Malaria risk perceptions and barriers for effective prophylaxis among sub-Saharan African `visiting friends and relatives´ travellers in Hamburg, Germany

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1 Introduction

1.1 Travel medicine

Travel Medicine is a broad and dynamic term used to describe the finding, treatment, prevention and management of health problems and challenges of the international traveler. It encompasses a traveler's personal risk assessment, knowledge of and susceptibility to destination-specific risks, and general health security. The area of great importance is the provision of targeted advice on risk management measures and procedures aimed at good health promotion, safety and deterring adverse health outcomes and complications during travel [1]. This may involve safety pre travel precautions such as vaccinations, drugs, protective gear among others [2]. This is a vital field of medicine even proven to be more crucial with the recent COVID19 pandemic. With the frequency of travel from country to country, airport to airport, city to city and home to home, communicable diseases are easily widely spread. Knowing the great risk involved, travel medicine aims at solving the issues that arise in order to make travel safer for the average traveler. The major challenge in travel medicine is how versatile and traveler-specific it is [3]. Any advice given must factor in the location, existing culture and behaviors, concomitant diseases, current health status and medical history, immunization history and ever-changing patterns of diseases just to mention a few. Another challenge is that, it is not always recognized nor considered in pretravel plans [1, 2, 4, 5]. With advancing research, training and initiatives, more and more people are being sensitized to travel medicine and its importance [6].

1.2 Travel health education

Primarily, it falls on travelers to equip themselves with the necessary information needed to ensure good general health before, during and after travel. However, health institutions have a role to play to ensure the provision of adequate travel health information. Major barriers affecting seamless transfer of information include travellers' negligence and carelessness. Travel health education involves pre and post travel consultation where an individual is advised on the health risk, preventative measures and emergency protocols concerning upcoming trips.

The travel destination, patients' health history, risk perception, finances and cultural backgrounds are among the many other factors considered [5]. With every destination comes various factors which determine the form and approach to providing medical travel advice and its same with each risk group as well. With every traveler who receives adequate travel health education, the general health risks are mitigated [7] [8, 9] [6].

1.3 Malaria in the context of travel medicine

Malaria is one of the major global infectious diseases and it is caused by the parasite Plasmodium. As a parasitic disease, the life cycle of *Plasmodium sp.* is complex and involves development in the insect vector *Anopheles* and transmission to the human host by the bite of the female mosquito. Due to its significant impact on human health, malaria has been an important driver of genetic mutations in the human genome conferring comparative survival advantage. While significant progress has been made in the control of malaria globally since the turn of the millennium, progress has stalled since 2015. Malaria therefore remains one of the main challenges of human health in the tropical and subtropical regions of the Global South and an important travel associated infection in travellers to malaria endemic countries.

1.4 Epidemiology of malaria

Malaria is one of the notable causes of deaths in the world [10]. In 2022, close to 249 million cases of malaria were recorded in 85 malaria endemic countries with Nigeria, Congo, Uganda and Mozambique contributing to approximately half of these cases globally [11]. The data translates to a malaria case incidence of 58 per 1000 population at risk in 2022. Globally, the malaria mortality rate (i.e., deaths per 100 000 population at risk) reduced by a half from about 29 in 2000 to 15 in 2015. It then continually declined slowly to 14 in 2019. In 2020, an observed increase in the mortality rate to 15.2 was recorded, before decreasing slightly to 14.3 in 2022 [11]. In Africa, many initiatives have been introduced to help combat infection, spread and transmission. This includes measures in prevention, prophylaxis and most recently vaccination. Taking a look at the global north, also characterised as malaria non-endemic countries, these countries have recorded significant number of cases of malaria due to many factors, one of them being the migration of malaria from endemic to non-endemic countries through 'visiting friends and relatives'(VFR) travellers [12-14].

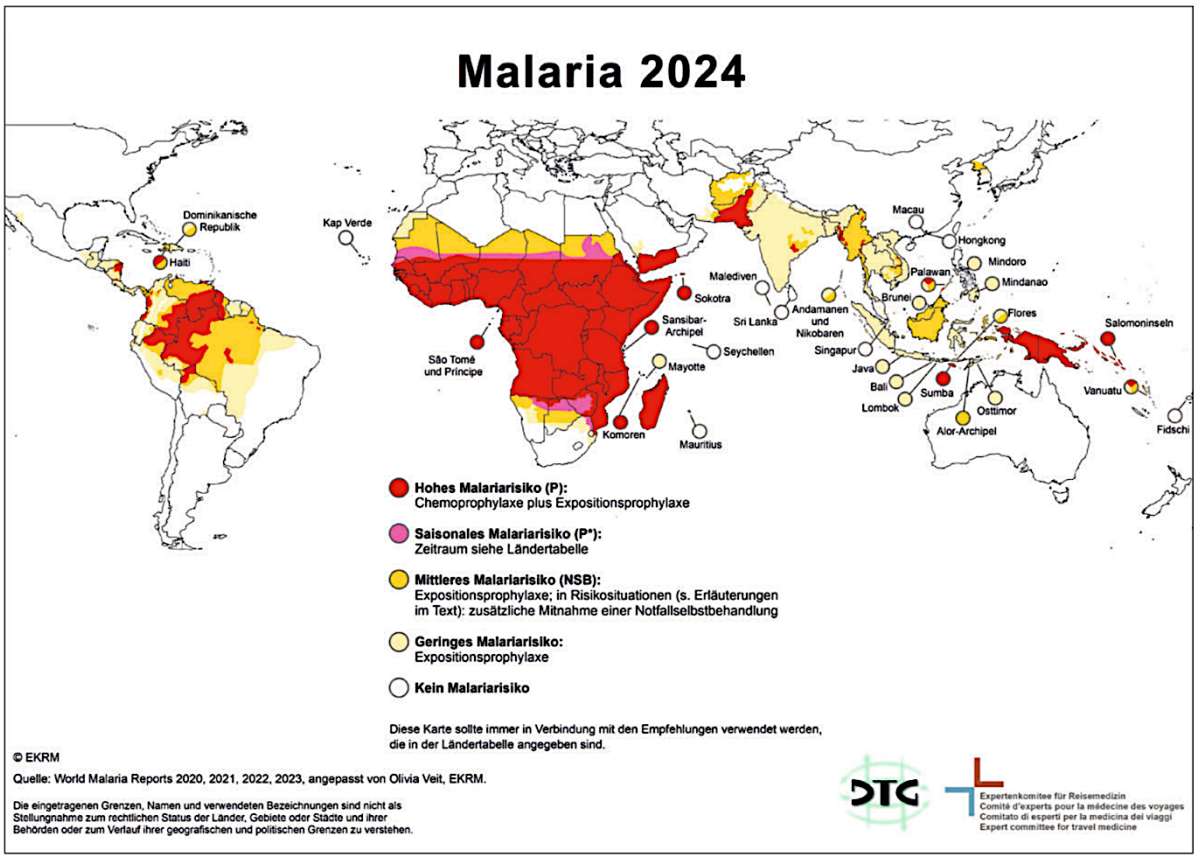

Figure 1: Epidemiology of malaria in the world

Source: World Malaria Reports 2020, 2021, 2022; adapted by Dr. Olivia Veit, ECTM and Ula Maniewski, ITM

Germany is among the top ten countries with a high flow of sub-Saharan Africans coming in every year. In recent years 2001-2016 (pre-pandemic), an average range of 526-1063 malaria cases per year were reported in Germany [15]. The majority of the malaria cases were acquired in sub-Saharan Africa (SSA) [16-18]. VFR travellers accounted for about 65% of these infections [18, 19]. Hamburg is home to one of the largest West African communities in Germany. In concordance with these national statistics, about 60-80% of patients hospitalized for acute malaria at the University Medical Center Hamburg-Eppendorf are of West African descent (own data). Recent studies in the USA, France, UK and Netherland among others seek to explain the cause of this phenomenon but very few establish a link between the German VFR travellers and imported malaria [20-23].

1.5 Parasitology and transmission

Malaria is a disease acquired by frequent exposure to Plasmodium carrying vectors known as mosquitoes. These vectors are commonly found in endemic countries. The five plasmodium species causing malaria in humans *are P vivax, P malariae, P ovale, P knowlesi and P falciparum* which is the most widespread parasite species in Sub Saharan Africa [10, 24]. The specific species known to carry these parasites is the female *Anopheles* mosquito.

A bite from the female anopheles mosquito carrying Plasmodium starts infection and progressing symptoms develop in about 10-15 days after [25]. During this bite, plasmodium sporozoites are injected into the skin. These sporozoites travel into the peripheral circulation and gradually migrate into the liver hepatocytes [25]. There, replication occurs and merozoites are formed. Merozoites enter red blood cells and develop through the different stages of ring, trophozoites and schizont then become new daughter merozoites which are later released and reinvade RBCs and destroy them [26, 27]. Gametocytes then develop in this blood stage which are needed for the transmission of malaria. The female *Anopheles* mosquito during blood feeding takes in these gametocytes which mate in its gut and after 10-18 days a sporozoite is formed and transferred through a bite to humans acting as a vector causing the cycle. This is the usual cycle of human infection, which starts again when another person is bitten by the same mosquito [25, 28-30].

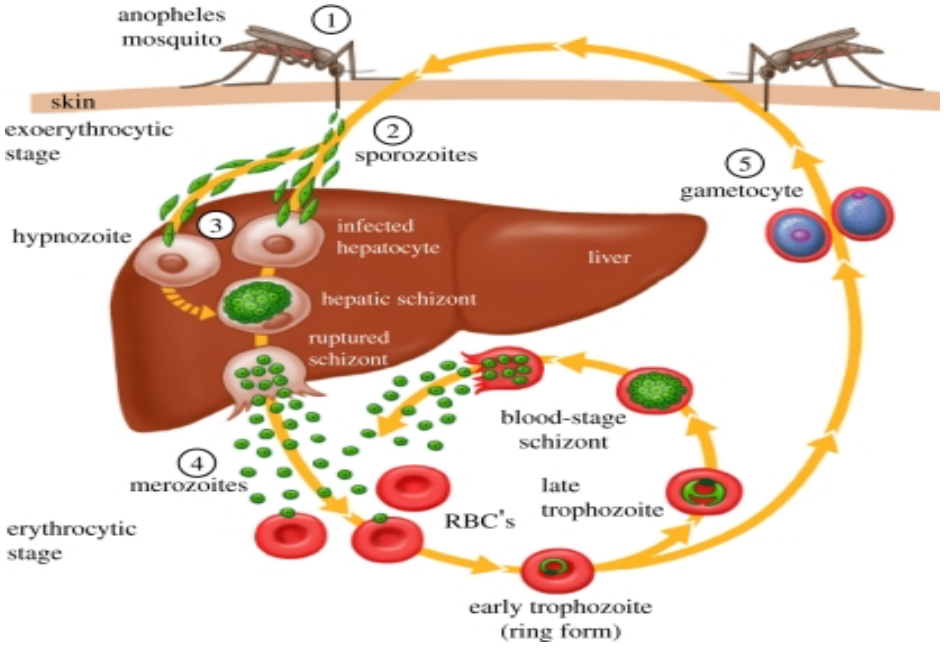

Figure 2: Transmission and infection of malaria parasites in human host

https://commons.wikimedia.org/wiki/File:Vaccines-against-malaria-rstb20110091-g1.jpg; Accessed 23.07.2024

1.6 Disease pathophysiology and clinical manifestation

Symptoms of malaria tend to appear in tandem with the rupture of infected erythrocytes and release of malaria toxins into the bloodstream. Usually after the first round of ruptured erythrocytes in the blood stage development, the symptoms are not yet manifest [31]. It is when the asexual cycle repeats every 24 to 48 hours that symptoms start to show.

