitable breeding sites for mosquitoes are shallow stagnant water bodies. In lakes, rivers or larger canals mosquito eggs or larvae will easily be flushed away. In the Dutch province of North Holland the common small polder-ditches were excellent places to be used as breeding sites for An. Atroparvus (Swellengrebel & de Buck, 1938).

Re-allotments (“ruilverkavelingen”) often result in a decrease in the number of polder-ditches and the water storage capacity of the polder becomes less. Although re-allotments may reduce the number of suitable breeding sites for An. atroparvus, it is not an important factor for the disappearance of malaria in the province of North Holland since until the 1960s only 3% of the available land in this province has been re-allotted (Van Seventer, 1969).

Availability of blood meals

An. atroparvus semi-hibernates in winter. Regularly it needs a blood meal in order to survive. Livestock farms were the most important habitats for semi-hibernation, since it provides shelter and it provides an easy blood meal. In the Netherlands An. atroparvus was mainly found in pig-sties (Swellengrebel & de Buck, 1938). Experiments showed that An. atroparvus is mostly attracted by pigs (Laarman, 1955). Over the years the number of pigsties declined, resulting in a decrease of suitable habitats for the mosquito to semi-hibernate and to collect blood meals (Van Seventer, 1969). Others suggest that an increase in farm animals reduced malaria incidence. A correlation was found between the increase in cattle population and the decrease of malaria incidence (Kuhn et al., 2003). Perhaps the increase in livestock diverted the mosquitoes from biting humans. The correlation may also be due to a decrease in the number of livestock farms, like proposed by Van Seventer (1969).
Other factors
Swellengrebel (1950) discussed some factors or theories in order to explain the intervals between each major epidemic. He discussed the influence of wars, the introduction of new plasmodium carriers and immunity towards *P. vivax*. None of these factors however could fully account for the intervals of the different epidemics.

For the reduction of *An. atroparvus* population sizes and the elimination of malaria in Western Europe, other factors are also known to be important. Water pollution with fertilizers, detergents, insecticides and other chemicals seems to be an important factor for the decrease in the *An. Atroparvus* population size in the 20th century, at least in the province of North Holland (Van Seventer, 1969). The pollution of the breeding sites influences the development of larvae directly or indirectly, for example through a change in the vegetation pattern of standing water.

Insecticide use also directly had an influence on adult mosquitoes. Since the 20th century the use of effective insecticide strips in pigsties and other types of stables increased. Also the selective spraying with DDT directly influenced adult mosquitoes (Swellengrebel, 1950; Van Seventer, 1969).

3.4 Comparison of environmental factors between the malaria endemic period and present times
Following the discussion on the determinants of malaria epidemics and the disappearance of malaria, it may be useful to see what the present situation is. Since malaria disappeared in the 1960s several factors may have changed, making conditions for *An. atroparvus* and malaria transmission possibly more favorable. In this section, several important factors or indicators for the presence of *A. atroparvus* and malaria during malaria endemic times (around 1930) are compared with today’s situation. Malaria incidence was already declining before the 20th century, but due to the lack of exact data, the first part of the 20th century is used as a reference point. This section focuses only on the province of North Holland, since in this region malaria incidence was relatively high and it was one of the last regions in Western Europe from which malaria disappeared.

Figure 3.10 shows the results of the comparison (cf. appendix C). The population of North Holland increased by approximately 70 percent. Also the climate factors have increased, while a decrease is shown for the other selected factors. The factors from this comparison will be discussed in more detail in the next sections of this chapter.

![Relative factor comparison between malaria epidemic period (blue) and present times (red) for the province of North Holland found. 1900-1930=100.](image)
Climate factors
The average annual temperature and the average annual total precipitation over 30 years were used to compare the past (1906-1936) with the present situation (1980-2010). Comparison between the two periods shows that both average temperature and precipitation have increased. The average temperature increased from 9.25°C in the first part of the 20th century to 10.13°C in present times. The average annual rainfall increased from 701.5 millimeters to 805.4 millimeters. Increased temperature can result in an increased malaria transmission rate, since both mosquito and parasite development increases (Kuhn et al., 2003). As mentioned in paragraphs about precipitation it is possible that the increase in precipitation is deteriorating conditions for malaria to be present.

Landuse
Figure 3.11 shows the changes in landuse from 1850 till 1995 (Knol, Kramer, Van Dorland, & Gijsbertse, 2003). Remarkable changes are seen in water, grassland, urban area and agricultural land. The change in water area is due to reclamation of land and transforming it into agricultural area, especially before 1930. The other important change is the percentage of grassland area. It should be noted that grassland also includes wet or marshy types of grassland, thus suitable areas for mosquitoes to breed. Marshlands in figure 3.11 mainly comprise reed marshes and no other types of marshlands. Both marshland and grassland in this figure can be seen as areas with suitable breeding sites for An. Atroparvus. The figure shows that the available area with suitable breeding sites (marshland and grassland) for An. atroparvus has declined over the decades.
Water chlorinity
As mentioned earlier, up till 1960 the chloride concentration in North Holland did not decrease. Until then, the average chloride concentration of the water on 89 different locations varied around 770 mg/L (Van Seventer, 1969). Since the 1960s the chlorinity of many waters slowly decreased due to changes in water management. In present times the average chlorinity is about 284 mg/L (HHNK, 2010). This value is the average of samples taken in the month of July in about the same manner as Van Seventer (1969) proposed. As the average water chlorinity decreased significantly in less than half a century, the conditions for suitable *An. Atroparvus* breeding sites also decreased. Figure 3.9 shows that water with a chlorinity of about 290 mg/L is more suitable as a breeding site for *An. messeae* than for the malaria vector *An. atroparvus*.

Figure 3.12 shows the average annual Cl\(^-\) concentration of the water in North Holland. The most likely explanation for the increasing trend are changes in water management since more or less a decade ago. If the increasing trend continues in the same way, it will still take many decades before the chlorinity is at the same level as in the 1930s.

![Water chlorinity in North Holland from 1990 to 2010](image)

**Figure 3.12** Annual average Cl\(^-\) concentration of the water at 49 different measuring points in the province of North Holland between 1990 and 2010 (After: HHNK, 2010).

