Malaria in Myanmar

Causes, treatment, prevention and prognosis of malaria, and the occurrence in the endemic Myanmar and non-endemic Norway

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Project thesis
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This report covers the work done on the mandatory project thesis during my medical study at the Faculty of Medicine, University of Oslo. The work on the project thesis has involved collecting and evaluating information.

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Abstract

Malaria is a vector-born disease, protozoa are transmitting through bites of the mosquito anopheles. Four species of plasmodium can infect humans, destroying red blood cells and causing clinical symptoms like fever and other typical symptoms of infection. Diagnosis is based on results from microscopy of blood and rapid diagnostic tests. Recommended antimalarial treatment is largely based on artemisinin-based combination therapy. This treatment is threatened by developing drug resistance. Preventing the spreading of the disease involve vector control and surveillance, mechanical and prophylaxis like insecticide treated bed nets and drug prophylaxis. Vaccination projects are launched by the World Health Organization. The tropical parasitic disease is distributed mostly in the African, Southeast Asian and Eastern Mediterranean region. In 2010, the number of cases was estimated to 237 million (95% CI: 218-278 million) worldwide, followed by 216 million (95% CI: 196-263) cases in 2016. Still causing one of the highest burdens of infectious diseases worldwide, the numbers have been markedly declining. This is also happening in the endemic country Myanmar. Myanmar has detected resistance to artemisinin-based combination therapy, and work on measures in order to stop the spread, which include stopping substandard treatment. Myanmar has several challenges, including a low health budget. Currently, the country plans to launch universal health care as part of a national health plan, reaching out to rural areas with health staff, malaria prophylactic measures and effective antimalarial treatment. The aim is to be malaria free by 2030. Norway is not a malaria endemic country and cases of malaria mainly originate from travelling and tourism. Norway has a well-built health care system and antimalarial measures mainly consist of travelling advice and the offer of prophylactic drugs.
Abbreviations

ACT  Artemisinin-based Combination Therapy
ALT  Alanine Transaminase
AMT  Artemisinin-based Monotherapy
ASEAN Association of South-East Asian Nations
BMJ  British Medical Journal
CI   Confidence Interval
CRP  C-Reactive Protein
DDT  Dichlorodiphenyltrichloroethane
HIV/AIDS Human Deficiency Virus/Acquired Immunodeficiency Syndrome
HRP2 Histidine-Rich Protein 2
IRS  Indoor Residual Spraying
ITN  Insecticide Treated Bed Net
LD   Lactate Dehydrogenase
MeSH Medical Subject Headings
MSIS Norwegian Surveillance System for Communicable Diseases
NIPH Norwegian Institute of Public Health
PCR  Polymerase Chain Reaction
PICO Population/Intervention/Comparison/Outcome
RDT  Rapid Diagnostic Test
UHC  Universal Health Coverage
USAID/PMI United States Agency for International Development/President’s Malaria Initiative
WHO World Health Organization
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1 Introduction

The aim of this report is to give an overview of trends of malaria occurrence, mortality and morbidity in a malaria endemic country, Myanmar, and compare this to Norway, a non-endemic country. The report will answer the following research questions:

*How has the occurrence of malaria changed in endemic Myanmar and non-endemic Norway over the last decade, and which are the main factors that influence the occurrence of malaria?*

In order to answer the research questions, several aspects of malaria will be discussed. This includes occurrence globally, in South East Asia, Myanmar and Norway, general pathophysiology, diagnosing methods, prevention, treatment options and drug resistance. Both existing and new cases are considered, and both preventative measures and the measures initiated when people are infected will be discussed.

Myanmar was chosen due to the challenges the country has faced and still faces regarding the spread of drug resistant malaria. In addition, challenges are related to the economic and political situation. Myanmar has recently moved from a military rule towards a more democratic government more attentive to public health. Global efforts are needed to fight malaria, and Myanmar has opened up to for collaboration with the world. According to the Myanmar National Health Plan 2017-2021(3), the country now plans on increasing the national budget on health. This may help reducing the occurrence of infectious diseases, including malaria, in the coming years. Norway was chosen as it is a country quite the opposite of Myanmar, and where malaria mainly is transferred by travellers from endemic countries. Malaria is today present in several regions of the world, including Southeast Asia where it causes a threat to both locals and travellers. As malaria is not eliminated in Myanmar, the country faces the challenge of the disease responsible for a vast number of cases, 142 600 estimated in 2016 (4), with both high mortality and morbidity. However, the prevalence of malaria decreases worldwide (5).

2 Methods

The literature collected consists of publicly available books and scientific articles as well as web pages from national and international public health services and organisations.

Literature searches were done using online search engines. It was decided to use search terms that would ensure a sufficiently wide selection of responses. Keywords used were “malaria”, “Myanmar” and “Norway”, supplemented with keywords such as “incidence” and “epidemiology”.

In order to get an overview of epidemiology globally and in Myanmar, the World Health Organisation’s (WHO) malaria page (6) proved useful, supplying national fact sheets and country profiles that showed statistics and trends. WHO World Malaria Report (5) and Global Technical Strategy for Malaria 2016-2030 (7) were also downloaded from the organisations’ web page. To obtain a more comprehensive understanding of malaria occurrence, searches were done in PubMed (8), using MeSH (Medical Subject Headings) and clinical queries.

Concerning Norway’s epidemiology, statistics were collected from the Norwegian Surveillance System for Communicable Diseases (MSIS) (9) and Norwegian Institute of Public Health (NIPH) (10). Relevant references were selected. NIPH described the trends to a greater extent,
in addition to supplying information about Norwegian guidelines concerning malaria, especially prophylaxis.

Concerning diagnostics and treatment, the search engine McMaster plus (11) was used with the search word “malaria”. Further, overviews were explored in UpToDate (12) and supplemented by WHO guidelines (13) and British Medical Journal (BMJ) Best Practice (14). These web pages provided useful information about treatment and pathophysiology. UpToDate’s references were explored to find single articles. Concerning vaccination, PubMed was used, with keywords such as “malaria” and “vaccination”, “vaccine”, “prophylaxis”, “prevention”. PubMed was also used throughout the exploration of the subjects in order to obtain individual scientific articles regarding epidemiology, diagnostics, treatment and symptoms. Cochrane library (15) was used to identify randomized controlled trial studies about treatment options. A selection of studies concerning treatment, based on date and relevance were explored further. PICO (Population/Intervention/Comparison/Outcome), a method used to form and answer health care related questions, was used as a strategy in the literature search.