This is because of a multiplication in parasitaemia which in turn results in an increased immune response [25, 30]. With an increased immune response and the release of inflammatory cytokines, clinical symptoms develop which include fever, headache, chills, sweating, anaemia, vomiting, muscle ache, abdominal discomfort among others [28, 32]. The higher the level of parasitaemia the more severe the clinical picture [32]. Uncomplicated malaria presents as a mild clinical picture and it is well treatable with oral antimalarial drugs and most patients are able to clear the infection if treated with good drug compliance. Chronic comorbidities paired with malaria infection may however lead to more severe symptoms. If uncomplicated malaria is not diagnosed quickly and treated adequately, progression of disease to severe malaria may occur. This is mostly the case in *P. falciparum* infection but may also regularly occur in *P. knowlesi* infection [26, 30, 33]. Less commonly the so-called "benign" forms of malaria caused by *P. vivax, P. ovale* and *P. malariae* may cause severe disease. Severe malaria is characterised by progressing organ failure that most commonly affects the kidneys, lungs, central nervous system but may also include severe anaemia or jaundice, bleeding and shock.

1.7 Diagnosis and treatment

Infection can result in death if it is not diagnosed and treated quickly. As any treatable disease, early diagnosis is imperative for management. Malaria infection is usually suspected when signs of fever or a history of fever is observed in a patient. Because signs and symptoms of malaria are non-specific, diagnosis are not based on clinical presentation but rather by using more specific and sensitive diagnostic tests. The value of every diagnostic test is its ability to differentiate infected from not infected individuals with high specificity and sensitivity. The standard for malaria diagnosis includes the direct detection of parasitaemia by light microscopy, immunochromatographic rapid diagnostic tests (RDTs), and increasingly by molecular tests such as PCR.

1.7.1 Polymerase chain reaction tests (PCR)

PCR tests detect parasite nucleic acids. It amplifies specific DNA segments by repeatedly and cyclically denaturalizing using heat, annealing with defined DNA primer pairs, and primer extension mediated by heat-resistant DNA polymerase isolated from a thermophilic bacterium. They are highly sensitive and effective in detecting mixed infection at low parasite densities otherwise undetectable by microscopy or RDTs. However, they are not recommended for routine diagnosis nor are they used in clinical management of malaria due to cost and accessibility issues [34]. Hence it is of most use for confirming malaria parasite species after the initial diagnosis has been established using microscopy or RDTs. Aside the above-mentioned tests there are indirect signs which may be used in addition to clinical and parasitological parameters that may trigger the suspicion of malaria. In some studies, thrombocytopenia is reported as a predictor for acute febrile illness in endemic area with 79.5% sensitivity and 86.3% specificity in malaria diagnosis [35].

1.7.2 Rapid diagnostic tests (RDTs)

In endemic areas where microscopy is not always readily available, RDTs are used on a large scale. These are immune-chromatographic tests which detect parasite-specific antigens through a finger prick blood sample [36]. These tests can in principle, detect either of the species namely *P. falciparum, P. vivax, P. malariae,* and *P. ovale*. However, sensitivity is best for *P. falciparum* species. A main advantage of this method is its ease of use and interpretation of results. Also, they are available in various formats such as cassettes, dipsticks and cards making it easy to be used where they are most needed. One goal of diagnosis with microscopy or RDTs, is to reduce overconsumption of antimalarial drugs in endemic countries by clearly identifying patients with malaria and treating them exclusively while avoiding offering antimalarial drugs to every patient with fever or other symptoms consistent with malaria. This allows the distinction between malarial and non-malarial fevers for appropriate and effective treatment.

1.7.3 Light microscopy

With light microscopy, thick/thin blood smears are examined under the microscope to reveal the presence of Plasmodium parasites in blood. It is a highly sensitive and specific test which also allows for the parasites to be quantified and the specific infecting species to be identified. Additionally, the developmental stages of the parasites can be evaluated. It requires well trained and competent microscopists to come out with accurate diagnosis which can be costly.

1.8 Treatment

1.8.1 Treatment of uncomplicated malaria

WHO defines a case of uncomplicated malaria as "a patient who presents with symptoms of malaria and a positive parasitological test (microscopy or RDT) but with no features of severe malaria". The objective here is to eliminate all parasites present in blood as quickly as possible, prevent severe disease progression, limit transmission of infection to others and prevent the formation of antimalarial drug resistance. Drug resistance is one of the most important challenges in the treatment of *P. falciparum* malaria. Artemisinin-based combination therapy (ACT) is today the standard of care for uncomplicated malaria cases. The treatment options are; artemether-lumefantrine (AL), artesunate-amodiaquine (AS+AQ), artesunate-mefloquine (ASMQ), dihydroartemisinin piperaquine (DHAP), artesunate + sulfadoxine-pyrimethamine (AS+SP) (contraindicated in first trimester of pregnancy) and artesunate-pyronaridine (ASPY) (2022) (contraindicated in first trimester of pregnancy) [37].

1.8.2 Treatment of severe malaria

Parenteral artesunate has been shown to be more effective and safer than quinine in the treatment of severe malaria, with a lower risk of mortality and fewer side effects. World Health Organization recommended it as the first-line treatment for severe malaria in all age groups [37]. Artesunate works by rapidly reducing the parasite load in the blood, leading to a quicker resolution of symptoms and a faster recovery. It is vital to note that parenteral treatment should be given immediately after the diagnosis of severe malaria is made, as delays in treatment can increase the risk of complications and death. In addition, a full course of oral ACT should be given after the initial parenteral treatment to ensure complete clearance of the parasites from the body. Note that, timely and appropriate treatment with parenteral artesunate is crucial in the management of severe malaria which is why it is recommended as the first-line treatment for all cases of severe malaria to improve outcomes and reduce the risk of mortality [38].

1.9 Methods to prevent malaria

Since malaria is a potentially life-threatening disease, preventing the infection is an important means to reduce malaria related morbidity and mortality. Due to its complex life cycle, malaria transmission can be prevented by multiple means including the prevention of infectious mosquito bites, the treatment against liver stages of Plasmodium or the suppression of the blood stage development after patient infection.

1.9.1 Vector Control

Mosquitoes are the vectors which transmit malaria parasites through bites when in contact with the skin. Vector control is the main stay against malaria infection. The use of pyrethyroid-only long-lasting-insecticides (LLIN) nets are recommended for use in endemic areas for both children and adults. In areas where there is pyrethroid resistance, pyrethyroid-PBO insecticide-treated-nets are used instead [34]. These nets are cost-effective and most importantly deter mosquitoes by relying on 3 main mechanisms; the construction of a physical barrier between human and mosquito vector, repulsion of mosquitoes by insecticides used to treat the nets and if the mosquito gets through the net, it usually rests on the nets after biting and may be killed upon contact with insecticide [39-41]. Insecticide-treated-nets are essential in the way that they offer personal protection, reduce transmission from mosquitoes to human by preventing bites and above all contributing to and fostering community protection by reducing the duration of the various stages in the life cycle of mosquitoes as well as disrupting the feeding cycle [39, 42-44]. Insecticide combinations also called mixtures may also be sprayed on breeding sites to kill mosquitos. These mixtures are recommended because they have different modes of action and guard against quick resistance formation [34]. Other methods such as use of insect-repellant creams (on exposed skin) and sprays (on clothing and indoor residual spraying), wearing long sleeved clothing when outdoors at night and sleeping in airconditioned rooms among others are also suggested and particularly useful for short term travellers.

1.9.2 Malaria chemoprophylaxis

Another recommended prevention strategy that is gaining momentum in the fight against malaria is preventive chemotherapies. This form of therapy is commonly prescribed for travellers consisting of malaria naïve (non-immune) individuals and sub-Saharan African VFR travellers (with partial immunity). They implore the use of antimalarial medicines to prevent malaria infection and disease. There are 3 classes of these drugs according to chemical structure and mode of action; aryl-amino-alcohol compounds (e.g., mefloquine), antifolate compounds (e.g., proguanil) and artemisinin compounds (e.g., artemether). Within these broad categories, some drugs are combined with artner substances. Atovaquone is combined with proguanil to enhance its antimalarial prevention potency. Besides atovaquone-proguanil, mefloquine is the second most widely used drug. Certain antibacterial drugs such as tetracycline and doxycycline are also used in chemoprophylaxis [45]. The use of these drugs varies from risk group to risk group and would be further explained in the coming paragraphs.

1.9.2.1 Atovaquone/Proguanil (Tradename Malarone®)

Atovaquone/proguanil is a widely used antimalarial drug in Europe with tradename Malarone®. It is a combination of two compounds atovaquone and proguanil hydrochloride. Atovaquone works by selective inhibition of the mitochondrial electron transport in parasites in this case plasmodium and proguanil inhibits dihydrofolate reductase in plasmodium and disrupts deoxthymidylate synthesis. With both inhibition pathways occurring, the biosynthesis of pyrimidines required for nucleic acid replication is hampered. For malaria chemoprophylaxis adults are prescribed 250mg of atovaquone/100mg of proguanil daily, taking orally every day, starting from 1-2 days before trip to malaria endemic country, every day during trip and continuing for up to 7 days after trip. It is recommended to take with fatty food or milk for maximum efficacy. Common side effects include abdominal pain, nausea, vomiting, headache, diarrhea, myalgia, gastritis among others. It is contraindicated in patients with hypersensitivity to atovaquone, proguanil or any other substance in the compound and also in patients with severe renal and hepatic impairment. Efficacy for malaria prevention is indicated above 95% [46].

1.9.2.2 Mefloquine (Tradename Lariam®)

It is used in prophylaxis against *P. falciparum* and *P. vivax*. This drug acts as a blood schizonticide which attacks developmental stages that invade red blood cells. The recommended dose is a weekly dose of 250mg (one tablet), starting two weeks ahead of arrival in an endemic country, once each week while in the endemic area and 4 week after return from endemic area [17]. Side effects include nausea, vomiting, diarrhea, abdominal pain, dizziness and vertigo and neuropsychiatric effects such as headache, somnolence, insomnia and abnormal dreams.

It is contraindicated in persons with hypersensitivity to mefloquine or other related compounds, people with history of convulsions, people suffering from depression, anxiety disorders, psychosis, schizophrenic disorders and any other major psychiatric disorder. It is very effective in preventing malaria outside of regions with mefloquine resistance such as South East Asia.

1.9.2.3 Doxycycline

It is a derivative of tetracycline and belongs to the same class of antibiotics. It is FDA approved for use as prophylaxis against *P. falciparum* in short term travellers in areas with chloroquine and/or pyrimethamine-sulfadoxine-resistant strains. It is a blood-schizonticidal-agent which acts by effectively killing malaria parasites at the asexual and erythrocytic stages. The recommended dosing regimen for adults is 100mg tablets/capsules per day for 1-2 days before entering an endemic area, each day during stay and continuing 28 days after leaving endemic area. Severe side effects include, gastrointestinal symptoms, pruritic skin reactions, photosensitivity, esophageal cancer and vaginal yeast infections. It is contraindicated in individuals with known hypersensitivity to tetracyclines and in pregnancy [47]. Despite being highly efficacious (92-98% for P falciparum and vivax) to drug-resistant malaria, adherence to the recommended regimen progressively decreases over time especially in the post travel period due to long duration as compared to shorter-regimen drugs like atovaquone-proguanil [17]. With its additional protection against anthrax, it is widely used in the military.