**Availability of blood meals**
To compare the availability of blood meals over the two periods, the number of pigs and pigsties are compared. Both the number of pigs and the number of pigsties show a difference between the malaria endemic period and the present. The number of pigsties in malaria endemic areas has decreased from almost 100,000 in 1934 (Van Seventer, 1969) till less than 750 in 2010 (CBS, 2010b). The number of pigs shows a smaller decline. Especially the number of pigs per farm has increased drastically. One may say that it is much harder these days for a female *An. atroparvus* to find a suitable place for semi-hibernation and blood meals. There is still a suitable number of pigs, but on much fewer locations.
3.5 Conclusions

So far, the most important factors related to malaria epidemics and the disappearance of malaria from Western Europe have been described and compared with present times. The available data showed that malaria epidemics reoccurred with a periodicity of 20 to 25 years. It is still unclear how this periodicity was regulated, but from this study it seems that the severity of an epidemic is related to annual precipitation. Because many other factors also influence malaria incidence, the exact context of this relation remains unsolved. Climate factors, like temperature and precipitation are also not likely to be strongly correlated with the disappearance of malaria in Western Europe. Other factors did influence An. atroparvus mosquitoes and the disappearance of malaria. The drainage of many wetlands in coastal areas reduced the number of breeding sites. The reduction of wetlands negatively influenced mosquito populations. Changes in socio-economic factors reduced the change of getting bitten by infected mosquitoes. The discovery of anti-malaria drugs became an effective tool to reduce parasite infections in people. Insecticides finally helped to reduce the number of mosquitoes in houses and stables. All these changes together resulted in the disappearance of malaria in Western Europe.

The comparison of different factors between the malaria endemic period en current times shows that conditions have become much less favorable for An. atroparvus and thus malaria transmission. Nowadays there are much less suitable breeding sites. Many water rich places have disappeared and the average chlorinity of the water is often not favorable for An. Atroparvus development. Also the way in which people were keeping cattle and pigs have changed significantly since malaria disappeared. The number of pigsties has decreased strongly, while the number of pigs per pigsty has increased. Also the type of housing has changed. All of these changes make it much more difficult for adult female An. Atroparvus mosquitoes to find suitable blood meals and shelter these days, especially during semi-ibernation.
4. THE SPREAD OF THE ASIAN TIGER MOSQUITO

4.1 Introduction
Since malaria disappeared there are no endemic mosquito-borne diseases left in Western Europe. However, global transportation makes rapid invasions of new species possible. One of the most successive examples of such an invading species is the Asian tiger mosquito or *Aedes albopictus*. This mosquito was able to invade large parts of the world and transmit different diseases like dengue and chikungunya onto humans (Benedict et al., 2007). Research showed that climate conditions are suitable for *Ae. albopictus* establishment in Western Europe, for example in The Netherlands (Takumi et al., 2009).

Sections 4.2 and 4.3 present the factors that make *Ae. albopictus* such a successful invading species. This gives more insight in the risk of *Ae. albopictus* establishment in Western Europe. Also the factors related to disease transmission by this mosquito are studied.

4.2 Spreading around the globe
In the 1970s, *Ae. albopictus* began to spread around the globe. Originally this species is found in tropical and subtropical regions in Southeast Asia (Gratz, 2004; Hofhuis et al., 2009). *Ae. albopictus* is known to be a tropical forest mosquito, with treeholes or other small standing water bodies surrounded by vegetation as breeding sites (Eritja et al., 2005).

The transport of used tires is the most important route by which this species has spread around the globe. Used tires have proven to be excellent breeding sites for *Ae. albopictus* (Benedict et al., 2007; Randolph & Rogers, 2010; Tatem, Hay, & Rogers, 2006). The long-lived eggs are relatively resistant to hard conditions like cold (Benedict et al., 2007) and the eggs can withstand desiccation (Straetemans & ECDC consultation group on vector-related risk for chikungunya virus transmission in Europe, 2008). These properties make the spreading around the world in used tires and containers so successful.

Another observed transport route is via shipments of plants like “Lucky bamboo” (*Dracaena sanderiana*). This route resulted in the introduction of *Ae. albopictus* in southern California (Madon, Mulla, Shaw, Kluh, & Hazelrigg, 2002) and The Netherlands. In The Netherlands this mosquito was discovered in greenhouses of Lucky bamboo importing companies. (Scholte et al., 2007; Scholte et al., 2008)

Short and medium range spreading of the mosquito can be attributed to public or private transport by car, boat or plane. Visitors in areas where *Ae. albopictus* is endemic, can accidently take mosquitoes or eggs with them by car or in their luggage and transport them into new regions. The mosquito itself can also actively invade new areas in close vicinity which are suitable for establishment (Straetemans & ECDC consultation group on vector-related risk for chikungunya virus transmission in Europe, 2008).
4.3 Establishment of *Ae. albopictus*

*Ae. albopictus* is not only suitable to spread rapidly due to global transportation, but it also was able to settle in many countries. The mosquito was first detected in Albania (1979) and 6 years later in the United States. After its introduction in the United States it was able to invade and establish in most of the southeastern parts, and was even found as far north as Minnesota (Benedict et al., 2007).

Before *Ae. albopictus* is able to establish in a newly invaded area, certain climate conditions need to be fulfilled. The invading temperate strain of the mosquito is able to establish under a variety of conditions. The female mosquito is able to lay diapausing eggs induced by shortened photoperiod and lower temperatures. These diapausing eggs hibernate and are able to withstand desiccation and to survive in regions with coldest month isotherms of -5°C. At least 500 millimeters annual precipitation is needed in order to fulfill the conditions for *Ae. albopictus* establishment (Eritja et al., 2005). Due to its success in adapting to the human environment it is also suitable to live and breed indoors, making the risk of possible virus transmission even higher (Dieng et al., 2010).

4.4 Risks of *Ae. albopictus* establishment

*Ae. albopictus* is an unusually aggressive day-time biter causing lot of nuisance in areas where it becomes established. Besides the biting habit the major risk is the fact that this species can serve as a vector for many pathogens. In the original distribution range of Southeastern Asia there has been outbreaks of dengue where *Ae. albopictus* has served as the vector. Laboratory experiments showed that this mosquito can serve as a vector for at least 22 arboviruses (Gratz, 2004). Some suggest that the globalization may have positive effects, because it is able to compete with the close relative *Aedes aegypti*, that is often considered as a more efficient vector Dengue virus (DENV) and Yellow Fever virus (YFV). Nevertheless are adaptations in arboviruses to *Ae. albopictus* possible, which may change the vector status of this mosquito (Lambrechts, Scott, & Gubler, 2010). Also the emergence of chikungunya virus (CHIKV) changed the relative innocent vector status of *Ae. albopictus* (Paupy, Delatte, Bagny, Corbel, & Fontenille, 2009).

In 2007 the first outbreak in Europe occurred of an arbovirus spread by *Ae. albopictus* in Europe was a fact. In Italy an outbreak of chikungunya occurred with 205 reported cases and one fatal incident. The virus was probably transported by a human host from India, visiting family in a small town in the province of Ravenna. Because population densities of *Ae. albopictus* were sufficiently high, it was possible for the virus to be transmitted to other humans (Rezza et al., 2007). Several factors are required to start a chikungunya epidemic: First, an infected patient must import the virus during the infectious stage. Due to increased travelling, this occurs more and more. Secondly, a suitable vector is required to replicate the virus and to transmit the virus to other people. Thirdly, the viral load in patients must be high enough before a mosquito can get infected. Finally certain environmental and ecological factors need to be sufficient to initiate and enhance an epidemic (Charrel, de Lamballerie, & Raoult, 2008). The outbreak of chikungunya in Italy showed that there is a serious threat for the introduction of new diseases even in countries with a temperate climate.
4.5 Possible establishment of *Ae. albopictus* in Western Europe

*Ae. albopictus* mosquitoes have been spotted in Western Europe several times. The first time was in Belgium in the year 2000. A larva and a pupa were found at used tires of a recycling company that imports used tires from the United States and Japan. Because premature stages of *Ae. albopictus* were discovered in tires laying there for more than 4 months it was suggested that the mosquitoes had reproduced on site (Schaffner, Van Bortel, & Coosemans, 2004).