Direct search on Myanmar Ministry of Health and Sport’s home page (16) provided useful reports and surveys, including Myanmar’s National Health Plan (3) and a demographic and health survey (17). References were selected from reports and papers. Open searches (Google) were used to identify a concluding report of the demographic and health survey (18). Furthermore, a malaria symposium (19) for Myanmar was used to supplement Myanmar’s country malaria profile along with several articles selected from WHO’s homepage (20) and The Lancet (21), specifically concerning malaria elimination and the management of drug resistance.

3 Malaria in a global perspective

The tropical disease malaria is one of the world’s most common infectious diseases. Despite a steady decline in malaria incidences throughout the world (7, 22), it continues to have a great impact on people’s health worldwide. The number of people at risk of acquiring the infection was in 2013 estimated to an 3,2 billion people, almost half the world’s population across 97 countries (7, 23).

3.1 Global occurrence

WHO’s World Malaria Report of 2017 (5) describes a worldwide decrease in the number of cases of malaria during since 2010 (figure 1). In 2010, the number of cases was estimated to 237 million (95% CI: 218-278 million) worldwide, followed by 216 million (95% CI: 196-263) cases in 2016. The mortality in 2016 was estimated to 445 000 deaths globally, while in 2015 there were 446 000 estimated deaths. The decrease in malaria cases is believed to be a result of proactive efficient use of mosquito nets and insecticides and more effective treatment (5, 23, 24). In recent years, several countries have been declared malaria free: United Arab Emirates (2007), Morocco (2010), Turkmenistan (2010), Armenia (2011), Sri Lanka (2016) and Paraguay (2018). Together with other Southeast Asian countries, Myanmar has the same goal.
Bringing malaria to extinction is a on-going multifaceted challenge. In its World Malaria Report (5), WHO points out financial funding, drug resistance and insecticide resistance to be factors that are of high importance, that are not yet fully controlled.

Drug resistance affects the Greater Mekong Subregion in particular, Myanmar included. Histidine-rich protein 2 deletions (HRP2) causes a higher amount of false negative malaria antigen tests (25) as the lack of protein expression makes parasites unidentifiable. Consequently, fewer patients are diagnosed and treated against malign malaria caused by *p. falciparum*.

The observed reduction in number of malaria cases is explained by improved monitoring of the effect of treatment and continuous updates and improvement of treatment policies (5, 23). Global targets for 2030 (7) is preventing re-establishment of malaria in disease-free areas, and reduction of both worldwide mortality rates and case incidences by 90%. Methods will among others include vector control and chemoprevention. Global challenges concerning drug and insecticide resistance will be discussed later in the report.

3.2 Global distribution

Malaria is mainly found in the tropical regions of the world, where nearly half of the world’s population is living. Malaria is very unevenly spread out (6). The distribution of the disease includes the Sub-Saharan Africa with the by far highest burden of disease (90%), followed the Southeast Asia region (3%) and the Eastern Mediterranean Region (2%). The Western Pacific and Europe are also affected (26). Sub-Saharan Africa accounts for 91% of all malaria deaths, the majority of these being caused by *p. falciparum* (99%) (27). In 2015, the following six African countries reported approximately 60% of deaths caused by the infection: Nigeria, The Democratic Republic of Congo, Burkina Faso, Ivory Coast and Mali (10).

The presence of the different parasite subgroups varies in different regions of the world:

- *P. vivax*, responsible for the highest amount of benign cases of malaria (28, 29), is more common in the Americas and western Pacific.
- *P. falciparum* is more morbid and is common in Sub-Saharan Africa (28). In the rest of the world, *P. falciparum* and *P. vivax* are equally common.
- *P. ovale* and *P. malariae*, the two other subgroups, are less common in general but are evenly distributed throughout the tropical zones (22). *P. ovale* is rarely found outside Africa.
- *P. knowlesi* is a subtype that has not yet be found to be transferred from humans to mosquitoes (30, 31). It is found in In Myanmar, Thailand, Malaysia and the Philippines.

The malaria distribution also varies within endemic areas. Subgroups of people with human deficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), infants and children under the age of five years, pregnant women and non-immune travellers are more susceptible to acquiring the disease, in addition to a more severe disease progression (6, 32, 33).

3.3 Occurrence in Southeast Asia

According to the WHO, the Southeast Asia Region accounted in 2016 for 3% of malaria cases worldwide, a 1.4 million cases were confirmed. A total of 1.35 billion people were at risk, 49% of the global population at risk (34, 35). A long road toward extinction of malaria remains in Southeast Asia, however the number of new cases and deaths have been decreasing in the region between 2010 and 2016 by 48% and 60% respectively (35). This is explained by several factors;
- extending the provisioning conservative prophylaxis,
- more rapid methods of diagnosis, and
- effective artemisinin-based combination therapies

*P. falciparum* infections vary greatly in Southeast Asia, from 0% to 91%, while *p. vivax* infections in Southeast Asia causes a high burden of disease in the region, accountable for 58% of the global incidence of *p. vivax* infections (35).

As artemisinin resistance is spreading and threatening the decline in number of cases, representatives from several Southeast Asian countries agreed in 2017 on accelerated action in order to eliminate malaria in the Greater Mekong Subregion by 2030 (36). The countries involved requested support from WHO, funders and other partners and agencies in order to ensure full funding, along with increasing domestic funds, in order to meet their goals. Other crucial steps involve improving the cross-border collaboration (37, 38) and ensuring availability of diagnosis and treatment interventions, also for mobile and migrating populations.

3.4 The impact of climate changes

Anticipating the impact of climate change on the spread of malaria is of high interest, and also vital in order to preserve the decline in occurrence, facilitate activities aiming for further elimination and secure the prevention of reintroduction of the disease. Research indicates there is a connection between malaria occurrence and climate change (39), and that the effect is a general increase of incidence. However, this effect is not uniform across countries. The future is still uncertain also due to other parameters that must be considered. Of these, evolving drug resistance and socioeconomic development are considered main factors.

The climate change may influence the transmission of malaria by several mechanisms. These include in particular an increased number of rainfall events followed by flooding and increased temperature. Developing nations are particularly susceptible to increased infection rate due to flooding (40, 41). Increased global temperature would be favourable to the spread of vector-borne diseases including malaria (42), and a global net increase in the population at risk is expected (43). On the other hand, certain areas would be expected to experience a decrease in
malaria cases, for example Sub-Saharan areas where climate change is expected to cause less rainfall.