1.9.2.4 Tafenoquine

It is an 8-aminoquinoline used for malaria prophylaxis under the tradename Arakoda®, prescribed for up to 6 months of continuous use in 18 years and older individuals. It is indicated under 2 main conditions due to its unique mechanism of action: as primary prophylaxis while in an endemic region because it acts against all pre-erythrocytic(liver) and erythrocytic (blood) stages of Plasmodium species and as post exposure protection toward the end of stay and after stay in endemic county due to its ability to kill hypnozoites of *P. falciparum* and *P. vivax* which are undetectable by diagnostic tests and can latently reside in the liver for months to years and later differentiate resulting in clinical manifestations [17]. The recommended and approved dosage by CDC and FDA for malaria prophylaxis is a loading dose of 200 mg (2 × 100 mg tablet) once daily for 3 days before travel to a malaria-endemic area, followed by a maintenance dose of 200 mg once weekly while in the malaria area, followed by one 200 mg dose 7 days after the last maintenance dose post travel [17, 34].

The majority of the studies on tafenoquine as a malaria chemoprophylactic drug are fairly recent, hence data on adverse effects is probably not yet providing a full picture. However, headache, dizziness, back pain, diarrhoea, vomiting, increased alanine aminotransferase, motion sickness, insomnia, depression, abnormal dreams, and anxiety have been observed.

Contra-indications include glucose-6-phosphate dehydrogenase deficiency (G6PDH) or unknown G6DPH status due to risk susceptibility to haemolytic anaemia, breastfeeding by lactating mother with baby with G6PDH deficiency or status unknown. Therefore, whether tafenoquine should be added to the trio of drugs used in malaria prophylaxis might rely on the provision of "feasible, reliable, time-saving G6PDH deficiency test that can be implemented at travel clinics; if not the case, the alternative is only to initiate laboratory G6PDH testing in advance of the clinic visit." as suggested by Schlangenhauf et al. [48]. The safety and tolerability in pregnant or breast-feeding women, children, G6PDH-deficient and elderly, comorbid travellers with poly-medication, which form a significant fraction of travellers, should be further explored.

It is important to note that artemisinin-combination therapies are not recommended for use for chemotherapy.

TABLE 2

Medications for malaria prophylaxis or standby emergency treatment, modified from (23)

Dosage of antimalarial drugs for prophylaxis and treatment in adults		
Medication	**Prophylaxis**	**Standby emergency treatment (SBET)**
Atovaquone/proguanil[*1]	From 40 kg BW: 1 tablet daily (= 250/100 mg); between 1–2 days before and 7 days after stay in a malaria area	From 40 kg BW: 4 tablets (= 1000/400 mg) as a single daily dose on 3 consecutive days
Doxycycline[*2]	1 Tablet daily (= 100 mg); between 1–2 days before and 4 weeks after stay in a malaria area	Suitable only as part of combination therapy
Mefloquine[*3]	• Special precautions to be followed according to the product information; – Under 90 kg BW: 1 tablet per week (= 250 mg) – From 90 kg BW: 1½ tablets per week (= 375 mg) – From 120 kg BW: 2 tablets per week (= 500 mg) • Between 1–3 weeks before and 4 weeks after stay in a malaria area	No longer recommended: approval in Germany withdrawn in 2016
Artemether/lumefantrine[*4]	Not suitable	From 35 kg BW: initial 4-tablet dose (= 80/480 mg); followed by 4-tablet doses after 8, 24, 36, 48, and 60 h
Dihydroartemisinin–piperaquine[*5]	Not suitable	• Currently not approved for SBET[*5] • Therapeutic dose in uncomplicated malaria: 4 tablets (= 1 280/160 mg) daily on 3 consecutive days

Overview of the most important medications for malaria chemoprophylaxis and standby emergency treatment (SBET). Attention should be paid to the product information.
A dosing table according to body weight for children can be found in the *eTable*
[*1] To be taken with food (including dairy products) at the same time every day
[*2] To be taken with food and plenty of fluid, not together with dairy products; formally off-label use; the monohydrate formulation has better gastrointestinal tolerability
[*3] For first-time mefloquine prophylaxis, start 2–3 weeks before departure to malaria area and check tolerability
[*4] To be taken with food (including dairy products)
[*5] To be taken with fluid between meals. Need for ECG monitoring due to QTc prolongation. Piperaquine is a weak CYP3A4 inhibitor. No more than two treatments permitted within a 12-month period. Due to piperaquine's long elimination half-life, no second treatment should be performed within 2 months of the first treatment cycle. Not suitable for the treatment of complicated *Plasmodium falciparum* malaria.
BW, body weight; SBET, standby emergency treatment

Figure 3: Malaria chemoprophylaxis options and dosages

https://www.aerzteblatt.de/int/archive/article/219179/Medical-advice-for-travellers Accessed:09/07/2024

1.9.3 Standby emergency treatment of malaria (SBET)

SBET is an intervention introduced in circumstances where emergency malaria treatment is needed in a low to moderate risk area, where there is no medical attention available or accessible.

This is self-administered by the traveller or used under medical supervision after a malaria diagnosis is confirmed [49]. It is intended to be used in life saving situations when malaria is suspected. According to WHO, SBET is recommended in circumstances such as the following as summarized by Tan and colleagues;

"

a) travellers staying in remote locations unable to seek medical attention within 24 hours of the onset of fever,
b) travellers in some occupational groups making frequent short stops to countries or areas with malaria risk over a prolonged period of time and
c) short-term travellers spending ≥1 week in certain remote rural areas where there is a very low risk of infection." [50, 51]

There are disparities over the use of this drug due to the variation in the definition of low to moderate risk areas and difficulty in pin-pointing specific areas where this measure can be used. Others argued that SBET can serve as chemoprophylaxis when used in combination with mosquito bite control measures. Also, with the prevalence of counterfeit antimalarial drugs in high to low-risk areas, it is advisable for travellers to carry SBETs for effective antimalaria treatment [49]. The challenges observed in a systematic review by Tan and colleagues, show poor adherence to the stipulated recommendations in case of fever [52]. Although it is advised to use SBETs when medical attention is inaccessible, travellers used it regardless. Also noted was that most travellers didn't see a healthcare practitioner after use of SBETs. Furthermore, several travellers took a false dosage schedule of SBETs. To combat these challenges, the use of maximum recommended therapeutic dose (mRDT) to prevent over-dosage on SBETs and also proper training of travellers with clearly written and defined instructions on the indications and application of SBETs to avoid misinterpretation of results. All in all, the effective and correct use of SBETs relies strongly on travellers' behaviours, how well travel medicine and health advisers explain its use in the time given for it [50, 51].

1.10 Malaria prevention for travellers

Travellers to malaria endemic countries can be classified based on reason for stay, length of stay, financial standing and risk susceptibility to diseases. Under these classifications we have tourists, business travellers, leisure travellers, long term travellers, short stay travellers, low-income travellers, high income travellers, disease naïve travellers, semi-immunity travellers and visiting friends and family travellers.

When it comes to malaria prevention in travellers the main interventions used are bed nets, repellants and antimalarial drugs. With first time travellers to malaria endemic countries, they are more anxious and likely to use some form of protection. We notice high patronage and adherence in this group. Caucasians have a high-risk experiencing life-threatening complication and severe disease manifestations after infection because they possess no form of semi-immunity towards infection and are regarded as malaria naïve individuals. Short-term travellers are more likely to use the complete dose of antimalarial drugs as compared to long term travellers this includes VFRs, backpackers and cultural exchange/study individuals [53, 54].

With VFRs or regular visitors to such areas, there is a lower adherence and overall use of malaria prevention due to low-risk perception. These factors make these two groups at high risk of infection and the specific malaria prevention methods should be prescribed taking into account the culture, behaviors, challenges and lifestyle of each individual. A major hindrance fighting adherence is the dosage of most antimalarial drugs. Take mefloquine for example, is taken once a week at least 2 weeks before visiting malaria endemic country, every week during stay at 4 consecutive weeks after return [55]. Depending on travel itinerary and family/social obligations following this dosage strictly may be cumbersome. Others avoid such drugs due to various side effects which include dizziness, anxiety, vivid dreams and visual disturbances and difficulty in speaking just to name a few in regards to mefloquine. Even vector control methods have some challenges. Travelers complain about heat when using bed nets, harshness of the insecticides used in bed nets and repellants causing dermatological side effects such as rashes and burns. Therefore, it seems that with every method comes different challenges hence advice on this should be individualized during consultation and not a one size fits all approach. Every risk group should have access to tailor-made malaria prevention options to suit their unique needs. For purposes of this paper, we will focus on VFR travellers.

1.11 Visiting friends and relatives as a risk group

Visiting friends and relatives (VFR) travellers are a specific group of people with characteristics that make them a risk group to various neglected tropical diseases. A stereotypical African VFR can be described as follows: A 35-year-old man born in Ghana but migrated to Germany when he was 20, currently has 3 children and visits his extended family in the village every year with his family. This model example depicts an individual who migrated and settled in a country, usually a high income and high resource country, and takes regular trips to their country of origin, usually a low income and low resource country to visit friends and family and for various occasions including funerals, weddings and birth ceremonies [56, 57].

Hence a VFR traveler of sub-Saharan descent, is an individual who was originally born in an African country to African parents and later migrated to the global north and frequents this said country regularly. Despite this prototypical definition of the VFR, this term has been expanded to include 2nd and 3rd generation immigrants, spouses of different ethnic background and others [58].

These individuals defer from tourists, backpackers and business trip visitors in that they have lived in the country they are visiting for a significant number of years. They are aware of the culture and usual day to day living and well experienced in finding their way around town. This comes with a level of confidence likened to a native dweller and they are not so cautious about various diseases they may be exposed to. In the year 2020, 406.3 million international travels were recorded and 72,132.34 were international travellers on VFR trips [59, 60]. VFR travellers are susceptible to various travel-associated infections such as malaria, sexually transmitted diseases, hepatitis and typhoid fever amongst others. This is because they are more likely to have long term travels as compared to tourists visiting the same region, their destinations may have high disease transmission regions leading to increased exposure and travels maybe impromptu and therefore include inadequate time to explore preventive measures. They have increased exposure to various diseases because they are less likely to make use of vector control measures, more likely to stay in indigenous homes with friends and family and readily participate in routine family activities and events like going to the farm, drinking tap water, sleeping in open air environment and eat food from roadside canteens [61].

1.12 VFR travellers & their characteristics in travel-related malaria epidemiology

The global burden of malaria has reduced significantly with the introduction of evidence-based interventions which have helped to mitigate disease complications and decrease infections. On the other hand, imported malaria cases in countries with high immigration rates have increased with most of these cases (approx. 56%) originating from West Africa [10, 62, 63]. In 2017, 2,161 confirmed malaria cases were confirmed in the US with 73% occurring in VFR travellers and 86% originated from Africa (67% from West Africa precisely). These numbers were further validated by data collected by the GeoSentinel global surveillance networks clinics (2003-2016) when the recorded 53% of malaria diagnosed patients returning from a trip as VFRs out of whom 83% were infected in sub-Saharan Africa [61]. A study done in the Netherlands, stated that between 2007-2011, 240 malaria cases were reported annually which were imported from Ghana (23%), Nigeria (14%) and Gambia (7%) by VFR travellers [64]. In Aragon, Spain, another study done in 2019; 609 cases (1996-2017) and 95.2% of cases from sub-Saharan Africa [13].