During inspections by the Dutch Plant Protection Service in 2005, *Ae. albopictus* mosquitoes were detected in and around three greenhouses of Lucky bamboo importing companies in the northwest of the Netherlands. In the following years the mosquito was detected at more Lucky bamboo importing companies (Hofhuis et al., 2009).

Although *Ae. albopictus* has been spotted several times at different locations in Western Europe, there is no evidence that the mosquito was able to settle in this region. Several studies show however that the climate conditions in large parts of Western Europe are suitable for establishment of temperate strains of *Ae. albopictus* (Benedict et al., 2007; Schaffner et al., 2009; Takumi et al., 2009). Due to global warming the seasonal activity may increase (Alto & Juliano, 2001). Because this species is able to adapt in urban areas and conditions for establishment already seem to be suitable, it may only be a matter of time before this species becomes established in Western Europe if no action is undertaken.

4.6 Conclusions

*Ae. albopictus* was able to spread rapidly around the globe due to shipments of used tires and lucky bamboo plants. On the other hand lies its success in the ability to adapt to temperate climates. The eggs of this mosquito can survive under relatively extreme conditions. It has adapted to live in urban areas very well, making the chances to come in contact with people very large. As the climate is becoming warmer in many regions it is likely that the range of where *Ae. albopictus* has become endemic will increase.
5. EPIDEMIOLOGIC MOSQUITO-BORNE DISEASE MODEL

As shown in chapters 4 and 5, the epidemiological cycle of mosquito-borne diseases is very complex. Many factors influence if and how diseases are spread by mosquitoes in certain areas. Often factors also influence each other, making it very hard and complicated to understand the system of mosquito-borne diseases entirely. A useful tool researchers often use to study and predict the presence and outbreaks of mosquito-borne diseases is an epidemiological model.

One of the most simplistic compartment models in epidemiology is an SIR model, first proposed by Kermack and McKendrick (Kermack & McKendrick, 1927). This model consists of a susceptible compartment (S), an infectious compartment (I) and a recovered compartment (R). A set of differential equations describe the changes in these compartments over time. If an infection has long incubation periods in humans, an extra compartment is needed. For such infections an SEIR model is more useful. Such a model includes an exposed compartment (E). When people are infected with a pathogen, they first stay in the exposed compartment. During this time people do not show symptoms and are not able to infect others. After the incubation period they will reach the infectious compartment. Then people show symptoms of the infection and are also capable of infecting others.

5.1 Mosquito-borne disease compartment model

Figure 5.1 illustrates the compartment model for malaria. Within the human population susceptible persons can be infected by infectious mosquitoes. When people are exposed to the malaria parasite they are able to infect susceptible mosquitoes after a certain incubation period (exposed). Especially *P. vivax* malaria in Western Europe had very long incubation periods (Swellengrebel & de Buck, 1938). After being infected for a certain period of time, people recover and become immune. For malaria, this immunity is not infinite; people can become susceptible to malaria infection again. The human part of the model is an SEIR model, but humans cannot infect other humans. Therefore there also is a mosquito part in the model. The mosquito part is largely the same as the human part, but mosquitoes will not recover from a plasmodium infection. Another difference is that births and deaths are included in the model because the lifetime of a mosquito is much shorter than the lifetime of a human and is also dependent on several environmental factors.

![Figure 5.1 Illustration of a compartment model for malaria. (After: Koella & Antia, 2003).](image)

An important number in epidemiology is the basic reproduction rate ($R_0$), which gives information about the severity of an epidemic. It represents the average number of secondary cases derived from one infected case introduced into a potential host population. When $R_0 < 1$ an infection will die out. If
The basic reproduction rate, $R_0$, is defined as the expected number of secondary cases of an infection produced by a single infected individual in a completely susceptible population (Lindsay et al., 2010; Schroeder & Schmidt, 2008). There are several ways to calculate the basic reproduction rate. For vivax malaria in Western Europe, the following equation is often used (Lindsay & Thomas, 2001; Lindsay et al., 2010; Martens et al., 1999):

$$R_0 = \frac{ma^2bp^n}{-\ln(p)\gamma}$$  \hspace{1cm} (1)

In this equation, $p$ is the daily survival probability of adult mosquitoes, $b$ is the proportion of infected mosquito bites that result in infection, $\gamma$ is the rate at which malaria-infected humans recover from the infection, and $ma$ is the expected number of mosquito bites per person per day. The feeding rate $a$ (bites/person/day) can be calculated using:

$$a = \frac{h}{u}$$  \hspace{1cm} (2)

where $h$ is the proportion of mosquito blood meals taken from people and $u$ is the period in days of the interval between laying eggs and a next blood meal (also called the gonotrophic cycle). The length of the gonotrophic cycle can be calculated with the following equation:

$$u = \frac{f_1}{T - g_1}$$  \hspace{1cm} (3)

where $f_1$ is the number of degree days, $g_1$ is a threshold below which development ceases, and $T$ is the temperature. In equation (1), $n$ is the period of parasite development in female mosquitoes in days (also called the sporogonic cycle) and can be calculated with:

$$n = \frac{f_2}{T - g_2}$$  \hspace{1cm} (4)

where $f_2$ is the time to complete development in degree days, $g_2$ is a development threshold below which development ceases, and $T$ is the temperature.