A Chinese study (44) discussed the spread of vectors, including the two most prevalent vectors in Myanmar, an. dirus and an. minimus, using species distribution models for the 2030s and 2050s. Estimations concluded with an increase of the environmentally suitable area for an. dirus and an. minimus by 49% and 16% respectively, thus leading to a substantial net increase in the population at risk in the coming decades (44). In addition to facilitating spread of the disease, increased temperature may also affect the mortality directly. A study shows a non-linear relationship between temperature and malaria mortality (45). Mortality increases at temperatures over 21°C, while the for children increased mortality is observed at a lower temperature, 19°C. In 2016, 70% of the deaths occurred in children below the age of five years. The same study estimated that child mortality may increase by up to 20% in certain areas by the end of the century, due to climate change (45). Climate change is in addition expected to have an economic impact; an African study shows an increased expected inpatient treatment cost (39).

4 Malaria key facts

4.1 Causes

4.1.1 Vector

The vector-borne disease malaria transmits through bites of the female mosquito anopheles, causing the bitten to be infected with plasmodium protozoa. Only the female mosquito bites humans, as it requires blood to lay eggs. The mosquito is typically found in warm and moist tropical climate, making Africa, Southeast Asia and the Eastern Mediterranean susceptible for disease outbreaks (26). The reason for increased prevalence in subtropical and tropical areas is that warmer temperatures favour and shortens the life cycle of the parasite, increasing the chance of completing the reproduction cycle within the mosquitoes two months life span. There are 400 mosquito species, of which 80 transfer malaria (46). An. minimus and an. dirus are the major malaria transferring species in Myanmar (19).

4.1.2. Parasite

Five species of the plasmodium may cause human malaria:
- p. falciparum
- p. vivax
- p. malariae
- p. ovale
- p. knowlesi

The five subtypes of malaria are divided into benign and malign malaria. The benign types are p. ovale, p. vivax and p. malariae. The malign are p. falciparum and p. knowlesi. P. knowlesi mostly infects animals, but also infects humans occasionally and like p. falciparum it may cause a severe disease outbreak (47).

Incubation time differs: p. falciparum has 12-14 days of incubation, p. malariae is about 18 days. P. vivax and p. ovale also have about 12-13 days, although outbreak of the disease may occur several months after initial infection due to the parasites residing in the liver in a dormant state, at this point being called hypnozoites (46, 48). The incubation time can in rare cases be
longer, but symptoms of infection with *P. falciparum* is most often within six months after exposure.

These species are able to infect both blood and tissue. They require mosquitoes to enter the stage of reproduction (46). Several morphological features characterise the species of plasmodium. Morphology studies are therefore essential in order to differentiate the species clinically which is a prerequisite to apply the correct treatment strategy. Morphology characterisation includes evaluation of the shape and size of trophozoites, schizonts and gametocytes, and also the number of merozoites. *P. ovale* and *P. vivax* invades immature, young red blood cells, In contrast, *P. falciparum* is not selective when it comes to what red blood cells to invade (46). All malaria species transferable to human may cause death, although *P. falciparum* has by far the highest probability of causing mortality if left untreated (6).

4.2 Pathogenesis and pathophysiology

4.2.1 Life cycle of malaria

When biting, the mosquito injects sporozoites into the human, which infects the parenchymal liver cells (figure 2). Asexual reproduction in the liver cells is called the exoerythrocytic cycle. The cycle length varies between the different malaria species. *P. vivax* or *P. ovale* can enter a dormant state as hypnozoites (46). *P. falciparum* does this to a less degree, as this subgroup more quickly goes over into the blood stream. *P. malariae* does not go dormant and thus cannot cause a relapse infection. Schizonts are formed, which rupture and release daughter parasites (merozoites) into the blood stream. Entering the red blood cells, they are at an early stage, before forming merozoites. The ring stage (trophozoites) is formed within the red blood cells, where they either mature and turn into schizonts that eventually rupture, again releasing merozoites to the blood stream, along with toxic cellular debris and haemoglobin (46). The trophozoites may also develop to gametocytes.

The parasitemia (parasites in the blood stream) of a malign course of a *P. falciparum* infection is quick to increase, increasing approximately 30 times every two days. The antigen production of a developed parasite will lead to knobs on the red blood cell, causing it to attach to the walls of blood vessels. This will clog smaller veins, giving anaerobic glycolysis, and in the next round possibly causing lactic acidosis. Mosquitoes sucking blood from an infected human will ingest the gametocytes and thus carry the infection onward, as the formation cycle in the mosquito leads to the release of sporozoites into the mosquito’s spit. As malaria is dependent on functioning red blood cells, certain red blood diseases in the host can protect against malaria. Among these are red sickle cell anaemia where a recent study shows that the trait’s resistance is caused by oxygen-dependent growth inhibition (49). The body responds to the malaria infection, creating an antibody response resulting in immunity if the subject is chronically exposed to the protozoa.
4.3 Diagnosis

4.3.1 Clinical manifestations

One of the main symptoms of malaria is an intermittent fever with or without chill, the length of the fever period varying between the subgroups of Plasmodium. *P. vivax* and *P. ovale* typically last for two days and *P. malariae* for three days. *P. falciparum* has no specific pattern. Typical symptoms following the fever are headache, myalgia, arthralgia, malaise, abdominal pain and diarrhoea, in short; flue-like symptoms. In addition, general symptoms in children are anorexia and irritability, although fever is not necessarily present. All subgroups of malaria will cause the same pattern of symptoms, however the symptoms of *P. falciparum* may worsen faster than the others. Complications can be severe, especially in *P. falciparum* with serious parasitemia. Complications may also occur for *P. knowlesi* and *P. vivax*. Among the typical complications are cerebral malaria that may cause seizures and coma. This is due to microvascular obstruction that takes place due to the parasite’s pathophysiology. In children, 10% have neurological sequelae. In addition to cerebral malaria, cramp can also be caused by hypoglycaemia and fever. Other complications are shock, disseminated intravascular coagulation, anaemia, hypoglycaemia, acidosis and haemolysis, liver dysfunction, renal insufficiency and non-cardiogenic lung oedema (50). The clinical pattern also presents itself as
low amounts of blood cells and blood platelets: leukocytopenia, thrombocytopenia and later haemolytic anaemia. The C-reactive protein (CRP), an inflammation marker, can often be found in the range 40-100mg/L. Plasma alanine transaminase (ALT) and creatinine are usually also increase (51).

4.3.2 Diagnostic tests

The diagnosis is built on the recognition of a clinical pattern and the detection of parasites in the bloodstream. The latter is done if a malaria infection is clinically presumptuous. Tests should be quick and exact, to make quick intervention possible. Positive traits would include the possibility to survey and screen for the disease. Malaria should always be suspected if a fever exceeds 37.5°C and there is a history of exposure. Concerning children in high risk areas, who are especially susceptible for obtaining the infection, malaria should also be suspected if the haemoglobin level drops below 8 g/dL or if palmar pallor is present.