In Germany from 2005-2015, about 401 imported cases were recorded annually. [62] In the last decade, 800-1000 imported cases of malaria into Germany were recorded yearly by the Robert Koch Institute with more than 95% of these cases were from VFR travellers returning from Africa [65]. In addition to the factors discussed in the earlier paragraphs, VFRs are a major risk group because of their perceived immunity against malaria and low risk perception [10]. Most VFRs are unaware of the waning semi-immunity against clinical complications and high parasitemia which they formerly developed as a result of residing in high malaria transmission areas and continuous exposure to mosquito bites. Mischlinger et al used the term naturally acquired immunity to malaria to describe immunity developed due to repeated exposure over several years. However, this natural protection wanes after absence of continuous exposure which is the case in most VFR travellers. The longevity of this immunity is yet to be explicitly determined with different studies recommending it at approximately 16-20 years after initial absence of exposure due to migration from endemic country to non-endemic.

Today it is only partially understood why VFRs have such an increased risk of contracting malaria as well as other travel-related health problems [66-68]. Reasons may include that VFR travellers usually spend a longer time in their home country as compared to tourists, have access to and generally frequent rural and high-risk areas and have close contact to the locals and even participate in social cultural behaviors and practices. It is suggested that VFRs underrate their susceptibility to infection, possess low level of knowledge of diseases as well as the misconstrued belief that the few measures taken would suffice may be causative factors [66, 69]. Young children and pregnant women are the most at risk groups to malaria infection and death. Preventative methods ensure a reduction in malaria related deaths in high transmission areas. Such measures include vector control which involves the use insecticides, pesticides, bed nets and destroying mosquito breeding areas. Chemoprophylaxis is the use of antimalarial drugs to prevent infection and constitutes the mainstay tool in the prevention of malaria in VFR travellers [10, 34, 70, 71].

Malaria can be reliably prevented by regular administration of a prophylactic drug. High uptake of malaria chemoprophylaxis among VFR travellers would significantly reduce the number of malaria cases imported into Germany. In addition, improved access to travel medicine consultations for VFR travellers would probably also lead to a lower incidence of other preventable infectious diseases as well.

Despite these interventions we still observe a low use of preventive measures against malaria amongst the VFR population mentioned in similar studies done in the USA, France, UK, Italy, the Netherlands and Spain [72-74]. Possible reasons for the apparently lower use of travel medicine consultations or prophylactic measures by VFR travellers could be manifold, ranging from a lack of financial resources to pay for travel advice to a mistaken belief that they are protected against infectious diseases, especially malaria, by being born in an African country or by belonging to a certain ethnic group [13, 20, 67, 75]. However, a similar systematic investigation of the reasons for this lower use of travel medicine consultations or prophylactic measures by VFR travellers has not yet been conducted in Germany as is the case in our European counterparts.

1.13 Scope of thesis and research questions

Our aim was to systematically assess and characterize the attitudes, practices and experiences of VFR travellers with regard to travel medicine and malaria prevention measures. To better understand the reasons for the disproportional risk of malaria among VFR travellers, we designed a survey to assess the knowledge, attitudes and practices of VFR travellers regarding malaria. With this survey, we aim to provide the scientific basis for targeted and effective interventions to improve the travel medicine care for VFR travellers.

2 Materials and methods

2.1 Study design

This study was a cross-sectional questionnaire study to assess the knowledge, risk assessment, travel medicine counselling practices and chemoprophylaxis use of VFR travellers returning to Hamburg after a trip to SSA or embarking on a trip to SSA.

The study involved the development of a questionnaire to be administered anonymously to VFR travellers. This questionnaire covered topics on malaria transmission, risk assessment, prevention, prophylaxis and general behaviour towards seeking medical travel advice.

The questionnaire consisted of 36 multiple-choice options and free-text questions. It was designed to be administered by trained staff who interviewed travellers and recorded their responses to the various questions. It was mainly administered in English, German and French. On very few occasions, the survey was conducted in Twi (a local Ghanaian language) for better understanding. The survey was conducted from January to July 2023 at the arrival and departure terminals of the Helmut Schmidt Hamburg Airport, Hamburg, Germany.

2.2 Target group

Passengers were eligible if they were about to check in for flights to African destinations and arriving from African countries as well as family and friends accompanying them or awaiting their arrival. Flight times and destinations were monitored to ensure access to the target group. The target group consisted of travellers over 18 years of age, of sub-Saharan Africa origin, currently living in Hamburg and having visited an African country in the last 10 years. Based on these inclusion criteria, travellers were interviewed on-site.

2.3 Validation of the questionnaire

After the initial questions had been drafted, a pilot survey was carried out at the aforementioned airport in December 2022. The aim of this pilot survey was to validate the questionnaire to ensure that the questions were understandable, that the responses were consistent and that the coding process was standardized. It was also used to assess the feasibility of administering the questionnaire in a reasonable amount of time.

A total of 20 people were interviewed in the pilot survey. On the basis of this experience, the questions were edited to be more specific and to ensure that they were understood equally by the interviewers and the respondents. In addition, the pilot survey allowed to set the logistics to be established to determine flight schedules, travel times and best ways to approach travellers to maximize response rates. Interviewing skills and proper understanding of responses were further trained as the project progressed.

As most of the participants did not have sufficient knowledge about malaria, a special educational leaflet about malaria and its prevention was produced. This leaflet was given to participants at the end of the interview process as an additional individual benefit for taking part in the survey. This aim of this measurement is to educate more people about malaria and encourage visits to health facilities before and after travel.

2.4 Data collection, data management, statistical analysis

Data were collected by trained interviewers using specially designed paper-based questionnaires. No identifiable information (name, date of birth, etc) was collected. Data were transcribed into a custom-built electronic database (Google Forms and Google Sheet). Data quality was assessed manually by two investigators and queries were generated for incorrect data entries which were subsequently resolved. Data were extracted for further analysis using a commercially available software package (STATA®). Descriptive summary statistics of consequential outcomes were generated from the data collected. Median (IQR) and mean (95%CI) were used where appropriate. No formal statistical hypothesis testing was pre-set in this descriptive study. Further statistical analysis was performed relating specific subgroups such as gender, country of origin, educational background and financial situation to the endpoints; knowledge of malaria, travel medicine prophylaxis, length of stay. Post-hoc statistical hypothesis testing was performed to generate exploratory hypotheses for associations or causal relationships between exposure variables and outcomes. Data analysis was presented as statistical tests and graphs.

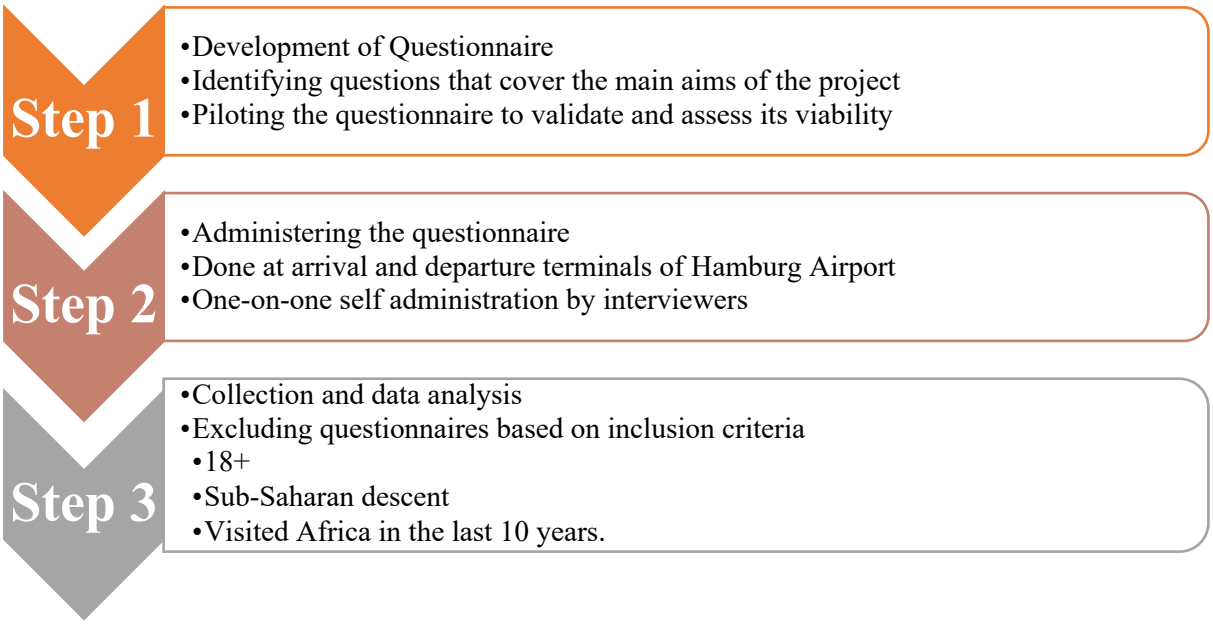

Figure 4: Step by step approach to study design

2.5 Ethics

This survey was submitted to the Ethics Committee of the Hamburg Medical Association (2022-300275-WF) According to the Ethics Committee no ethical approval was required for this study as no identifiable personal information was collected and there were no plans to contact participants after the survey. Therefore, no written informed consent form was necessary for this study. Permission to conduct the survey at the airport was sought and obtained from the Hamburg Airport Authority.

This project was funded by the German Centre for Infection Research (DZIF project number: TI 07.003_014) through a doctoral dissertation grant and a seed grant of the German Society for Tropical Medicine, Travel medicine and Global Health.

3 Results

3.1 Demographic information

Over a period of eight months, from January to August 2023, 400 participants agreed to be interviewed at the airport (**Figure 5**). Five respondents were excluded because the last time an African country was visited was more than ten years ago. A further six respondents were excluded because the data entered for country visited and year visited were inconclusive. This resulted in 389 respondents who met the inclusion criteria and were therefore included in the analysis.

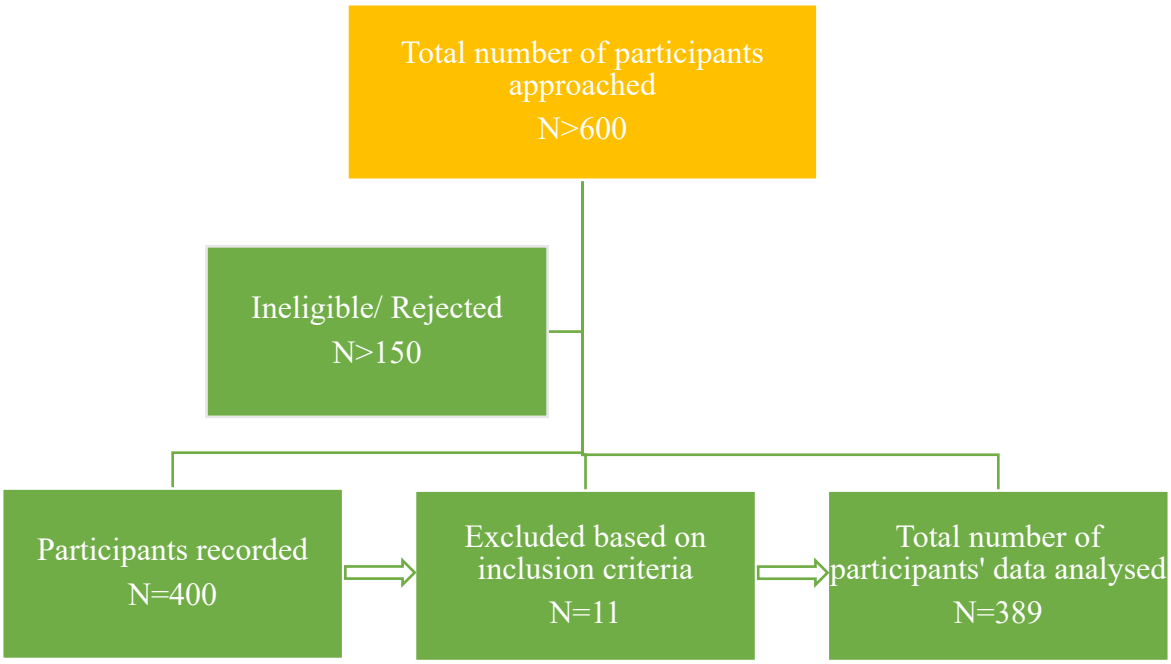

Figure 5: Flowchart of the Hamburg Airport Survey. The participants approached, interviewed and questionnaires in the study are shown as well as exclusions

In terms of general demographics, 265 (68%) of travellers were male **(Table 1**). Median age was 38 (IQR: 25%-28, 75%- 50). The most frequent age groups were 18-29 (28%) and 30-39 (24%). Data on 92 children were also collected from the adults who accompanied them on their trip. We recorded the country of origin using the origin of their parents or grandparents. The majority came from Ghana (n=173; 44%), Nigeria (n=54; 14%), Togo (n=29; 7%), Cameroon (n=22; 6%), Gambia (n=16; 4%) and Kenya (n=15; 4%) (**Table 2**).