Before the compartment model can be constructed in Stella it is necessary to understand how the different compartments change over time. As mentioned, the human part of the model is basically an SEIR-model. The only difference is that the number of new infections depends on the ratio of infectious mosquitoes instead of infectious humans. The human compartments will change over time in the following way:

$$\frac{dS_H}{dt} = -\frac{\beta_H \cdot S_H \cdot I_M}{N_M}$$  \hspace{1cm} (5)

$$\frac{dE_H}{dt} = \frac{\beta_H \cdot S_H \cdot I_M}{N_M} - \kappa_H \cdot E_H$$  \hspace{1cm} (6)

$$\frac{dI_H}{dt} = \kappa_H \cdot E_H - \gamma_H \cdot I_H$$  \hspace{1cm} (7)

$$\frac{dR_H}{dt} = \gamma_H \cdot I_H$$  \hspace{1cm} (8)
$S_H$: Susceptible humans  
$E_H$: Exposed humans  
$I_H$: Infectious humans  
$I_M$: Infectious mosquitoes  
$R_H$: Recovered humans  
$N_M$: Total mosquito population  
$\beta_H$: Human infection rate  
$\kappa_H$: Human infectious transition rate  
$\gamma_H$: Human recovery rate

The mosquito part is somewhat different since there is no compartment for recovered mosquitoes and birth and death rates are included due to the short life-span of a mosquito. The following equations explain the change of the different mosquito compartments over time:

$$\frac{dS_M}{dt} = N_M \cdot \lambda_M - \frac{\beta_M \cdot S_M \cdot I_H}{N_H} - \mu_M \cdot S_M \quad (9)$$

$$\frac{dE_M}{dt} = \frac{\beta_M \cdot S_M \cdot I_H}{N_H} - \kappa_M \cdot E_M - \mu_M \cdot E_M \quad (10)$$

$$\frac{dI_M}{dt} = \kappa_M \cdot E_M - \mu_M \cdot I_M \quad (11)$$

$S_M$: Susceptible mosquitoes  
$E_M$: Exposed mosquitoes  
$I_M$: Infectious mosquitoes  
$I_H$: Infectious humans  
$N_M$: Total mosquito population  
$N_H$: Total human population  
$\beta_M$: Mosquito infection rate  
$\kappa_M$: Mosquito infectious transition rate  
$\mu_M$: Mosquito death rate  
$\lambda_M$: Mosquito birth rate

The basic reproduction rate can be incorporated into the compartment model because of the following notion:

$$R_0 = \frac{\beta}{\gamma} \quad (12)$$

The infection rates of both humans and mosquitoes can be calculated as follows:

$$\beta = R_0 \cdot \gamma \quad (13)$$

For calculating the human infection rate, the human recovery rate is used. The mosquito part does not consist of a recovery part, therefore the mosquito death rate is used in the equation instead of the recovery rate. Although recovered people do become susceptible after a certain time, it is not implemented in the model. Therefore the model is not suitable to accurately simulate many years at a single run, since the susceptible compartment will become empty at a certain time at a certain $R_0$ value.
5.2 Constructing a Mosquito-borne disease model

With the theory from the previous section, the malaria compartment model can be constructed in Stella. Figure 5.2 gives a schematic overview of the different compartments and equations that are used. The Stella model is presented in appendix D. Several variables can be changed within the model and assessed in order to understand the effects of these changes. The standard values of the variables for calculating $R_0$ and the Stella model are also presented in appendix D.

![Figure 5.2 The vivax malaria compartment model as it is modeled in Stella.](image)

Calculate $R_0$ values

It would be possible to calculate $R_0$ values directly in the Stella model, using equation (1). Because the model can become very complex when all the different variables necessary to calculate $R_0$ are implemented in the model, it was decided to calculate $R_0$ in an excel sheet. In the excel sheet all the variables can be changed in order to assess the effect of these changes on the $R_0$ value. Also historic temperature data can be implemented in order to calculate the $R_0$ values for times when malaria was present. The results from excel can then be used as an input for the Stella model.

Assessment of the model

The effects on $R_0$ of changing the variables from equation (1) were assessed in excel. In the Stella model the effect of changing $R_0$ values were studied. In the model a converter is included that calculates the attack ratio (the cumulative incidence of infections) of both the human part as well as the mosquito part. The attack ratio is also a sort of indicator of the severity of an epidemic.

5.3 Model results

Stella results

Figure 5.3 shows the results of analyzing different $R_0$ values in Stella. At an $R_0$ value of 3 or higher, the human attack ratio will finally reach 100%, although this may still take several years. The mosquito attack ratio will never reach 100% as the birth rate is higher than 0. As the $R_0$ value will become higher, the attack rate of both humans and mosquitoes will become larger and it will reach the maximum attack rate sooner.
In figure 5.4 the Stella results of two epidemics with different $R_0$ values are presented. From this figure it can be seen that an epidemic with a constant $R_0$ value of 2 can persist for a very long time before no humans are exposed to or infected with malaria anymore. Even after 5 years, the infection is still present, although then it is on its return for several years. An epidemic with a constant $R_0$ value of 5 reaches much sooner the maximum size. After one year the number of infectious humans reaches its peak. The peak is also higher, so more people are infectious at a certain time, than with a lower $R_0$ value.

**Figure 5.3** Results of the Stella model with varying $R_0$ values. Both the maximum attack ratio, as well as the time (in days) to reach this ratio ($T_{max}$) are presented for humans and mosquitoes.

**Figure 5.4.** Results for both $R_0=2$ (dashed lines) and $R_0=5$ (solid lines) are shown. In this figure, “E” represents exposed humans, “I” infectious humans, and “R” represents the recovered humans.
The $R_0$ value is not the only part that can be changed in the model. Also population sizes (compartment sizes), infectious rates, human recovery rate, birth and death rate can be changed as well. It is however, for the validity of the model results, better to keep these variables constant. In general, but not in the model, these variables influence the $R_0$ value. For example, when changing the mosquito population size from 10,000 (the chosen standard value) to only one mosquito, the results of the model regarding the number of exposed, infectious, and recovered humans over time will exactly be the same. This is the consequence because the number of people becoming exposed is dependent on the ratio of infectious mosquitoes with the total mosquito population size. Changing the initial mosquito population size will not change the ratio since this ratio is zero at the start of a run.

To observe the effects of a changing mosquito population size, the $R_0$ value simply needs to be changed. When the mosquito population increases it can be expected that the amount of bites per person per day will increase and thus the basic reproduction rate.

**Excel results**

Figure 5.5 and figure 5.6 show the results of the Excel sheet when different variables are changed. The “normal” line represents the $R_0$ values at different temperatures when all the other variables (see appendix E) are set to normal (Lindsay & Thomas, 2001; Lindsay et al., 2010; Schroeder & Schmidt, 2008). It is clear that $R_0$ values will become larger at higher temperatures. The variables that are varied can also change the size of $R_0$. As the number of bites per person per day increases, $R_0$ will also increase. The same holds for the rate of recovery, the survival probability of a mosquito, the proportion of blood meals taken from humans and the proportion of mosquitoes developing parasites after taking an infective blood meal. When these variables become larger, $R_0$ will also increase and vice versa.

![Figure 5.5](image.png)

**Figure 5.5** The results of $R_0$ calculation from equation (1) at different temperatures. The normal line is the standard input of variables. The red line shows the results when the number of bites per person per day is smaller ($m*a$). The blue line shows the result when the rate of recovery ($r$) is larger than normal. Finally the green line gives the results when the daily survival probability of mosquitoes ($p$) is smaller than normal.
Figure 5.6 The results of $R_0$ calculation from equation (1) at different temperatures. The normal line is the standard input of variables. The two outer lines are the results when the “proportion of female mosquitoes developing parasites after taking an infective blood meal” variable ($b$) is changed. The remaining two lines show the results of changes in the “proportion of mosquito blood meals taken from people” variable.