The most common ways of detecting malaria are briefly described below.

**Light microscopy:** Light microscopy of giemsa stained blood smear is the first choice (52). The test can be used both for identification and for quantification. In addition, other tropical diseases may also be detected, e.g. filariasis and trypanosomiases. The downsides are the time consumption, access to necessary equipment and variability and deviations between therapists when it comes to both preparation and interpretation which to a large degree may depend on experience. Another downside related to the use of light microscopy is that low parasitemia, <5 to 10 parasites/mL, may not be detected. (53) Thick and thin blood smear both provide unique information. Both use capillary blood or anticoagulated venous blood. Thin smears allow the observation of the morphology of the red blood cells, including parasites within the cells. This enables the possibility to identify different species of plasmodium along with staging of the disease. Using morphology alone, benign and malign malaria can be differentiated and diagnosed. Thick smears cause lysis of the red blood cells, so malaria can be detected independently based on structures of the red blood cells. Regarding the execution of the tests, 1000x enlargement and oil immersion technique should be used to provide optimum conditions.

**Rapid diagnosis tests (RDTs):** Quick methods of malaria diagnosing are detecting the antigens histidine-rich protein 2, plasmodium lactate dehydrogenase (LD) and aldolase. Host-produced antibodies may also be detected (54). Antigen testing can distinguish *p. vivax* and *p. falciparum* cases. These rapid diagnostic tests are less prone to variation among the personnel performing the tests hence can easily be carried out as they require little training of personnel. A considerable downside with RDTs is the lack of ability to quantify the parasitemia. Another challenge is false negative results, leading to an inexpedient retention of treatment. Standard and recommended procedure in many endemic areas, especially Africa, is to treat presumed malaria-caused fever outbreaks with antimalarial medication (55-57).

4.4 Prevention

4.4.1 Vector control and surveillance

Malaria is a disease that is both curable and preventable. WHO visions a malaria-free world with a reduction of mortality rates and case incidence by at least 90% compared with 2015 by 2030 (5). WHO’s global technical strategy describes clear goals and puts up requirements to enable the goals to be met within the time set (7).
A key factor is vector surveillance and control. Surveying entomology and researching factors concerning the anopheles mosquito is crucial, including surveying the development of insecticide resistance.

Mechanical protection with clothing, blankets and nets is effective prophylaxis, especially if impregnated like permethrin-treated bed nets. Along with indoor spraying, this are most important prophylactic interventions in endemic areas, although a study shows less effect of insecticide-treated bed nets in Asia than in Africa (58). Expanding the use of this intervention in high risk areas would be a major step towards WHO’s goals. Any prophylaxis in regard to reducing the transmission of the parasite to the mosquito will also give protection against other diseases borne by the vector, including dengue fever, zika fever, chikungunya fever and Japanese encephalitis.

4.4.2 Vaccination

There has been a considerable international cooperation between research environments over the last years. Genetic variation amongst malaria parasites might demand different vaccines.

An 18 month follow up study of a vaccine candidate, mosquirix, showed a reduction of approximately a quarter of malaria cases in the study population, thus preventing a substantial number of cases (59).

WHO launched a vaccination pilot project in 2018. Mosquirix is the world’s first malaria vaccine and secures humoral and cellular immunity in the vaccinated (60). The project takes place in Ghana, Kenya and Malawi. The vaccine offers protection in small children, and is considered a part of the treatment, not a replacement of provisional measures. If the vaccine proves to have an effect, it may become a part of the core package that WHO recommends, which involves prevention, diagnostics and treatment (6). The vaccination will first of all naturally be aimed at people in high-endemic countries and is, until further, limited to infants in Sub-Saharan.

4.4.3 Drug prophylaxis

Chemoprophylaxis protects the non-immune and is important in vulnerable groups of people. As pointed out earlier, being exposed on a regular basis builds up malaria immunity in the host. This partial immunity will however gradually disappear if there is no longer exposure to the parasite.

For people being occasionally exposed, there are several prophylactic drugs to choose from. No drug prophylaxis gives a 100% resistance and they may have different side effects. Inadequate drug prophylaxis may prolong the parasite’s incubation time, causing a disease outbreak when the drug use ceases. Recommendations for the most suitable drug treatment may depend for example on the duration of the exposure (typically, a trip/stay duration) and the specific country, region or even the local place travelling to (10). The latter is due to possible drug resistance which may vary over short geographical distances.

For travellers visiting Myanmar, conservative prophylaxis like mosquito nets, spray and skin covering clothing is recommended in all regions of the country, including bigger cities like Yangon and Mandalay. Outside these cities, drug prophylaxis is also recommended. These recommendations take drug resistance into account. For example, due to mefloquine resistance, atovaquone/proguanil, or doxycycline, is recommended in parts of the Shan State or in Kayin close to the border to Thailand and China, while in the rest of the country, mefloquine remains an option (10).
4.5 Treatment

4.5.1 Artemisinin-based combination therapy

Malaria treatment requires a double focus: firstly, to combat the parasite itself, secondly, to provide symptomatic treatment in order to avoid morbid complications (61). Uncomplicated infections are distinguished from severe malaria. The former includes all cases where malaria is detected but with the most serious symptoms excluded.

Artemisinin-based combination therapy (ACT) is a pillar in the treatment of both benign and malign malaria. Such treatment is strongly recommended in the WHO 2015 report and is building on high quality evidence (62). ACT is a combination of a fast-acting artemisinin derivate and a partner drug that stays in the body for a longer time. Artemisinin and its semi-synthetic derivates artesunate, artemether and arteether are a fundamental part of the treatment of uncomplicated malaria (63). Artemisinin’s mechanism of action is to a certain extent unknown. In a chemical proteomics analysis study from 2016 exploring this subject (64), artemisinin was found to covalent bind to essential proteins causing the parasite’s death. Haem, produced by the parasite in early ring stage and from haemoglobin digestion, is responsible for activation of artemisinin. Attacking the parasites in both sexual and asexual stages of the life cycle (65), artemisinin has proven itself to be an effective drug (66), with a faster killing rate than other available drugs. Leaving a small number of parasites, it also reduces the chance of the parasites developing resistance to artemisinin’s partner drug (46). However, due to the short active killing time of artemisinin, multitherapy is required in order to avoid microbial resistance. Combined with a longer acting partner drug, the ACTs are first line option worldwide.

The recommended treatment duration of the uncomplicated *p. falciparum* is three days (67). Treatment of symptoms and complications are not discussed in detail in this report but are considered important in the clinical setting.