When asked about the highest level of education completed, 188 (48%) responded with tertiary education, 168 (43%) with secondary education and 20 (5%) with primary education. Ten respondents 10 (3%) did not finish primary school.

A total of 336 (87%) respondents were employed either by an employer or self-employed, 27 (7%) were unemployed and 10 (3%) were retired. The respondents were also asked about their net household income per month: 118 (30%) earned more than 3000 Euros, 72 (19%) between 2000-3000, 55 (14%) between 1500-2000 and 46 (12%) less than 1500 (**Table 2**).

3.2 Travel profile

A total of 33 countries were recorded as having been visited by VFR travellers in the last ten years. Forty respondents (10%) travelled between 2013 and 2017 and 349 respondents (90%) travelled between 2018 and 2023. These most visited countries were Ghana (n=172; 44%), Nigeria (n=56; 14%), Togo (n=27; 7%), Cameroon (n=24; 6%), Gambia (n=16; 4%), Kenya (n=14; 4%) and Ivory Coast (n=11; 3%) (**Table 1**). Most respondents (n=320; 82%) were born in Africa and later moved to Germany. The main residence status of the respondents was in Germany (98%), the rest lived in other European countries. The median duration of the trip recorded by travellers who answered this question was four weeks (IQR 25%=3, 75%=6). Six travellers (about 2%) could not remember the duration of the trip. More than half of the total participants travelled alone (n=241; 62%), others travelled with family or friends (n=148; 38%). Sixty respondents out of the number travelling with others (60/148: 41%) travelled with children.

3.3 Knowledge about malaria

The mode of transmission of malaria was asked and multiple answers were possible. Only 260 (67%) of the participants chose the bite of the Anopheles mosquito as the only mode of transmission, 49 (13%) chose this answer in addition to other transmission factors (**Table 3**). Food and water were chosen by 63 (16%) and direct person-to-person contact by 11 respondents (3%). Other responses included dirty environment, sun exposure, bacteria, airborne, dust inhalation and staying in humid areas. Ten percent stated that they did not know how malaria is transmitted.

Regions	Country visited	Frequency	Percentage	Percentage	Frequency	Country of origin
West Africa	Ghana	172	44.33	44.47	173	Ghana
	Nigeria	56	14.43	13.88	54	Nigeria
	Benin	7	1.80	2.86	8	Benin
	Burkina Faso	4	1.03	1.29	5	Burkina Faso
	Cape Verde	1	0.26	0.26	1	Cape Verde
	Gambia	16	4.12	4.11	16	Gambia
	Guinea	5	1.29	1.29	5	Guinea
	Guinea-Bissau	3	0.77	1.54	6	Guinea-Bissau
	Ivory Coast	11	2.84	2.83	11	Ivory Coast
	Liberia	2	0.52	1.03	4	Liberia
	Togo	27	6.96	7.46	29	Togo
	Niger	1	0.26	0.51	2	Niger
	Senegal	5	1.29	1.03	4	Senegal
	Sierra Leone	2	0.52	0.77	3	Sierra Leone
				0.26	1	Mali
East Africa	Kenya	14	3.61	3.86	15	Kenya
	Tanzania	2	0.52	0.26	1	Rwanda
	Uganda	2	0.52	0.51	2	Uganda
	Eritrea	2	0.52	1.03	4	Eritrea
	Ethiopia	5	1.29	0.51	2	Ethiopia
	Somalia	1	0.26	0.26	1	Somalia
	South Sudan	1	0.26	0.26	1	South Sudan
	Sudan	2	0.52	0.26	1	Madagascar
Southern Africa	Mozambique	1	0.26	0.26	1	Mozambique
	Namibia	2	0.52	0.26	1	Namibia
	South Africa	5	1.29			
	Zambia	2	0.52	0.51	2	Zambia
	Zimbabwe	2	0.52	0.51	2	Zimbabwe
	Angola	1	0.26	0.51	2	Angola
Central Africa	Cameroon	24	6.19	5.66	22	Cameroon
	Republic of Congo	4	1.03	0.26	1	Republic of Congo
	DR Congo	-	-	0.26	1	DR Congo
	Equatorial Guinea	2	0.52	0.26	1	Equatorial Guinea
	Gabon	2	0.52	0.51	2	Gabon
North Africa	Morocco	1	0.26			

Table 1: Country of origin of participants from the 2nd and 3rd generation and country visited

The symptoms compatible with malaria were also asked as a multiple-choice questions with 289 (79%) selecting fever, 179 (46%) headache and 79 (20%) vomiting (**Table 3**). Another 86 respondents (22%) mentioned other symptoms, especially jaundice, itching, body aches, dizziness, and sweating. Twenty-eight respondents (7%) did not know the symptoms of malaria. When asked about prevention methods, 212 (54%) mentioned bed nets, 174 (45%) mosquito repellents, and 73 (19%) mentioned keeping the environment clean. Other responses included drinking clean water, using traditional herbs and root tonics, burning incense/prayer and vaccination.

Demographics		(N=389), n(col%)
Gender	Male	265(68)
	Female	124(32)
Age	18-29	11(28)
	30-39	93(24)
	40-49	78(20)
	50-59	70(18)
	60+	37(10)
Educational level	Primary school	20(5)
	High/Secondary school	168(43)
	Higher Education	188(48)
	None	10(3)
	No answer	3(1)
Monthly net household income	0-500€	4(1)
	500-1000€	19(5)
	1000-1500€	23(6)
	1500-2000€	55(14)
	2000-3000€	72(19)
	More than 3000€	118(30)
	No answer	98(25)
Employment status	Employed	325(83)
	Mini-job	1(0.3)
	Retired	10(3)
	Unemployed	27(7)
	Unemployed but spouse works	9(2)
	Self-employed	11(3)
	No answer	6(2)
Duration of trip	4 weeks and below	259(67)
	More than 4 weeks- 24 weeks	118(30)
	More than 24 weeks	6(1.5)
	Can't remember	6(1.5)

Table 2: General characteristics of 389 participants included the study in relation to general demographics, occupation, education, trip duration and finances

How does one contract malaria? Multiple responses	N(col %)
Bite from Anopheles mosquito	308(79)
Food and water	63(16)
Direct human to human	11(3)
I don't know	38(10)
Other	25(6)
What symptoms of malaria do you know?	
Fever	289(74)
Headache	179(46)
Sweating	29(7)
Nausea	30(8)
Vomiting	79(20)
Loss of appetite	64(16)
Cold-like symptoms	43(11)
Weakness	63(16)
Joint/body pain	44(11)
Diarrhoea	17(4)
I don't know	28(7)
Others	86(22)

Table 3: Knowledge of mode of transmission and symptoms of malaria. More than one answer is possible to each question hence total percentage for each question may be > 100%

What measures of exposure prevention against malaria are you aware of and which did you take during your last journey to Africa? (multiple answers are possible)	N=389
Bed net	212
Mosquito repellent	174
Impregnation of clothing with mosquito repellent	8
Wearing of clothing with light colour	6
Clean environment/ good hygiene	73
None	20
No answer	25
Other	81

Table 4. Malaria prevention methods used by travellers during their trip in SSA. More than one answer is possible to each question hence total percentage for each question may be > 100%

3.4 Risk assessment

Travellers were asked questions to assess their perceptions of malaria infection. When asked how dangerous malaria was, 247 (64%) said it was very dangerous, 43 (11%) said it was dangerous and 99 (25%) said it was not dangerous at all (Table 6). When asked to estimate their personal risk of contracting malaria during a trip to any sub-Saharan African country, 126 respondents (32%) considered it high, 64 (16%) medium and 171 (44%) low.

	n (%)
How high would you estimate your personal risk to fall ill from a malaria infection?	
High	126(32)
Intermediate	64(16)
Low	171(44)
No risk	27(7)
No answer	1(1)
Who is most at risk of getting malaria? Multiple responses	
Children	145(37)
Poor people	47(12)
Other races	23(6)
Pregnant	16(4)
People of a particular blood group	11(3)
Old people	54(14)
Everyone	91(23)
Africans	13(3)
I don't know	15(4)
No answer	4(1)
Other	35(9)
How dangerous do you think malaria is?	
Very dangerous	247(64)
Dangerous	43(11)
Not dangerous	99(25)

*Table 5: Risk perception of VFR travellers interviewed in this survey. *Multiple answers were applicable here summing up to 454 given responses*

Another 27 respondents (7%) said they had no risk of contracting malaria while travelling. Participants were also asked who they thought was most at risk of malaria. The most common responses were children (n=126; 37%), poor people (n=47; 12%), other races (n=23; 6%), pregnant women (n=16; 4%) and old people (n=54; 14%).

3.5 Medical travel advice

To properly study the behaviour of VFR travellers, they were asked whether they had sought medical advice before their trip, if so, where and if not, why not. 208 (53%) sought medical advice. Of these, 61% (127) went to a general practitioner and 26% (51) to a tropical medicine institute. The most frequently stated reasons why many travellers did not seek travel advice were "I don't think it's important" (n=71; 39%) and "I didn't think of it" (n=64; 35%). Other selected responses are shown in **Table 6**.

3.6 Medical prophylaxis

In total, 311 (80%) participants were recommended antimalarial drugs by a health worker, family and friends and the internet. Of those, 194 (62%) took the medication. 34/194 (18%) used mefloquine, 31/194 (16%) used atovaquon-proguanil and 107/194 (55%) could not remember the name of the drug. Chloroquine, sulfadoxine, doxycycline and artefan were also used by some travellers. In total, 156/194 (80%) bought these drugs in Germany, 31/194 (16%) bought them in the visited country and 6 (3%) bought them in other non SSA countries. See **Table 7** for more information.

Reasons for not taking prophylaxis included low risk of disease (n=74, 38%), "was not recommended" (n=39/194, 20%), and "malaria is not dangerous for me" (n=28, 14%) (**Table 7**) Another reason provided by respondents was that they were strong African men hence not susceptible to malaria infection. Side effects, if any, were also noted: 36 respondents (19%) had side effects, the most common being headache (n=19; 8%). See **Table 7** for other reported side effects. When the respondents who did not take medical chemoprophylaxis (194) were asked if they had ever been recommended antimalarials, 117 (60%) said that they had, 69 (36%) said that they had not, and 8 (4%) did not remember.