5.4 Model discussion and conclusions
The results from Stella and Excel give insight in the way malaria was spread and reasons for its disappearance from Western Europe. Many factors influence the basic reproduction rate and therefore the onset and the size of an epidemic. Within a year many factors will change and the $R_0$ will also vary greatly. The variability of the $R_0$ value is clearly visible when looking at the seasonal variability of malaria as discussed in chapter 3. Because the variability of the basic reproduction rate within a year, it was not useful to model an epidemic over the years according to actual data.

The way the $R_0$ value has been calculated is very likely to be different from what happened in North Holland. There the basic reproduction rate may have been less dependent on temperature as humans became primarily infected during autumn when mosquitoes were entering houses. When looking only at temperature, one would expect that during summer most people would become infected since $R_0$ values would be the highest.

Nevertheless is it possible to assess the consequences when the factors discussed in chapter 4 are changing. Although temperature influences several variables according to the $R_0$ equation that is used, its direct influence on malaria transmission in North Holland remains unclear. Also the way precipitation influences the model is uncertain. It is known that it can influence the chlorinity of water bodies suitable as breeding sites for mosquitoes. Therefore the birth rate and the number of susceptible mosquitoes may increase. On the other hand is it likely that the $R_0$ will also be influenced by precipitation for example by increasing the daily survival probability.
Especially “the availability of blood meals” factor and the related number of pigsties can be very well assessed by the model. The product $m\cdot a$ (the number of mosquito bites per person per day) may be influenced by the number of pigsties and the way in which these stables are connected to houses. On the other hand may the number of cattle influence “$h$”, the proportion of blood meals taken from humans (Kuhn et al., 2003). On the other hand is it also possible that the number of mosquito bites per day also will be influenced by the size of the mosquito population. Nevertheless will these factors influence the $R_0$ value and thus the way an epidemic progresses over time.

In principle this model can also be used for other mosquito-borne diseases. If certain diseases can also be transmitted vertically (the virus is transmitted from mother mosquito into her eggs), however the model needs to be adjusted. Then, not only births are a flow into the susceptible mosquito compartment, but also in the other mosquito compartments.
6. GENERAL DISCUSSION

6.1 Malaria in Western Europe
The part of this research about malaria in Western Europe showed that many interacting factors played a role in the epidemic character and the disappearance of the disease. Still many questions remain unsolved about the epidemiology of malaria. It is still not clear why malaria epidemics occurred regularly every 20-25 years. Also the onset and peaks of epidemics showed large differences in time, even between neighboring villages. The studied factors did not give a conclusive explanation for these characteristics. One could question whether the used data is accurate enough. The climate data is an average of that from Den Helder and De Bilt. Therefore the data may deviate from the actual situation in Wormerveer. Nevertheless did temperature variation and precipitation show a correlation with malaria incidence. One can doubt about the value of these correlations because leaving a few data points out of the assessment can result in data that is not correlated. Also the data for malaria incidence is very different between villages in North Holland. Therefore a correlation between malaria incidence and weather conditions in Wormerveer, does not have to mean a correlation between weather conditions and malaria incidence in other villages. To say more about the different climate factors it is necessary that also data from other villages are assessed, although the question is whether accurate malaria incidence data from other places is available.

Also the differences in comparing historic chloride content with current chloride contents of water bodies in North Holland may be due to inaccurate data. The average historic chloride content was based on 89 measuring points, while 49 measuring points were used to calculate the current average chloride content of the water. Nevertheless is it fair to say that water in certain areas in North Holland still contains a suitable chloride concentration for An. atroparvus mosquito to be used as breeding sites. But the number of breeding sites with a suitable chloride content have very likely decreased since the 1960s as the average chloride content over the different measuring points is much lower these days.

Although the statement that there is an increasing risk for malaria in Western Europe may be legitimate, it still remains to be seen whether this risk is substantial. For example, experts think that the fear for the return of malaria is overrated and other factors will prevent new outbreaks of malaria in the Netherlands (Takken et al., 1999). Also the comparison in this research showed that many factors in malaria epidemiology have changed during the last century in such a way that the statement of reoccurring malaria seems unfounded.

The model is a useful tool to learn more about mosquito-borne disease epidemiology. The basic reproduction rate (\(R_0\)) was used as an input for the model. An equation from literature was used to study the effect of changes in several factors. One may argue whether this equation is suitable enough for studying malaria in Western Europe. The basic reproduction rate will become higher if the temperature increases according to the equation. Therefore one could expect that a warmer year would result in a higher basic reproduction rate. However this research showed that there is no correlation between malaria incidence and temperature. Nevertheless, the Stella model showed that the higher the basic reproduction rate, the higher the attack ratio. The peak of an epidemic will also be higher and will be reached faster. It seems that the model is working properly, but it is hard to calculate the input (\(R_0\)) accurately since it is dependent on many variables. The Stella model can also be used for other mosquito-borne diseases, but changes should be made for viruses which can be transmitted vertically (also a “births” flow into the “infectious mosquitoes” compartment is necessary) and several basic settings need to be adjusted according to the specifications of the mosquito and pathogen. For this thesis the model has only been used for studying malaria epidemiology and not to model other mosquito-borne diseases (e.g. a chikungunya epidemic transmitted by Ae. albopictus mosquitoes) due to insufficient time. Nevertheless, it should be interesting to model the outbreak of chikungunya in Italy for example.
6.2 Invasion of the Asian tiger mosquito

Current scientific literature in the field of mosquito-borne diseases often focuses on *Ae. albopictus*. It is seen as one of the most successful invading species of the last decades. Although the transport of used tires and lucky bamboo are known as successful invasion routes for this mosquito, other routes may also be present. For example, short-term distribution routes through cars and trucks. Therefore more research is needed to identify alternative transport routes in order to reduce the chances of mosquito invasions through these routes (Straetemans et al., 2008).

Many experts characterize the invasion of *Ae. albopictus* into many countries as a lack of policy measures by governments. The threat of this mosquito species was underestimated for a long time. In Europe policy makers became more aware of this problem after the outbreak of chikungunya in Italy (Schaffner et al., 2009). Before this outbreak *Ae. albopictus* had the chance to invade many countries very easily, as economic values were seen more important than public health. Often it is necessary to react very rapidly to new introduced species in order to prevent establishment and further spread (Lodge et al., 2006).

As climate conditions in certain parts of Western Europe seem to be suitable for *Ae. albopictus* establishment, there may be a serious threat for public health. Especially with the knowledge that the mosquito has been imported into Western Europe several times (Schaffner et al., 2004; Scholte et al., 2007). Since *Ae. albopictus* was first discovered in greenhouses in the Netherlands, the import of lucky bamboo has not been restricted. Many companies however do spray with insecticides regularly in order to exterminate mosquitoes. So far, it seems that this method is successful (Scholte et al., 2008).