Treating severe malaria requires optimal supportive care and monitoring, which itself often is a challenge in endemic areas with a substandard provision of health care services. Intravenous or intramuscular artesunate followed by per oral ACT is recommended (62). This can reduce a mortality from around 100% to 1-20%.

Recurrent infection can result from both a reinfection and failure of treatment. Separating these requires polymerase chain reaction (PCR) genotyping. Failure in therapy is due to either reduced medicine quality, suboptimal exposure to the drug or drug resistance. Drug change is then recommended. ACT is also the treatment of choice in non-immune travellers, and also plays a central role in treating *p. vivax*, *p. ovale*, *p. malariae* and *p. knowlesi*, along with mixed infections. Chloroquine, an option to ACTs, can also be used for the benign subgroups, although local existing resistance to the drug must be considered (66).

4.6 Prognosis

4.6.1 Morbidity and mortality

The BMJ Best Practice states that diagnosis delay increases both morbidity and mortality. If untreated, the transition between asymptomatic and death can be as little as 36 to 48 hours (68). Malaria is also responsible for a considerate health risk in travellers, with mortality ranges from 0.4% to 10 % if left untreated (69). Children under the age of five, pregnant women, tourists, old people and people affected in areas where malaria is less common are considered to be at
an elevated risk of a fatal outcome (70). A UK cohort study concludes mortality of cerebral malaria ranges from 10% to 20% in non-endemic, high-developed countries (71). There are reasons to believe that this mortality is higher in endemic, non-industrialized countries with a less developed health care system.

A study of severely *p. falciparum* infected Papua New Guinean children concluded that protective genetic factors, along with good nutrition and/or infrequent coincident sepsis may result in a lower mortality (72). The study indicated the same results for *p. vivax*. Coinfections of *p. falciparum* and *p. vivax* were associated with the worst prognosis.

4.7 Drug resistance in malaria

4.7.1 Geographical developing of drug resistance

Several factors impact on the emerging drug resistance, including environmental and climatic, political, movement of populations and war. These may all lead to increasing spread of the parasite, possibly causing epidemics. Development of effective drugs must battle time and the rapid changes of drug resistant malaria.

Artemisinin resistance is spreading (73, 74). It is prevalent in Cambodia, Lao People’s Democratic Republic, Thailand, Vietnam and Myanmar. The Greater Mekong Subregion faces a challenge as artemisinin drug resistance sprouts in several places in the area. Resistance to artemisinin also results in a higher selective pressure on the partner drug, further on leading to resistance also in this drug. Artemisinin drug resistance is related to a mutation in the Kelch gene on chromosome 13 of *p. falciparum* (k13), leading to a longer ring stage and an increased stress response at this time that in turn increases the parasite’s survivability (75-77). A study from 2014 (78) discusses the spreading threat of the artemisinin resistant *p. falciparum* in Southeast Asian mainland. In 2014, prolonged courses of ACT were still effective in regions where three days of treatment failed. In addition to the artemisinin resistance in falciparum, there is a known spread of chloroquine resistance in *p. malariae* and *p. vivax*. As per 2015, Southeast Asia remains a low risk area for chloroquine resistant *p. vivax* (62).

4.7.2. Artemisinin-based monotherapy

A key in avoiding developing drug resistant is stopping the use of artemisinin-based monotherapy (AMT). In 2017, oral AMT was still considered to be of high availability and distribution, as non-oral and oral AMT included nearly 20% of the national market volume for the different classes of antimalarial drugs (79). WHO Global Malaria Programme’s urge on out phasing of the cheaper AMT (80) showed results in 2006 as several manufacturers agreed to the out phasing of the single oral drug (81).

Causing a threat both locally and globally, Myanmar’s extensive use of AMT in the eastern part of the country raised alarm. As a result of this, measures were taken in order to squeeze monotherapy out of the market and launch economically competitive ACT. The Artemisinin Monotherapy Therapy Replacement project took place between 2012 and 2014 in order to remove the monotherapy from the private sector (82, 83). The project was considered successful. Myanmar had in 2013 previously not registered artemisinin resistance. A study at this point showed prolonged treatment time using artesunate in the southern part of Myanmar, and a resistance was believed to be either emerging or spreading from western Cambodia (84). From 2015, studies showed emerging resistance of artemisinin along the China-Myanmar border and in the Northern Kayin State related to mutations in the k13 gene. Divergent mutations point towards an independent evolution of resistance. Migrating populations may contribute to high allele variation across short distances (85).
4.7.3 Mass drug administration

Mass antimalarial drug administration has occurred several times over the last decades. It involves giving therapeutically doses of antimalarial treatment to a greater part of the population, for the purpose of reducing transmission, cure asymptomatic disease and stop reinfection in post treatment prophylaxis (86). A good short term effect has been reported (87, 88), though there is a lack of long term studies, especially in relation to drug resistance (89).

5 Malaria in Myanmar

5.1 Sociodemography and health indicators

Myanmar lies amidst Asia’s monsoon region hence hosts tropical climate. In the north, the average temperature is 21°C, while the southern coastline offers a higher temperature of an average of 32°C. The country’s economy is mostly made up of agriculture, mining, industries, oil, gas, plantations, forestry and fishing (19). Townships, wards and villages merge into districts, which further make up the administrative units of Myanmar: states, regions, union territories and self-administered zones and divisions. Roughly speaking, the regions are mainly inhabited by the Bamar, the dominant ethnic group, whilst the states holds the remaining ethnic minorities. In 2011, concluding a governing by a military junta since 1962, Myanmar started implementing several reforms leading the people on down the road towards a more democratic future.

In 2016, Myanmar’s population was estimated to approximately 53.9 million people (90), whereof 34% live urbanely. The majority of the population lives rurally. Although still lowest among countries included in Association of Southeast Asian Nations (ASEAN) (3), average life expectancy and healthy life expectancy has improved by 4.5 years since 2000 and currently are 66.6 years and 59.2 years, respectively. The reduction of infections has contributed to this increase (90). Still, tuberculosis and HIV prevalence are the second highest among ASEAN countries (3). The probability of premature death has since 2005 been stable for males and declining for women, however, neither of the projected linear trends meet global targets (91). The under-five mortality rate is declining, in 2016 being 72 deaths per 1 000 live births (92). Myanmar is not favourably compared to neighbouring Cambodia and Thailand, where the corresponding rates are 29 and 12, respectively (3). In 2016, non-communicable diseases accounted for 68% of the deaths in Myanmar. The two largest contributors to mortality in Myanmar this year were cardiovascular diseases, which accounted for 25% of the deaths, and communicable, maternal, perinatal and nutritional conditions, which together accounted for 24% of the deaths. Concerning life style risk factors, obesity is increasing. On the other hand, tobacco smoking has been steadily declining during the last decade (91).