	Overall (N = 389)
Before your last journey to Africa, did you seek medical travel advice?	N (col %)
Yes	208(53)
No	181(47)
Where did you seek travel medical advice?	(N=208)
Institute for tropical medicine	51(26)
Medical practice specialized in travel medicine	8(4)
General practitioner	127(61)
Pharmacy	5(2)
Internet	5(2)
Friends and family	7(3)
No answer	1
Other	4(2)
What was the reason for not seeking travel medical advice?	N=181(%)
I don´t think it's important	71(39)
I did not think of it	64(35)
I didn't have time, because I had to travel on short term notice	9(5)
Travel medical advice was too expensive	2(1)
I didn't have time, because I had to work	5(3)
I only sought travel medical advice for the vaccination against yellow fever and my vaccination was still valid	3(2)
Other	24(13)
No answer	3(2)

Table 6: Travel medical advice responses as given by the 389 participants

	Overall (N = 389)
During your last journey to Africa, did you take medical chemoprophylaxis?	
Yes	194(50)
No	194(50)
No answer	1
Why did you NOT take any prophylaxis against Malaria?	**N=194**
I am concerned about the side effects	8(4)
It hasn't been recommended to me	39(20)
Malaria is not dangerous for me	28(14)
I can just treat it if I get it	3(2)
I think the risk to fall ill is low	74(38)
The medication was too expensive	3(2)
I just didn't take it	1(1)
Because I don't think it works	6(3)
Others	32(16)
Do you know of such medication and have they ever been recommended to you? (Responded "No" to "During your last journey to Africa, did you take medical chemoprophylaxis?")	**Overall (N = 194)**
Yes	117(60)
No	69(36)
I don't remember	8(4)
Did experience any of the following side effects while taking the medication? (N=194)	**N(%)**
Nausea	5(3)
Diarrhoea	4(2)
Constipation	1(1)
headache	11(7)
Vertigo	2(1)
Insomnia	0
Depressive mood	1(1)
Skin rash	0
No	158(81)
Other	19(8)
Which medication did you take?	N=194
Malarone (Atovaquone/Proguanil)	31
Doxycycline	4
Lariam (Mefloquine)	34
Other	15
I don't remember	107
No answer	3
Did you finish the prescribed dose?	**N(%)**
Yes	149(77)
No	31(16)
I don't remember	14(7)

Table 7: Medical prophylaxis and its usage by participants

3.7 Adherence

The majority of respondents (n=149; 77%) who took antimalarial drugs completed the full dose, while 31 (16%) did not complete the dose and 14 (7%) did not remember.

3.8 Prevention methods

Participants were asked which prevention methods they knew about and which they used. As this was a multiple-answers-question, some participants mentioned more than one prevention method. Most of them (n=212; 54%) mentioned bed nets, 174 (45%) mentioned mosquito repellent, 73 (19%) mentioned clean environment and good hygiene and 20 (5%) did not know or use any. Other measures mentioned included impregnating clothing with mosquito repellent, using traditional herbs, vaccination and eating healthy foods. (Refer to **Table 4**)

3.9 Post-travel events

21 (13%) had symptoms compatible with malaria after their return. Of these, 9 (45%) sought medical attention, 1 (5%) did not and 10 (50%) self-medicated.
The 20 participants who experienced symptoms were asked if they had any concerns about seeing a healthcare provider; 16/20 (80) replied yes while 4/20 (20) replied no.

3.10 Participants´ history of malaria

In total, 115 (30%) respondents had had malaria in the past, 133 (34%) were not sure and 141 (36%) said they had never had malaria. Around half of the patients with a history of malaria (n=59; 51%), had their most recent malaria infection in the recent 10 years. The participants were not asked if they had malaria during their trip, although they were asked about their most recent malaria infection. However, during questioning, 9 participants explicitly mentioned they had malaria during their stay in the country visited. We compared the years they had malaria and the years they travelled to SSA and we were able to deduce 59/389 (15%) additional participants who may have had diagnosed and undiagnosed malaria during their trip.

3.11 Comorbidities and additional medication

62 respondents (16%) had other medical conditions. Out of those, the most frequent diseases were had hypertension (32/8%) and diabetes (type 1 and type 2) (12/3%). 80 (20%) people regularly took medication.

		N=389, N (%)
Have comorbidities	Yes	62 (16)
	No	324 (83)
	No answer	3 (1)
Pre-existing medical conditions	Hypertension (HTN)	32 (8)
	Diabetes mellitus	12 (3)
	Gastroenterology diseases (stomach ulcer, gastric reflux, gastritis)	4 (1)
	Respiratory diseases (asthma, cough)	5 (1)
	Others (dermatolysis, psychiatric issues, hemarrhoids, cancer, osteoporosis, psychosis, sickle cell anemia, hypo- & hyper-thyroidism, anemia, tendinitis, cardiac enlargement etc)	14 (4)
Health medication on a regular basis	Yes	80 (20)
	No	308 (79)
	No answer	1(1)
List of medications HTN drugs (amlodipine, ramipril, irbesartan, losartan, valsartan, bisoprolol, enalapril), vitamin D, glucophage, pain killers, anti-allergy drugs, azathioprine, insulin, siofol, traditional herbs, birth control, ibuprofen, omeprazole, loratadine, metformin, iron supplements, pantoprazole, thyroxine, cetirizine, linezolid, furosemide, aripiprazole and multivitamin nutritional supplements		

*Table 8: List of pre-existing medical conditions participants had and additional medications they were on. *Multiple answers were given in these free response question on medical conditions so total percentages may be >100*

3.12 Further analysis of special sub-groups of VFRs

With all the collected, different parameters were compared and studied to detect certain trends, connections, contrasts or correlations within the different sub risk groups and specific risk group within the VFR community were identified. Age, country of birth, gender, accompanied travellers, duration of trip, education, employment and finances were compared against the main aims of the study.

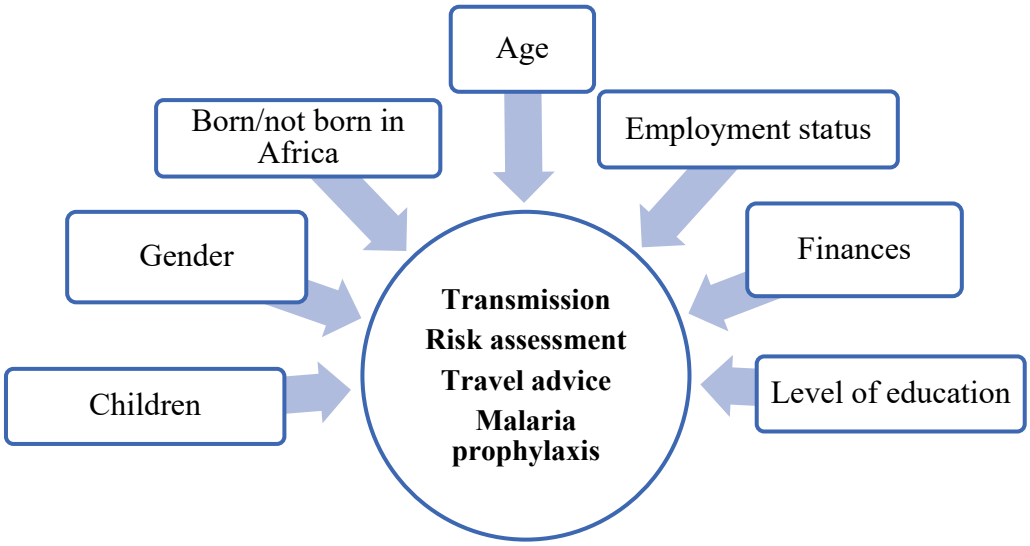

Figure 6: Sub-analysis comparing different parameters with the main aims of the study design

3.12.1 Special subgroups

3.12.1.1 Parents travelling with children

A section of the questionnaire included questions for participants travelling with children, a risk group we identified. They were asked questions pertaining to their children on general data, malaria prevention methods, chemoprophylaxis use among others.

Data for 92 children were taken obtained from 60 parent-participants who travelled with children.

I. Parental data

36/60 (60%) took antimalarial drugs for themselves and 23/60 (40%) did not. 37/60 (62%) sought personal travel advice and 23/60 (38%) did not. 41/60 (68%) parents purchased antimalarial drugs for their kids and 18/60(30%) did not. 1(2%) gave no answer no answer.

II. Children data

Fifty-nine (64%) were female and thirty-three (36%) were male. Sixty-four (70%) took antimalarial drugs. 40 (62%) could not name the drug used, mefloquine was used by 11 (17%) children and atovaquone-proguanil was used by 8 (13%) children. 70/92 (76%) children used a prevention method and 15/92 (16%) children did not.

Children's data	Total number: 92
Age	
Median	11
25% percentile	6
75% percentile	15
Gender	
Male	35(38%)
Female	57(62%)
During your last journey to Africa, did you take medical chemoprophylaxis?	
Yes	66(71%)
No	26(28%)
Which medication did you take? n=66	
Atovaquone-proguanil	7 (9%)
Mefloquine	11(12%)
I don't remember	41(44%)
No answer	7(8%)
Did you use any preventive method during your trip?	
Yes	61(66%)
No	15(16%)
No answer	16(17%)
Parents' Data	
Total number of participants travelling with kids	n=60
During your last journey to Africa, did you seek medical travel advice personally?	
Yes	37(62%)
No	23(38%)
During your last journey to Africa, did you take medical chemoprophylaxis personally?	
Yes	36(60%)
No	23(38%)
No answer	1(2%)
Did you purchase malaria chemoprophylaxis for kids during your last journey to Africa	
Yes	41(68%)
No	18(30%)
No answer	1 (2%)

Table 9: Data collected from parents travelling with children under 18

3.12.1.2 Born in Africa vs not born in Africa

The second risk group identified were those born in Africa. 320/389 (82%) were born in Africa. 255/320 (80%) of those born in Africa chose bite from Anopheles mosquito. 159/320(50%) of those born in Africa sought medical travel advice and 146/320(46%) took antimalarial drugs. In contrast, 69/389 (18%) were born outside Africa. 54/69 (78%) of the participants born outside Africa chose bite from Anopheles mosquito, 49/69 (71%) of those not born in Africa sought medical advice when travelling and 48/69 (70%) took antimalarial medication.

3.12.1.3 Vaccination

The third group identified were participants who believed were vaccinated against malaria. Thirty-seven respondents (10%) reported that they were either vaccinated against malaria or recommended vaccination as a prophylactic measure against malaria for adults and children.

3.12.2 Further analysis of main parameters

3.12.2.1 Knowledge of the mode of transmission and risk assessment against various parameters.

Seventy-nine percent (n=309) chose the correct mode of transmission (bite from the Anopheles mosquito). The responses of these 308 participants were further dissected and these were the results. Based on level of education, 160/188 (85%) of the total number people with higher education chose `bite from mosquito'. 11/20(55%) of participants who had completed primary education, 129/168(77%) of participants who had completed secondary education and 7/10(70%) of participants with little or no formal education, also chose this answer. In terms of age, more than 70% of respondents in each age group chose the correct answer. 15/20(75%) of participants who had completed primary education, 63/168(38%) of participants who had completed secondary education, 89/188(47%) of participants who had completed tertiary education and believed they were at low risk of contracting malaria in the country they visited.

3.12.2.2 Travel medical advice

Sixty-three percent (63%) of all women and 49% of all men sought medical advice. Sixty-one percent of people in the 30-39 age group did not seek travel medical advice, in contrast to the higher proportions seeking travel medical advice in the other age groups. The number of people who sought travel medical advice were 208/389 and out of the 208, 159 (76%) took antimalarials before or during their trip and 49/208 (24%) did not. 188/208 (90%) were recommended antimalarials and 20/208 (10%) hadn't heard of it or couldn't remember if it was recommended.