Because there is serious chance that *Ae. albopictus* will invade parts of Western Europe it is necessary to take policy measures in order to prevent its introduction. Regular surveillance of lucky bamboo importing companies and tire trading companies is therefore needed. When *Ae. albopictus* eggs, larvae or mosquitoes are detected, they should be eradicated as soon as possible. Although it is doubtful whether policy measures will prevent the introduction of *Ae. albopictus*, the process of invasion can still be delayed. If this species manages to establish itself, it is important to keep the populations as small as possible in order to reduce the chance of virus transmission. Inhabitants of regions where the mosquito is present should be made aware of it, so they can take precautions to reduce the chance of getting bitten.

In the meantime it is important that scientific research continues to learn more about the epidemiologic success of *Ae. albopictus*. On the other hand should scientific research also direct on finding vaccines for the most common viruses spread by *Ae. albopictus* and new ways to exterminate this mosquito.
7. CONCLUSIONS

Many different factors related to mosquito-borne diseases in Western Europe were addressed in this study. The results from the literature study show that several factors have changed over the years resulting in the disappearance of malaria from Western Europe. Especially the reduction of wetlands and the availability of (human) blood meals were important in the decline of malaria incidence. Although water chlorinity and climate factors are related to variations in malaria incidence, the role of these factors in the disappearance of malaria is limited. Because conditions are not suitable enough, it is unlikely that malaria will return in Western Europe anywhere soon.

The spread of *Ae. albopictus* around the globe is mainly due to shipments of used tires and lucky bamboo. Because this mosquito adapted very well to hard conditions like cold and drought and because it thrives very well in human environments it was able to establish in many regions where it got introduced. Conditions in many regions may become more suitable for *Ae. albopictus* due to climate change. In certain regions of Western Europe conditions are expected to be suitable enough already for its establishment. Because this species can serve as a vector for many arboviruses, it is a potential threat to public health.

The return of malaria in Western Europe is unlikely to occur. Therefore specific policy measures are unnecessary. The invasion of *Ae. albopictus* in to Western Europe is much more likely and policy measures are necessary to protect public health. Policy measures directed to prevent or delay the introduction and establishment in Western Europe should be the primary target. Even with such measures it is still possible that *Ae. albopictus* will settle, therefore also measures are necessary to keep mosquito populations as low as possible and to inform the public on protection against these mosquitoes.
8. ACKNOWLEDGEMENTS

This training thesis was carried out at the Center for Energy and Environmental Studies at the University of Groningen in the period September 2010 until June 2011. Of course I could not have done it without help and advice from my supervisors and other staff members who taught me research skills. Therefore I need to thank some people, now the report is almost finished.

First of all I would like to thank my first supervisor Ton Schoot Uiterkamp who helped me throughout the research and the writing of this report. His advises and also his enthusiasm helped me to get new insights into the subject and to stay motivated throughout the progress of this thesis. I also would like to thank my second supervisor Sjaak Swart for his critical comments on the report. For the modeling part I would like to thank René Benders for his feedback. Furthermore I would like to thank all other (IVEM) students and staff members who gave me advice or helped me find useful information and data on the subject.
9. REFERENCES


Lindsay, S. W., & Thomas, C. J. (2001). Global warming and risk of vivax malaria in great Britain. *Global Change & Human Health*, 2(1), 80-84.


Zwarteveen, J. (1948). Malaria in de noordoostelijke polder, onderzoek en bestrijding in de jaren ‘42-‘47’.

![Figure 9.1](image-url)
APPENDIX A: MALARIA IN WORMERVEER

In 1902 Dr. P.C. Korteweg started to diagnose malaria by finding the responsible plasmodium in the village of Wormerveer (Swellengrebel & de Buck, 1938). As Described by Swellengrebel (1950), the figures apply to a population of 3000 till 1926. From 1927 onward the figures apply to a population of 6,000, gradually rising to 10,000. The assumption is made that the rise of the population was linear, so that every year the population increased with 182 persons. In table A1 the population and the number of patients are shown from 1902 until 1949.

<table>
<thead>
<tr>
<th>Year</th>
<th>Population</th>
<th>Number of Patients</th>
<th>Year</th>
<th>Population</th>
<th>Number of Patients</th>
<th>Year</th>
<th>Population</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1902</td>
<td>3000</td>
<td>540</td>
<td>1918</td>
<td>3000</td>
<td>117</td>
<td>1934</td>
<td>7273</td>
<td>157</td>
</tr>
<tr>
<td>1903</td>
<td>3000</td>
<td>111</td>
<td>1919</td>
<td>3000</td>
<td>173</td>
<td>1935</td>
<td>7455</td>
<td>161</td>
</tr>
<tr>
<td>1904</td>
<td>3000</td>
<td>56</td>
<td>1920</td>
<td>3000</td>
<td>229</td>
<td>1936</td>
<td>7636</td>
<td>115</td>
</tr>
<tr>
<td>1905</td>
<td>3000</td>
<td>119</td>
<td>1921</td>
<td>3000</td>
<td>234</td>
<td>1937</td>
<td>7818</td>
<td>77</td>
</tr>
<tr>
<td>1906</td>
<td>3000</td>
<td>126</td>
<td>1922</td>
<td>3000</td>
<td>326</td>
<td>1938</td>
<td>8000</td>
<td>64</td>
</tr>
<tr>
<td>1907</td>
<td>3000</td>
<td>111</td>
<td>1923</td>
<td>3000</td>
<td>64</td>
<td>1939</td>
<td>8182</td>
<td>62</td>
</tr>
<tr>
<td>1908</td>
<td>3000</td>
<td>25</td>
<td>1924</td>
<td>3000</td>
<td>12</td>
<td>1940</td>
<td>8364</td>
<td>82</td>
</tr>
<tr>
<td>1909</td>
<td>3000</td>
<td>12</td>
<td>1925</td>
<td>3000</td>
<td>13</td>
<td>1941</td>
<td>8545</td>
<td>21</td>
</tr>
<tr>
<td>1910</td>
<td>3000</td>
<td>3</td>
<td>1926</td>
<td>3000</td>
<td>18</td>
<td>1942</td>
<td>8727</td>
<td>24</td>
</tr>
<tr>
<td>1911</td>
<td>3000</td>
<td>19</td>
<td>1927</td>
<td>6000</td>
<td>85</td>
<td>1943</td>
<td>8909</td>
<td>54</td>
</tr>
<tr>
<td>1912</td>
<td>3000</td>
<td>40</td>
<td>1928</td>
<td>6182</td>
<td>66</td>
<td>1944</td>
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<td>275</td>
</tr>
<tr>
<td>1913</td>
<td>3000</td>
<td>27</td>
<td>1929</td>
<td>6364</td>
<td>119</td>
<td>1945</td>
<td>9273</td>
<td>332</td>
</tr>
<tr>
<td>1914</td>
<td>3000</td>
<td>10</td>
<td>1930</td>
<td>6545</td>
<td>201</td>
<td>1946</td>
<td>9455</td>
<td>696</td>
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<tr>
<td>1915</td>
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<td>28</td>
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<td>1947</td>
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<td>305</td>
</tr>
<tr>
<td>1916</td>
<td>3000</td>
<td>25</td>
<td>1932</td>
<td>6909</td>
<td>25</td>
<td>1948</td>
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<td>21</td>
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<td>1917</td>
<td>3000</td>
<td>27</td>
<td>1933</td>
<td>7091</td>
<td>164</td>
<td>1949</td>
<td>10000</td>
<td>7</td>
</tr>
</tbody>
</table>