Myanmar’s total health expenditure as share of gross domestic product was 2.35% in 2015 (90). Myanmar offers low financial protection. Out of pocket expenditure, the patient’s expenses, was in 2014 over 50% of the health expenditure. 52% of families receive family planning, while 59% receive antenatal care (18). Other areas are less covered, including cervical screening. Infectious diseases are to a greater extent covered. 43% of the people had in 2015 access to affordable medicines and vaccination. Health worker density was in 2016 ca. 16 per 10 000 population.
5.2 Malaria occurrence in Myanmar

Myanmar Medical Association estimates that out of Myanmar’s population of approximately 53.9 million people, roughly 43.9 million are at risk of acquiring malaria (19). This involves 291 townships of the total 330 townships that are spread out across the 15 states and regions. Reported cases in 2016 were, according to WHO, estimated to 142 600 [120 600- 165 000], with 110 146 cases confirmed. Death count was 21, estimated to 240 [≤100-400] (4).

Between 2005-2014, an impressive reduction in annual incident, mortality and hospital admissions took place (figure 3) (24), with a decline of 81%, 94% and 87% respectively. Cases treated have increased since 2012 by approximately 20% and in 2016 were more than 80% of cases treated. Hospital admissions and deaths caused by malaria has also decreased since 2006 and resided in 2016 close to zero deaths (4).

The incidence of malaria changes in relation to the time of year and usually peaks between July and October due to the monsoon season. In all ages, cases of malaria are more common in male than female. In the reported cases where the infected persons were over the age of 15, the number of male cases was more than double the number of females affected (19).

Concerning the prevalence of the different subgroups of malaria in Myanmar, *p. falciparum* accounts for 60% of the plasmodia in the country, the remaining accounted for by *p. vivax*. 
Yangon Region was in 2015 the only area that was considered malaria free and this area includes 16% of Myanmar’s population (19). Regions with a high transmission status include the boarders against Thailand, China, India and Bangladesh and, to a lesser extent, the border against Laos. In total, this comprises roughly 3.5 million people which corresponds to 7% of the country’s population. The Chin State had in 2015 both the highest reported incidence and mortality, possibly more related to socioeconomic and geographical factors than the spread of artemisinin resistance (24). Although incidence varies in the different regions, incidence has declined throughout the country (figure 4). Myanmar uses active case detection of febrile cases at community level to monitor surveillance of the disease, which means systematically screening febrile patients.
5.3 Vector control

An. minimus and an. dirus are the most common anopheles transferring malaria in Myanmar. These are both susceptible to dichlorodiphenyltrichloroethane (DDT) and pyrethroids (19). Hence, the susceptibility of these mosquito types to the different insecticides is, according to Myanmar Medical Association, reassuring, although insecticide resistance has been reported along the Thailand-Myanmar boarder (96).

An. dirus is also susceptible for organophosphate (malathion), though there is a lack of data for an. minimus concerning this insecticide. Insecticide treated bed nets (ITN) were in 2001 available to all age groups, and was by 2003 free of charge (4). The coverage of ITNs in high risk population was reportedly increased to 100% by 2016, although a survey shows less than 20% use of ITNs. Indoor residual spraying (IRS) in high risk population was in 2016 almost non-existent.

5.4 Diagnosis and treatment

The Department of Public Health launched “Guidelines for Malaria Diagnosis and Treatment in Myanmar” in 2016 (19). Similar to the WHO guidelines (62), this gives information to health workers concerning both uncomplicated and severe malaria, including outbreaks and special risk groups.

Diagnosing malaria has been free of charge for decades in Myanmar (4). Uncomplicated malaria must be diagnosed at a peripheral level and involve rapid diagnostic blood testing performed by community health workers and village health volunteers (97). Concerning RDT, it has been in use since 2002 for *p. falciparum*, later extended to include *p. vivax*, as microscopy has reduced availability in rural areas and the patient might be too sick to await microscopy results.

Severe malaria requires a different course of action and higher-level facilities to better support patients. Cases of severe malaria in the periphery will if possible be referred to hospitals, as will patients where initiated treatment has failed. Intermediate levels of health organizations will be expected to be of a higher level concerning both staff and equipment, and to offer microscoping and classification of malaria subgroups. Hospitals in Myanmar provide a higher level of readiness concerning both diagnosing and treating malaria.

According to the Department of Public Health’s guidelines (19), first line treatment of uncomplicated *p. falciparum* malaria is artemether and lumefantrine. Other options include a combination of artesunate plus mefloquine and dihydroartemisinin plus piperaquine, all being ACT combinations. Guidelines on treatment exist also for special risk groups such as infants, young children and pregnant women, and for cases where a mixed infection is suspected. Since 2011, ACTs distributed in relation to reported *p. falciparum* cases has continuously been 100% (4). In 2003, ACT also became free of charge (4).

5.5 National health plans in Myanmar

Along with a low quality of the health service offer itself, years of neglecting the health sector has caused both underdeveloped infrastructures, a demand of human resources that is not yet met and high out of pocket expenses for patients. Prioritizing specialized care in urban areas has been at the expense of primary health care offer in rural areas, affecting a large number of Myanmar’s population (3). Over the years, big differences have developed between socioeconomical, geographical and ethnic groups.
In 2009, Myanmar spent 0.2% of the gross domestic product on health, lowest in the world. This has markedly been increased since, affecting the prevalence of the communicable diseases malaria, HIV/AIDS and tuberculosis (3). In an attempt to increase the nation’s health in general, Myanmar’s is now trying to reverse the ignoring of the population’s health and move towards a more just distribution that will include primary health care in townships. This is also expected to improve the country’s economy (3).

Myanmar is working to achieve universal health coverage (UHC) and to provide a basic essential package of health services to everyone by 2020 (3). The contents of this package will grow over time and lead to less out of pocket expenses. The package of health services will focus on main communicable diseases, some non-communicable and nutrition. WHO’s recommendation for human resources per 1,000 persons is 2.3 while Myanmar’s human resources were 1.33 health workers per 1,000 persons in November 2016. Not only is the number low but the health services are concentrated in urban areas like Yangon and Mandalay. Concerning infrastructure, both health facilities themselves and the transportation between them are causing problems in providing a sufficient health offer.