3.12.2.3 Medical chemoprophylaxis

Three hundred and eleven participants (311/389: 80%) had heard of or were recommended antimalarial drugs. 117/311(38%) did not take it despite the recommendation/knowledge of antimalarial drugs. (refer to **Table 7**). 20/208 (20%) who sought medical travel advice before their trip answered that they weren't recommended and neither have they heard of antimalarial drugs. 61% of all women used chemoprophylaxis. 62% of participants aged 30-39 years did not use antimalarial drugs. Regarding side effects, 9/36 experienced side effects from taking Atovaquone-proguanil, 6/34 from Mefloquine and 6/36 from other drugs. 15/36 of those who experienced side effects could not remember which drug they had taken. 311/389 (80%) were recommended antimalarial drugs and 194/311(62%) actually took them.

3.12.2.4 Adherence vs duration of travel

Eighty-one percent (109/134: 81%) of travellers who spent less than 4 weeks in the country visited, 68% (21/31) who spent 1-6 months and 69% (18/26) who spent more than 6 months completed the course of treatment. Refer to tables 2 and 6 for total values for trip duration and adherence.

3.12.2.5 Medical advice for next trip

The participants were also asked if they would seek travel medical advice before their next trip to Africa and 240 (62%) answered yes while 109 (28%) answered no. Forty respondents (10%) were not sure if they would or would not. Thirty-one (15%) respondents who took medical advice for their last trip decided not to do so for their next trip. The stated reasons for this decision were that they had all the required information now, it is expensive, sometimes not covered by insurance and the risk of possible infection is low in their regions of Africa. Of the 181 people who did not seek medical advice, 74 (41%) decided to do so on their next trip.

3.12.3 How to encourage malaria chemoprophylaxis use and seeking medical travel advice

As part of the study, participants were asked the best ways to educate the VFR community on malaria prophylaxis. The use of social media as an information dispersion tool was highly suggested. Some participants suggested the introduction of pop-up notifications on airline websites and third-party flight booking websites when any destination in SSA is entered. Adverts, talks/seminars and announcements on local radio stations and also in places frequented by the VFR community including African shops, religious places of worship, sport centres among others could be organised. Another way suggested was for travel agents and agencies to share pamphlets with information on malaria with clients travelling to SSA. Airports may also have such flyers at the info desks. General practitioners and family doctors should also readily share information on malaria prophylaxis when intent to visit SSA countries is mentioned. The target group identified by the respondents as more receptive to the information given was said to be young people 30 and below. Some participants also suggested visiting schools and universities as part of a malaria education drive may be effective. Also suggested was for more insurance companies to cover malaria prophylaxis to increase use.

4 Discussion

Specific risk groups in travel medicine are the elderly travellers, children, pregnant and lactating women, persons with co-existing medical conditions and individuals visiting friends and relatives in their countries of origin (VFRs) [76]. This study was conducted by interviewing 389 VFR travellers on their malaria risk perception and attitude towards as well as experience with preventive measures and travel advice. Most of the study participants were born in Africa and migrated to Hamburg which is consistent with other similar studies [56]. They originated predominately from Ghana, Nigeria, Togo and Cameroon. These VFRs majorly visited their countries of origin within the last 10 years.

4.1 What do VFR travellers know about malaria?

When the knowledge of malaria based on mode of transmission, symptoms and prevention methods was assessed, 21% did not know the correct mode of transmission of malaria. This means that still a significant percentage of the VFR population are unaware of basic information about malaria though they are at high risk of getting infected. The study conducted in the USA from 2016-2018 showed similar results, where 16.5% of VFRs listed the wrong mode of transmission when asked within the community and 27% of VFRs asked at the travel clinics listed the wrong mode of transmission as well [77]. In our study, those born and raised in Africa knew more as compared to those with African decent but born outside of Africa.

4.2 How dangerous is malaria to a VFR traveller?

44% of the participants thought they had a low risk of contracting malaria and 7% stated that there's no risk of getting malaria even though 64% viewed malaria as a very dangerous disease. Most VFRs are aware of how dangerous malaria is as a disease. However, they don`t believe they are at a high risk of getting malaria in their home countries when visiting. Reasons such as sustained immunity to malaria over the years, environments with low presence of mosquitoes, lifestyle etc could have influenced this opinion [78, 79]. Regarding which group of people, they thought were most at risk, 37% said children, 12% said poor people, 14% saying the elderly and 4% mentioned pregnant women.

Most VFRs are unaware of the reduced immunity after staying in a non-endemic malaria country over a long period of time [10].

4.3 Travel medical advice: patronage among VFR travellers

A significant percentage of 47% of the participants interviewed did not seek pre-travel medical advice before their trip. Based on our results and published literature, our hypothesis that within the VFR community, a high percentage do not seek pre-travel advice is valid [80]. The reasons for this decision include belief that they already have all the information they need, low level of importance or simply that they did not think of it. Other authors argued that the reasons for not receiving pre-travel medical include low level of trust in healthcare professionals, the assumption that healthcare professionals in Africa know better about malaria and its treatment, not covered by insurance, last minute travel plans, unaccommodating work schedules and other priorities [81].

Another factor was highlighted in a study by Shukri A. Hassan in the African immigrant community in King Count, Washington, United States. Most VFRs do not have the attitude of regularly seeing their doctors for check-ups but rather after their illnesses have significantly progressed. [82]. Contrary to our hypothesis and existing literature that finances and education should influence the decision to seek travel medical advice or use antimalarial drugs, our data showed no such findings [79]. Studies by Walz et al. and Hanna et al, the individual salaries (type of employment) determined if they had good insurance which covered such services while a lower level of education correlated with a lower knowledge on malaria prevention and attitudes toward seeking medical advice [83, 84].

4.4 Antimalarial drugs: Yes or No and Why

Of the 389 participants interviewed, 50% did not use antimalarial chemoprophylaxis before travelling to Sub-Saharan Africa. This finding is in line with academic literature where about 50% of the interviewed study participants took the same decision [84, 85]. In a 2022 study from Canada, only 37% used antimalarial drugs prescribed by the doctors in Canada as well as those getting antimalarial drugs through other means i.e., in home country or through friends and family. The author explained this number to be due to high cost of drugs no insurance coverage, low self-risk perception of malaria infection as well as they didn't find it important [20, 83]. Some expressed that using these drugs as well as vector prevention methods will highlight their differences from the local population. They risked being ridiculed or seen as disrespectful if they used them [20]. Many of these reasons are in line with what we speculated and also our results [84].

A few participants mentioned that they didn't use antimalarial drugs because they were "strong African men" and would not want to be viewed otherwise by their peers.
80% of the total number were aware or had been recommended antimalarial drugs but out of this percentage, 38% did not take it (refer to medical prophylaxis in further analysis section and **Table 7**). Despite knowing about the drug and its importance, quite a percentage of people still did not take them. This shows that knowledge of antimalarial drug is not enough to ensure total use. More can be done to encourage correct antimalarial drug use and adherence among the VFR community. A study compared knowledge of malaria to antimalarial drug use in VFR travellers and the results showed that those who used drugs unexpectedly scored lower on overall knowledge of malaria while those who didn`t use it scored higher [85].

From the results, more people experienced side effects after taking atovaquone-proguanil as compared to the group that took mefloquine. In literature, the high occurrence of side effects in patients who use mefloquine as compared to atovaquone-proguanil has been discussed [86]. Our results disagreed with this existing information. Taking into account the 15/36 of participants who could not remember the name of the drug they used, we are unable to make a valid claim. The randomised, blinded, controlled trial that most closely resembled actual travel medicine practice in Europe and Canada showed no significant overall difference in tolerability between atovaquone-proguanil and mefloquine (71.4% vs 67% of patients, respectively with a 4.1% difference) [87]. Both drugs are acceptable prophylaxis options [78].

4.5 Participants history of malaria

59/389(15%) listed that they had malaria within the last 10 years. Of this group, the majority did not seek medical advice (61%) nor did they take prophylaxis (53%). Considering our hypothesis and existing scientific literature, we expected a larger difference margin that could relate malaria infection susceptibility to not taking antimalarial drugs or seeking medical travel advice [88].

4.6 Preventive measures

Aside the use of bed nets (54%) and mosquito repellents (46%), another common answer was keeping clean environments and eating healthy food (19%). People thought keeping clean environments (19%) was a major preventive method which is not surprising since 16% stated food and water as a mode of transmission. A study conducted among the VFR community in London, participants stated that they didn't foresee staying in a mosquito-infested-environment before travelling. One study participant claimed that although they had a clean environment and used mosquito repellents, their neighbours did not so it still left them at risk. [20] In the same study people avoided using preventive measures despite being aware of them due to the discomfort and risk of insulting those hosting them by implying that their homes are not safe. In addition, when VFRs were compared to non-VFRs in a study about prevention, less VFRs used preventive antimalarial measures throughout their stay [77].

4.7 Post travel events

Coming back with symptoms (20/389(5%)), some participants (10/20:50%) chose to self-medicate and not see a doctor. There seems to be misconceptions around seeing a doctor abroad for tropical related diseases. Some assume the information given is from the internet anyway or the healthcare professionals aren't knowledgeable or experienced enough to handle patients which such diseases. Others expressed a fear of extreme measures such as quarantine maybe implemented over malaria infection which to them, is an everyday illness [83].

4.8 Children

70% of families travelling with children under 18 sought medical travel advice for the kids. Out of the 41 parents who gave antimalarial drugs to their children, 9/41(22%) didn't take any for themselves. (Refer to **Table 8**) This is based on the assumption that the children were more at risk of getting malaria because they weren't born in Africa nor had they lived in Africa hence have little to no natural immunity against malaria infection [63, 89]. Children born in malaria endemic countries naturally acquire immunity by repeated *P. falciparum* infections which lead to significant level of accumulated clinical immunity [10]. Needless to say, children born in non-endemic countries lack this repeated exposure. It is clear that risk perception greatly affects antimalarial drug use.

4.9 Vaccination

Almost 10% of the population interviewed claimed to have been vaccinated against malaria. We realised these participants either mistook the yellow fever vaccine for malaria vaccine or assumed it protected them against both. Some literature attributes this situation to miscommunication and inadequate clarification on vaccinations by healthcare physicians when giving travel advice to VFR patients [22, 78]. Such a perception is quite dangerous since people gave it as a reason why they neither used medical prophylaxis against malaria personally nor for their kids despite visiting malaria endemic countries after living abroad for some years now. RTS,S/AS01 is the initial and only vaccine approved by the WHO 2023 for use in areas with moderate-to-high transmission in children. As part of the Malaria Vaccine Implementation Program, this vaccine was tested in Kenya, Ghana and Malawi, and is now implemented in routine prevention programs in several countries including those mentioned above [89]. However, this vaccine is not licensed for use in adults and travellers to malaria-endemic areas [37].

4.10 Co-morbidities and drugs

16% of the people interviewed had existing illnesses. No participant stated having a concomitant disease as a reason why they did not use antimalarial drugs. Half of this specific population suffered from hypertension (52%) and 20% from diabetes. The CDC Yellow book outlines potential drug-drug interaction between antimalarial drugs and other drugs for the treatment of endocrine, respiratory, circulatory and digestive related diseases. Atovaquone-proguanil may interact with cimetidine, fluvoxamine, metoclopromide, rifabutin, rifampin, tetracycline and warfarin. Mefloquine may interact with antiarrhythmic agents, anticonvulsants, beta blockers, calcineurin inhibitors, calcium channel receptor antagonists, CYP3A4 enzyme inducers[4], CYP3A4 enzyme inhibitors[2], H1 receptor antagonists, lumefantrine, mTOR inhibitors, phenothiazines, protease inhibitors and tricyclic antidepressants.