Table A1: Malaria cases in Wormerveer from 1902 till 1949 (Reproduced from Swellengrebel, 1950).
APPENDIX B: STATISTICS

The statistical analyzing tool SPSS16 is used to investigate a possible correlation between the climatic factors and malaria incidence in Wormerveer between 1907 and 1949. Malaria incidence (per thousand inhabitants) is compared with temperature and precipitation in an entire year and in the summer months (June – August), the reproductive period of *An. atroparvus*. The climatic factors of a year (see table B1) are actually the numbers of the previous year (e.g. the factors in 1907 are actually those from 1906). The reason for this shift is the assumption that climatic factors may influence the malaria incidence in the next year due to the long incubation period of the malaria parasite in humans (Swellengrebel & de Buck, 1938).

<table>
<thead>
<tr>
<th>Year</th>
<th>Malaria</th>
<th>Temp (year)</th>
<th>Temp (Jun-Aug)</th>
<th>Precip (year)</th>
<th>Precip (Jun-Aug)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1907</td>
<td>37,0</td>
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<td>15,93</td>
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<td>143,3</td>
</tr>
<tr>
<td>1908</td>
<td>8,3</td>
<td>8,95</td>
<td>14,39</td>
<td>634,0</td>
<td>157,7</td>
</tr>
<tr>
<td>1909</td>
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<td>8,65</td>
<td>15,85</td>
<td>561,6</td>
<td>191,2</td>
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<tr>
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<td>1,0</td>
<td>8,44</td>
<td>14,48</td>
<td>760,2</td>
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</tr>
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<td>9,56</td>
<td>15,76</td>
<td>699,4</td>
<td>186,7</td>
</tr>
<tr>
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<td>13,3</td>
<td>9,96</td>
<td>17,30</td>
<td>618,2</td>
<td>114,6</td>
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<tr>
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<td>9,0</td>
<td>9,37</td>
<td>15,94</td>
<td>893,1</td>
<td>324,0</td>
</tr>
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<td>9,78</td>
<td>14,70</td>
<td>655,8</td>
<td>190,7</td>
</tr>
<tr>
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<td>9,87</td>
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<td>14,53</td>
<td>742,7</td>
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</tr>
<tr>
<td>1918</td>
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<td>8,48</td>
<td>16,85</td>
<td>762,6</td>
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<tr>
<td>1919</td>
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</tr>
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<td>171,3</td>
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<tr>
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<td>15,18</td>
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<tr>
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<tr>
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<td>15,64</td>
<td>800,5</td>
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</tr>
<tr>
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<td>9,46</td>
<td>15,63</td>
<td>767,8</td>
<td>203,7</td>
</tr>
<tr>
<td>1930</td>
<td>30,7</td>
<td>8,41</td>
<td>15,58</td>
<td>567,3</td>
<td>134,7</td>
</tr>
<tr>
<td>1931</td>
<td>15,5</td>
<td>9,81</td>
<td>16,72</td>
<td>832,9</td>
<td>307,3</td>
</tr>
<tr>
<td>1932</td>
<td>3,6</td>
<td>8,98</td>
<td>15,73</td>
<td>713,9</td>
<td>232,9</td>
</tr>
<tr>
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<td>16,94</td>
<td>685,1</td>
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<td>16,99</td>
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<tr>
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<td>16,32</td>
<td>667,8</td>
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</tr>
<tr>
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<td>9,81</td>
<td>16,88</td>
<td>826,7</td>
<td>170,2</td>
</tr>
<tr>
<td>1937</td>
<td>9,8</td>
<td>9,62</td>
<td>16,36</td>
<td>736,7</td>
<td>207,7</td>
</tr>
<tr>
<td>1938</td>
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<td>9,53</td>
<td>16,33</td>
<td>733,7</td>
<td>165,0</td>
</tr>
<tr>
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<td>9,86</td>
<td>16,28</td>
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<td>181,3</td>
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<tr>
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<td>9,71</td>
<td>16,76</td>
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</tr>
<tr>
<td>1941</td>
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<td>8,17</td>
<td>15,78</td>
<td>784,8</td>
<td>195,9</td>
</tr>
<tr>
<td>1942</td>
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<td>8,64</td>
<td>16,58</td>
<td>728,3</td>
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</tr>
<tr>
<td>1943</td>
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<td>8,39</td>
<td>15,64</td>
<td>798,2</td>
<td>289,5</td>
</tr>
<tr>
<td>1944</td>
<td>30,3</td>
<td>9,88</td>
<td>16,08</td>
<td>636,6</td>
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<td>16,35</td>
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<td>139,6</td>
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<tr>
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<td>73,6</td>
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<td>16,57</td>
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<td>190,6</td>
</tr>
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</tr>
<tr>
<td>1949</td>
<td>0,7</td>
<td>9,96</td>
<td>15,96</td>
<td>684,6</td>
<td>230,8</td>
</tr>
</tbody>
</table>

Table B1 List of the compared numbers of malaria incidence and climate factors between 1907 and 1949.
Table B1 is imported in SPSS and the different factors are compared with the malaria incidence to find the Pearson correlation coefficient. Figure B1 shows the result of the comparison of malaria incidence and total annual precipitation. Not all the data is presented in the appendices of this thesis, due to large amounts of used and assessed data. All other data is burned on a CD-ROM and available at IVEM.