Myanmar reached the millennium developmental goals related to malaria in 2014, target year being 2015. The country has also recently achieved several other key goals on the road to a country free of malaria. First of all, a national epidemiological situation analysis was carried out by 2015, followed by an external program review and micro stratification the following year. Plans were made in 2016; National Malaria Strategic Plan 2016-2020 (98) and National Malaria Elimination Plan 2016-2030 (99), along with documents related to vector control and surveillance and case management. In 2017-2020, the malaria global fund concept note involves 124 US dollars. The funding of the malaria treatment in Myanmar has been increasing every year since 2009, except for a drop in 2015 (figure 5) (4). Global funding is the major part, United States Agency for International Development/President’s Malaria Initiative (USAID/PMI) also contributed. In total, the available amount of money consisted of almost 65 million US dollars (4).

As part of the national malaria elimination plan, Myanmar visions to be malaria free by 2030. Myanmar’s National Strategic Plan 2016-2020 (99) has several objectives: reducing the reported incidences of malaria to less than 1 case per 1000 population in all states/regions, interrupting transmission of falciparum malaria in several states/regions, further on preventing re-establishment and preventing further spread and development of *p. falciparum* that is resistant to ACT. Key factors involve case detection, management and surveillance. Upcoming
challenges are several in addition to preventing artemisinin resistant malaria: maintaining provision of insecticides, nets and other mosquito prophylactic measures in moving populations and control malaria in areas where the disease is not yet under control by the government. Private sectors are planned to be engaged, and a good cooperation between implementing partners is vital.

6 Malaria in Norway

6.1 Sociodemography and health indicators

Norway, with a population of about 5.2 million people, is governed democratically and parliamentary and has a comprehensive welfare system, an offer largely made possible by the country’s petroleum industry. The country’s income relies on several other contributing industries like minerals, sea food, water power, timber and fresh water. Norway had in 2017 the world’s third highest contribution per inhabitant to the gross domestic product. The settlement pattern is quite unlike Myanmar, eight out of ten of the country’s inhabitants are located in densely populated areas, the number steadily increasing (101). The health sector is financed by the government. Compared to Myanmar’s 2.35%, Norway has a total expenditure on health of 9.7% of the gross domestic product (2014) (102). Life expectancy in Norway is 80.9 years for males, 84.3 years for females. Like most other western countries, cancer and cardiovascular disease claim the most deaths. Cancer is increasing, the number of deaths related to cardiovascular disease is on the decline (101).

6.2 Malaria occurrence in Norway

P. falciparum infections and malaria induced mortality are rare in Norway. Malaria has been reported and monitored in Norway since 1975. The incidences have been declining relatively steadily from 1997 until 2005 and stabilized on 30-40 cases between 2007 and 2012 (figure 6) (10). An increased incidence was observed in the time period 2013-15. This was mainly ascribed to a heavy increase of new immigrants from Eritrea, in addition to a more active collection of cases from Norway’s health system. In 2017, a total number of 61 cases were confirmed, p. falciparum accountable for 40 (10). The number of cases has been declining since 2014. In 49 of the cases, the infection of plasmodium took place in Africa. Severe disease and death due to malaria is extremely rare in Norway.

The people who return with malaria are only in few cases tourists. Of the 61 cases of infection in 2017, only 7 were due to tourism (10). Immigrants visiting their malaria endemic home country accounted for the most cases, along with migrating people already infected. One of the factors contributing to infection in immigrants revisiting endemic countries is loss of immunity against the parasite, as immunity requires continuous exposure to the parasite. Thus, staying in a non-endemic country for a longer period of time will cause immunity to decrease and disappear. Despite rising temperatures, malaria is unlikely to establish in Norway (103).
6.4 Diagnosis and treatment
NIPH regularly updates malaria guidelines (10). The guidelines focus on prophylactic measures, advising both conservative and drug prophylaxis. No drugs give 100% protection. In 2014, several drugs were available: atovaquone-proguanil, mefloquine, doxycycline hydroxychloroquine sulphate and proguanil. Malaria should be suspected when the patient has a fever and a history of travelling to a malaria endemic area. In Norway, blood smears are used for diagnosis, as no symptoms can give the diagnosis alone. RDT of parasite antigens may be used as supplement. The drug of choice for treatment of benign malaria in Norway is chloroquine/hydroxychloroquine. Primaquine is added if the plasmodium is *p. ovale* or *p. vivax*. For potentially malign malaria, the drug of choice is dihydroartemisinin-piperaquine or artemether-lumefantrine, proguanil-atovaquone or mefloquine (105).

7 Discussion: Trends in occurrence in Myanmar and Norway
A steady decrease in number of malaria cases: Reliable sources conclude that the number of malaria cases, both caused by *p. vivax* and *p. falciparum*, in Myanmar has markedly and steadily been declining for over a decade (4, 19, 24), reaching towards the country’s goal of elimination of malaria. Mortality and hospitalization of malaria infected patients has also been markedly declining (24). The main reasons are the country’s own strategy together with neighbouring countries and local contributors, in addition to increased awareness around the malaria’s burden of disease. Continuing the reduction of malaria incidence and prevalence relies on political, economic and scientific effort.

Vector control: Malaria incidence relates to vector prevalence, ecology and biology, its opportunity of transmitting the disease to humans and the host’s immune defence. Climate changes and deforestation both affect the mosquito biology and survivability. Studies of deforestation’s effect on malaria vectors claim opposite results and demand further studying on
the malaria vector’s biology along with other environmental factors and human population exposed of risk (106).

A study specific to the China-Myanmar border region shows increased survivability in deforested areas for anophales minimus, higher temperature and lower elevation contributing to survivability (42), while life-table studies conclude deforestation a contributor to development of anopholes min. larvae (107). The increased temperature as a result of climate changes is expected to increase the population at risk (44) by facilitating vector survivorship and the spread of malaria. Other events following climate change, such as flooding, problematizes malaria control the prevention of an increase of incidence.

Measures taken towards the population at risk are vital in order to control malaria. Migrating people impacts on the incidence of malaria. Different regions’ seasonal patterns of malaria incidence may vary, and in some places, peaks may occur more than once yearly (59, 108). Although the majority of the population lives in rural areas, Myanmar experiences a continuous urbanization (109). This change in population demographics is expected to influence malaria incidence as it affects the population at risk of acquiring malaria, as urbanization causes more people to move into areas of the country where malaria is less endemic, in this way decreasing malaria incidence.