4.11 Travel medical advice and chemoprophylaxis use: the way forward for VFRs

Physicians should be sensitised into giving tailored medical travel advice to VFRs with an understanding of the relationship between VFR and destination country of visit and origin as well general behavioural patterns [90]. Heywood wrote in his study that disregard for and initial opposition to pre-conceived beliefs of the VFR traveller regarding certain measures will result in equivalent disregard of recommendations and poor adherence to malaria chemoprophylaxis [90]. These microaggressions and microinvalidations hinder effective assimilation of information. He also recommended the use of supplementary written travel health information in order to overcome language barriers and reduce doctor-patient miscommunication [90]. VFR travel have the tendency to think like locals hence assume they have the same perception of disease risk as locals. General practitioners should therefore greatly emphasize malaria infection susceptibility and reduction in acquired immunity to malaria [83]. 5% of the respondents claimed to have not been recommended antimalarial drugs despite seeking medical travel advice. This can be attributed to forgetfulness, low information retention by travellers during consultation, alternative methods of prevention suggested based on uniqueness of the case and possible negligence of the physicians in question. This situation can be avoided by asking patients to relay information said to them to ensure that key information was well received and also offering pamphlets with prophylaxis information post consultation. Malaria education drives targeted at the VFR community in schools, universities, shops, places of worship, local radio stations etc with the main messages being increased risk susceptibility of the average VFR traveller, migratory malaria and available malaria prophylaxis drugs and insurance companies that cover them. The other means suggested by the respondents in the results section should also be considered.

4.12 Trust in healthcare providers; pre-requisite for effective malaria prevention

From our findings, 61% of the participants sought travel medical advice from their general practitioners (GP). (**Table 5**) This shows that general practitioners have the most contact with VFR travellers hence play a vital role in effective risk communication and education on malaria. GPs counselling this major risk group should do well to provide adequate travel advice on malaria prevention options when intent to travel is expressed [66]. As mentioned before, VFRs may confuse vaccinations with one another. The various vaccination recommended should therefore be explicitly explained as to what they protect against, dosage and efficacy.

During this survey, a number of people expressed their believe in being vaccinated against malaria and that this was recommended by their GPs. Such statements suggest a degree of miscommunication between the GPs and their patients. This may be due to inadequate explanation, poor comprehension or omission of vital information due to insufficient time and a language barrier [91]. Also observed is a mistrust in healthcare providers. Some travellers avoided travel medical advice and antimalarial drugs because they didn't trust the information they would receive as valid. They expressed fear of being misdiagnosed or given the wrong medication [20]. They opted to self-medicate in case of illness and this is reflected in the 50% of participants who self-medicated after having malaria-like symptoms post-travel. One major strength and advantage this study had over similar studies was that the administration of the questionnaires was done by trained personnel of similar descent. This created a trust and conducive environment which greatly influenced the process. Applying a similar strategy of training and introducing more healthcare providers of similar ethnic background to attend to this risk group will greatly improve overall trust and compliance. When it comes to healthcare, trust within the doctor-patient relationship is a fundamental feature. For patients to be well catered for, they have to believe that their physicians have their best interest at heart [92].

4.13 Limitations to the study

Overall, in our study we tried to collect an unbiased and highly representative data. Conducting this questionnaire at the airport exposed us to participants from various walks of life. Our trained personnel administered the survey in English, French, German and sometimes Twi to ensure better comprehension of questions asked and to include participants from non-English speaking countries as well. On one hand, our selected mode of admission of the questionnaire allowed us to properly assess the knowledge of malaria by not providing possible answers. On the other hand, a lot of free text was gathered leaving most of it to the interpretation of the investigator. Major limitations experienced include numerous rejections because participants were either in a rush to check-in and catch their flights or really couldn't be bothered upon arrival after a long and stressful flight. This caused the questionnaire implementation phase of the project to be extended beyond our set timeline. Nonetheless we prevailed in the summer months to reach our 400-participant-quota. Another limitation was that 25% of participant refused to provide salary information leaving us unable to accurately assess the trends and connection between finances and other parameters such as travel medicine, use of antimalarial drugs and overall knowledge of malaria.

5 Conclusion

Based on the understanding that VFRs are very susceptible to different infections especially malaria because they are frequent travellers, the low-risk perception observed in our survey is alarming. The better understanding of the perceptions of VFRs and the barriers to effective malaria prevention described in this study will assist in improving this status quo by providing healthcare services tailor-made for this group of travellers. This research will serve as a basis from which more ground-breaking implementations and measures in this area will be developed.

6 Zusammenfassung

Hintergrund: Die afrikanische VFR-Gemeinde (aus dem Englischen „visiting friends and relatives“) aus nördlichen Ländern hat ein höheres Risiko, sich während einer Reise in Subsahara-Afrika mit einer reiseassoziierten Infektionskrankheit anzustecken. Diese Studie untersucht das Wissen, die Risikowahrnehmung, die reisemedizinische Beratung und die Nutzung von Chemoprophylaxe innerhalb der reisenden VFR-Population. Sie versucht, ein Verständnis der Hürden für eine effektive Prävention zu erlangen und eine maßgeschneiderte Reiseberatung zu entwickeln.

Methode: Eine fragebogenbasierte Umfrage wurde zwischen Januar und Juli 2023 am Hamburger Flughafen unter erwachsenen sub-saharischen VFR-Reisenden, die aus Malaria-endemischen Gebieten in Afrika zurückgekehrt sind, durchgeführt. Ziel dieser Studie war es, die Wahrnehmung des Malariarisikos, die Einstellung zu prophylaktischen Maßnahmen und reisemedizinischer Beratung sowie die Erfahrungen vor und nach der Reise mit Reisemedizin und Malariaprophylaxe zu bewerten.

Ergebnisse: Insgesamt wurden 389 Teilnehmende befragt. Von diesen haben 67 % (n=261) ausreichende Kenntnisse über die Übertragung von Malaria. 51% (n=198) gaben an, dass sie während ihres Aufenthalts in dem Malaria-endemischen Land wenig oder kein Risiko sahen, sich mit Malaria anzustecken, und 10% (n=37) glaubten fälschlicherweise, sie seien gegen Malaria geimpft worden. Etwa die Hälfte der Teilnehmenden holte vor der Reise keinen medizinischen Rat ein und nahm keine Malariaprophylaxe ein, da sie das Risiko einer Erkrankung als gering einschätzten. Von denjenigen, die Malariamedikamente einnahmen, beendeten 77 % (n=149) die vollständige Behandlung. Bei der Rückkehr hatten 5 % (n=20) Symptome, die mit Malaria übereinstimmten. Unter diesen, suchten 55% (n=11) keine medizinische Behandlung auf oder nahmen Selbstmedikation ein.

Fazit: Das Malariarisiko wird von VFR-Reisenden fälschlicherweise als gering eingeschätzt, was zu einer geringen Inanspruchnahme von reisemedizinischer Beratung und Chemoprophylaxe führt. Ein Misstrauen gegenüber dem Gesundheitswesen wurde festgestellt. Erkenntnisse aus dieser Umfrage sind für Ärzte und Reisemedizin-Kliniken wertvoll und werden zu einer kulturell sensibleren und individualisierten Reiseberatung beitragen.

7 Summary

Background: The African visiting-friends-and-relatives (VFR) community in the global north is at high risk of contracting preventable travel-associated infections when travelling to sub-Saharan Africa. This study aimed to assess VFR travellers' knowledge, risk perceptions, travel medicine advice counselling and use of chemoprophylaxis for malaria to improve our understanding of barriers for effective prevention and to develop tailored travel counselling.

Methods: A questionnaire-based survey was conducted between January and July 2023 at the Hamburg Airport among adult sub-Saharan African VFR travellers returning from malaria-endemic destinations in Africa to assess malaria risk perception, attitudes towards prophylactic measures and travel medicine advice, and as well as pre- and post-travel experiences with travel medicine and malaria prophylaxis.

Results: A total of 389 participants completed the survey. Among these, 67% (n=261) had adequate knowledge of malaria transmission. Fifty-one percent (n=198) stated they had little or no risk of contracting malaria in the malaria-endemic country they visited, and 10% (n=37) mistakenly believed they had been vaccinated against malaria. Approximately half of the respondents did not seek medical travel advice prior to departure and did not take antimalarial prophylaxis due to a perceived minimal risk of disease. Of those who took antimalarial drugs, 77% (n=149) completed the full course. On return, 5% (n=20) had symptoms consistent with malaria and subsequently 55% (n=11) either self-medicated or did not seek medical treatment.

Conclusion: VFR travellers mistakenly perceive a low risk of malaria, resulting in low uptake of travel medical advice and chemoprophylaxis. Distrust of advice from healthcare providers was identified. Insights from this survey are valuable for practitioners and travel medicine clinics to provide more tailored and culturally sensitive travel advice to VFR travellers.

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9 List of Abbreviations

In order of appearance

Abbreviation	Description	Page
COVID19	Corona Virus 2019	6
VFR	Visiting friends and relatives	7
RDTs	Rapid diagnostic tests	10
PCR	Polymerase chain reaction	10
ACT	Artemisinin-based combination therapy	12
LLIN	Long-lasting-insecticides	13
FDA	Food and drug administration	13
CDC	Centers for disease control and prevention	15
G6PDH	Glucose-6-phosphate dehydrogenase deficiency	16
SBET	Standby emergency treatment of malaria	17
mRDT	Maximum recommended therapeutic dose	18
IQR	Interquartile range	24
DZIF	Deutsches Zentrum für Infektionsforschung	25
SSA	Sub-Saharan Africa	34
HTN	Hypertension	35
CYP	Cytochrome P450	45
GP	General practitioners	46
DFG	Deutschen Forschungsgemeinschaft	60

10 Tables of figures and indices

11 Declaration of own contribution

The following parts of this dissertation are based on my direct (collaborative) work under the supervision of Professor Dr. med. univ. Michael Ramharter:

- Drafting of questionnaire: I produced the draft with input from Dr. med. Thomas Brehm and Dr. med. Maria Sophia Mackroth
- Piloting and validation of questionnaire
- Administration of questionnaire and participant recruitment: with support from Pia Mitchelitch, Franck Mbassi Ekoka, and Kayode Ijagbemi
- Planning and implementation of statistical analysis: with support from Maximilian Rakotonirinaloloa
- Monitoring of recruitment process: with support from Pia Mitchelitch
- Database maintenance (data cleaning and verification)
- Interpretation of data and creation of tables
- Design of figures and illustrations
- Writing the dissertation, literature research and evaluation of data

12 Eidesstattliche Versicherung

Ich versichere ausdrücklich, dass ich die Arbeit selbständig und ohne fremde Hilfe, insbesondere ohne entgeltliche Hilfe von Vermittlungs- und Beratungsdiensten, verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die aus den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen einzeln nach Ausgabe (Auflage und Jahr des Erscheinens), Band und Seite des benutzten Werkes kenntlich gemacht habe. Das gilt insbesondere auch für alle Informationen aus Internetquellen.
Soweit beim Verfassen der Dissertation KI-basierte Tools („Chatbots“) verwendet wurden, versichere ich ausdrücklich, den daraus generierten Anteil deutlich kenntlich gemacht zu haben. Die „Stellungnahme des Präsidiums der Deutschen Forschungsgemeinschaft (DFG) zum Einfluss generativer Modelle für die Text- und Bilderstellung auf die Wissenschaften und das Förderhandeln der DFG“ aus September 2023 wurde dabei beachtet.
Ferner versichere ich, dass ich die Dissertation bisher nicht einem Fachvertreter an einer anderen Hochschule zur Überprüfung vorgelegt oder mich anderweitig um Zulassung zur Promotion beworben habe.
Ich erkläre mich damit einverstanden, dass meine Dissertation vom Dekanat der Medizinischen Fakultät mit einer gängigen Software zur Erkennung von Plagiaten überprüft werden kann.

Datum……22/10/2024……. Unterschrift: ……  ……

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