<table>
<thead>
<tr>
<th></th>
<th>Malaria (1/1000)</th>
<th>Precip (year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>20,923</td>
<td>711,360</td>
</tr>
<tr>
<td>Std Deviation</td>
<td>24,3055</td>
<td>98,6344</td>
</tr>
<tr>
<td>N</td>
<td>43</td>
<td>43</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Malaria (1/1000)</th>
<th>Precip (year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Correlation</td>
<td>1.000</td>
<td>-0.425**</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0.004</td>
<td>0.004</td>
</tr>
<tr>
<td>N</td>
<td>43</td>
<td>43</td>
</tr>
</tbody>
</table>

**. Correlation is significant at the 0.01 level (2-tailed).

Figure B1 Results of correlation analysis between malaria incidence and annual precipitation.
APPENDIX C: ENVIRONMENTAL FACTORS

<table>
<thead>
<tr>
<th>Factor</th>
<th>1930</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>1 509 587</td>
<td>2 669 084</td>
</tr>
<tr>
<td>Average temperature (°C)</td>
<td>9.25 (8.17-10.25)</td>
<td>10.13 (8.46-11.23)</td>
</tr>
<tr>
<td>Annual precipitation (mm)</td>
<td>701.5 (406.7-893.1)</td>
<td>805.4 (560.8-1112.0)</td>
</tr>
<tr>
<td>% Grassland</td>
<td>51.5</td>
<td>36.4</td>
</tr>
<tr>
<td>% Water</td>
<td>14.8</td>
<td>14.1</td>
</tr>
<tr>
<td>Water chlorinity (mg/L)</td>
<td>770 (600-1000)</td>
<td>284 (212-370)</td>
</tr>
<tr>
<td>Number of pigfarms</td>
<td>98 981</td>
<td>742</td>
</tr>
<tr>
<td>Number of pigs</td>
<td>790 931 (82 836)</td>
<td>611 045 (22 493)</td>
</tr>
</tbody>
</table>

Table C1: Comparison of the selected environmental factors between the malaria endemic period (~1930) and present times (~2010) in the province of North Holland.

In Table C1 the changes in more or less 80 years of the different factors are shown.

The historic population number is the outcome of a census in 1930 in North Holland (CBS, 2006). The number of the present population size is from January 1st 2010 (CBS, 2010a).

In this table, the average temperature and the annual precipitation are the average of daily data over 30 years in the periods 01-01-1906 till 31-12-1935 and 15-11-1980 till 16-11-2010 (KNMI, 2010a). It is the average of data from De Kooy (location code: 06235) and De Bilt (location code: 06260), since both data locations may not represent the temperature of North Holland (De Kooy is located far north on the mainland of North Holland and De Bilt in the province of Utrecht). For precipitation, data in the period 1906-1936 is used from Den Helder (location code: 009) instead of De Kooy (KNMI, 2010a), since precipitation measurements in De Kooy did not start until the 1970’s. The variation in average annual temperature and total annual precipitation are shown between brackets.

The recent and historic numbers for both grassland and water are reproduced from Knol et al. (2003). Note that the recent numbers are from 1995 instead of 2010.

The average chlorinity in 1930 is reproduced from Van Seventer (1969), from chlorinity data between 1939 and 1960 of 89 measuring points. It is approximately the value of the regression line in 1939. The average water chlorinity in present times was calculated by averaging the water chlorinity of 49 data points annually from 1991 until 2010 (HHNK, 2010). Measuring points from the isle of Texel and the Wieringermeer polder were excluded, since Van Seventer (1969) did also not include these points. The years 1996, 1998 and 1999 are not included in the calculation since some data points were lacking for those years. The location codes of the 49 data points are: 1003, 1007, 2002, 6002, 7001, 7002, 9001, 13001, 14001, 21001, 81001, 84001, 87001, 88001, 104302, 104401, 104502, 107201, 107301, 116102, 116501, 119201, 119202, 119203, 125202, 128204, 134401, 134601, 134603, 134604, 135101, 135105, 135201, 135202, 135301, 135601, 146301, 146401, 146402, 149102, 152302, 158102, 158201, 158202, 184201, 184501, 187103, 187202, 517006, 770206

The historic pig(farm) data is reproduced from Van Seventer (1969). Although there are some differences between figure 9 and 10 in the thesis by van Seventer, it is assumed that the total number of pigs and pigfarms in the year 1934 is from all malaria endemic provinces: North Holland, South Holland, Utrecht, Friesland and Zeeland. The recent numbers for both pigs and pigfarms are also the total of the mentioned provinces (CBS, 2010b). The number between brackets in the “number of pigs” section is the specific number for only the province of North Holland. The historic number for
pigs and pigfarms for the province of North Holland specifically was much harder to find since this
data was not available at the Central Bureau for Statistics. Finally information on historic pig numbers
in the province of North Holland was found via contact with the department of rural history
(Boeleman, J.) at the Wageningen University. The historic number of pigs in the province of North
Holland is from the year 1921 (Directie van den landbouw, 1922).
APPENDIX D: STELLA MODEL

Figure D1 The malaria model in Stella. $R_0$ (green) is an input variable for both the infection rate of the human part (blue) en the mosquito part (black) of the model.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$a$</td>
<td>Anopheles density</td>
<td>1/a</td>
</tr>
<tr>
<td>$b$</td>
<td>% developing parasites</td>
<td>0.19</td>
</tr>
<tr>
<td>$p$</td>
<td>Daily survival prob</td>
<td>0.97</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Rate of recovery</td>
<td>0.0167</td>
</tr>
<tr>
<td>$h$</td>
<td>Proportion taken from humans</td>
<td>0.42</td>
</tr>
<tr>
<td>$f_1$</td>
<td>Thermal sum</td>
<td>36.5</td>
</tr>
<tr>
<td>$g_1$</td>
<td>Threshold below development ceases</td>
<td>9.9</td>
</tr>
<tr>
<td>$f_2$</td>
<td>Thermal sum</td>
<td>105</td>
</tr>
<tr>
<td>$g_2$</td>
<td>$T_{min}$ for parasite development in mosquitoes</td>
<td>14.5</td>
</tr>
<tr>
<td>$S_H$</td>
<td>Susceptible humans</td>
<td>9900</td>
</tr>
<tr>
<td>$E_H$</td>
<td>Exposed humans</td>
<td>100</td>
</tr>
<tr>
<td>$I_H$</td>
<td>Infectious humans</td>
<td>0</td>
</tr>
<tr>
<td>$R_H$</td>
<td>Recovered humans</td>
<td>0</td>
</tr>
<tr>
<td>$\kappa_H$</td>
<td>Human infectious transition rate</td>
<td>0.005</td>
</tr>
<tr>
<td>$\gamma_H$</td>
<td>Human recovery rate</td>
<td>0.0167</td>
</tr>
<tr>
<td>$S_M$</td>
<td>Susceptible mosquitoes</td>
<td>10000</td>
</tr>
<tr>
<td>$E_M$</td>
<td>Exposed mosquitoes</td>
<td>0</td>
</tr>
<tr>
<td>$I_M$</td>
<td>Infectious mosquitoes</td>
<td>0</td>
</tr>
<tr>
<td>$\kappa_M$</td>
<td>Mosquito infectious transition rate</td>
<td>0.1</td>
</tr>
<tr>
<td>$\lambda_M$</td>
<td>Mosquito birth rate</td>
<td>0.03</td>
</tr>
<tr>
<td>$\mu_M$</td>
<td>Mosquito death rate</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table E1 Standard values for the different variables in $R_0$ equation and the Stella model