**International collaboration in surveillance:** Cross-border cooperation between nations and international non-governmental organizations has an impact on malaria control (37, 38), and concerted action with NGOs, UN agency and local governing is of major importance. As the regional action plan for Southeast Asian countries visions a malaria free area by 2030 (35), the focus on both reducing incidence and prevalence will strengthen. Actions towards reducing prevalence in Myanmar’s surrounding countries leads to a decreased number of imported malaria. Malaria prevalence in Myanmar’s boarder regions is higher than the remaining country (19). China launched a National Malaria Elimination Programme in 2010 (108), and as imported malaria from Myanmar was considered a problem, the boarder was targeted (110). The China-Myanmar boarder had a marked decrease in prevalence and cases of hospitalization in the period 2007-2013 (37, 110), in addition to resulting in an upscaling of the general health system and a more equal distribution of health services. Continuous surveillance and upscaling of the health care system along the border is still necessary (108). Despite socio-political cooperative challenges, emphasizing the importance of and continuing cross-border control of malaria is crucial. This includes efficient diagnostic methods and treatments, upscaling of conservative prophylaxis and mass drug administration (111).

**Health programs:** Studies on malaria preventative habits of the population show the importance of effective health education programs. They are vital in order to increase compliance of the use of prophylaxis such as ITNs, mosquito repellent and blankets (112). Local practice has used to be ill-informed and greatly influenced by traditional and cultural beliefs (113). The supplement of ITNs (4) has contributed to the decrease of incidences (24). However, studies report the use of ITN has less effect in Asia than in Africa (58) and thus early diagnosing and treatment is considered more cost effective. Supplying Myanmar’s rural population with ITNs is a challenge itself, and mass free distribution is a key factor (114) in order to supply people facing financial difficulties. Durability monitoring of the nets is essential in order to maintain this conservative prophylaxis. Although Myanmar Medical Association concludes both an. minimus and an. dirus still being susceptible to the most common insecticides (19), there is evidence of pyrethroid resistance along the Thailand-Myanmar boarder threatening vector control (96). Otherwise, as a measure in order to reduce the population’s susceptibility, a vaccine is yet not available.
National upscaling of health services: Rural Myanmar lacks necessary infrastructure and health facilities in order to provide sufficient health care, both concerning communicable and non-communicable diseases (3). An upscaling of the health offer to townships and villages now takes place as Myanmar’s political regime changes. Along with provision of ITNs to populations at risk and ACT, training and deployment of 40,000 community health workers has contributed to the marked decline in malaria (24). UHC is on the way and a health package is planned implemented by 2020 (3). As the package expands to involve more areas in health and nutrition, the burden of disease is expected to drop as the population is resistant to mortality caused by malaria.

RDTs that improve workflow and are sensitive in both asymptomatic and symptomatic cases are important in order to intervene with appropriate therapeutic response to a malaria infection (115). As Myanmar’s health facilities lack sufficient laboratory equipment, RDT is very useful as they require little equipment and are portable. RDT for both *P. vivax* and *P. falciparum* has been available in rural areas since 2011, although national recommended use is only when microscopy is not available or when the patient condition is severe and quick action is required (19). They are also easy to use and require little training, are cost effective, and provide quick results. New RDTs are currently on trial and are tried out in endemic areas (116). Diagnostic gaps are envisioned to be filled using innovative technological strategies, such as a new generation of RDTs (117).

Providing ACT according to national guidelines and recommendations from WHO will reduce prevalence of malaria. Regulatory authorities must inhibit false and substandard treatment by attend to the problem of monotherapy, which was banned in 2014, and falsified artesunate derivates (118). High failure rate of ACT with delayed clearance of parasites has been reported and calls for action in certain regions as artemisinin resistance develops (74). Preventative measures in addition to proper use of ACT may further down the line include mass drug administration in order to contain the resistant falciparum malaria (74, 88). Pilot studies in Myanmar have showed an effect of mass drug administration on the *P. falciparum* prevalence (87). As drug resistance threatens the decline of malaria incidence and drugs will be needed, several new agents are in clinical development. In addition, therapy including more than two drugs is under consideration for implementation (119).

Assessing the effect of actions: The possibility that incidence would decline even if no local or international efforts were made in order to reduce incidence of malaria in Myanmar needs to be considered. In that case, observations from countries with conflicts where less action is taken in order to reduce malaria incidence may be compared to Myanmar. This includes several African countries, among others Chad (120) which holds a large population of refugees that is difficult to reach with health services and malaria prophylaxis. Other countries where political instability and violence occurs are Congo and the Central-African Republic. When several countries in a region struggles in the fight against malaria, each individual country also misses out on the benefit of cross-border cooperation and decrease of imported cases from the surrounding countries. Chad, Congo and the Central-African Republic, left behind due to conflicts and war, all have an increase of case incidence from 2010 to 2017 (121), which supports the claim that the actions taken in Myanmar actually have the desired effects.

In non-endemic Norway the malaria incidence is low. The NIPH provides public information containing primary prophylactic advice, both drugs and insecticides, and the information is accessible for everyone. Health personnel informs tourists and travelers about the disease and risk of transmission in endemic areas. Drug prophylaxis is recommended, but none of the drugs offers a 100% guarantee of transmission prevention. In addition to drug prophylaxis, advice and guidance on conservative measures. Tourism accounts for a few amount of the total cases
of malaria, and the loss of immunity in previously exposed travelers contributes to the number of cases (10). It is for the Institute of Public Health to act towards this and provide information.

8 Conclusion

As a malaria endemic country, Myanmar has had a marked decrease in malaria incidence over the last decade. Norway, a non-endemic country, has had a decline since 2014. In the time period 2013-2015, incidence was higher after years of stable, low incidence.

The marked decrease in Myanmar’s malaria incidence is due to the effect of several actions taken on a national level in the wake of a shift in government more attentive to public health matters. Among others are

- the provision of rapid diagnostic tools in rural areas and evidence-based treatment in the form of artemisinin-based combination therapy
- the provision of insecticide treated bed nets and the deployment of health care workers in rural areas.

Further actions involve upscaling of the health care systems in rural parts of Myanmar, including facilities, infrastructure and staff. Continuous provision of insecticide treated bed nets will contribute to a further reduction of incidence, while adequate diagnosing methods and effective treatment in adequate facilities is expected to affect prevalence.

The decline in incidence so far is threatened as climate change and deforestation affect the ability to control the vector and antimalarial drug resistance threatens an effective treatment.

Myanmar has strengthened its efforts towards the rural border zones that are lagging behind in the combatting of the incidence rates compared to the more urban parts of the country.

Although challenges and uncertainties lie ahead, Myanmar, along with other Southeast Asian countries, envisions a malaria free future. In Norway, reducing incidence greatly depends on information and preventative measures provided to travelers, especially people who visit their home country. These are responsible for the highest amount of cases in Norway.
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